HEART FAILURE: PROGNOSTIC POINTERS

12 | BEDSIDE
Combined score using clinical, ECG, and echocardiographic parameters to predict left ventricular remodeling in CRT patients

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Background: Up to 30% of patients selected on guideline criteria fail to respond to CRT.

Methods: The derivation cohort consisted of 162 heart failure patients implanted with a CRT device. Baseline clinical, ECG and echocardiographic characteristics were entered into an univariable and multivariable model to predict reverse remodeling as defined by a ≥15% reduction in LVESV at 6 months (60%).

Results: A high significant incremental predictive value was noted when Septal Flash was added to an initial 4-factor model including left bundle branch block (difference between area-under-curve C statistics = 0.125; p < 0.001). The predictive accuracy using the L2ANDS2 score was then 0.79 for the C statistic. Application of the new score to the validation cohort (71% of responders) gave a similar response term L2ANDS2: Left bundle branch block (2 points), Age > 70 years, Non-ischemic etiology, LV end-diastolic Diameter –40 mm/m², and Septal Flash (2 points) was calculated for these patients. This score was then validated against a validation cohort of 45 patients from another academic center.

Conclusions: This L2ANDS2 score provides an easy-to-use tool for the clinician to assess the pre-test probability of a patient being a CRT responder.

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ACTN3 R577X polymorphism and long-term survival in patients with chronic heart failure

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Background: Previous studies have shown the occurrence of actinin 3 deficiency in the presence of the R577X polymorphism in the ACTN3 gene. A recent systematic review and meta-analysis brought a stronger evidence of the influence of the genetic profile with physical performance in athletes with positive association between ACTN3 R allele and power events. However, the impact of alpha actinin-3 deficiency caused by this polymorphism is still unknown in heart failure.

In this scenario, the main aim of our study was to assess whether ACTN3 R577X polymorphism is associated with mortality in a heart failure patient.

Methods: A prospective cohort study was conducted from 2002 to 2004. The eligibility criteria included diagnosis of chronic heart failure stage C from different etiologies. We excluded all patients with concomitant diseases that could be related to poor prognosis. ACTN3 rs1815739 (R577X) polymorphism was detected by polymerase chain reaction. Survival curves were calculated with the Kaplan-Meier method with the log-rank statistic. The relationship between baseline variables and the composite endpoint of all-cause death was assessed using a Cox proportional hazards survival model.

Results: A total of 463 patients were included in this study. The frequency of the ACTN3 R577X variant allele was 39.0%. The L VEF mean was 45.6±18.7% and the most common etiology of this study was hypertensive. After mean follow-up of 40 months, 239 (51.6%) patients met the pre-defined study endpoint. Survival curves showed higher mortality in patients carrying RX or XX genotypes compared with patients carrying RR genotype (HR 1.72, 95% CI 1.14–2.62, p = 0.01), whereas a score term RX or XX genotypes in Cox proportional hazards survival model, the presence of the RX or XX genotypes in the most common etiology of this study was hypertensive. After mean follow-up of five years, 239 (51.6%) patients met the pre-defined study endpoint. Survival curves showed higher mortality in patients carrying RX or XX genotypes compared with patients carrying RR genotype (HR 1.72, 95% CI 1.14–2.62, p = 0.01), after adjusted for covariates.

Conclusion: R577X polymorphism in the ACTN3 gene was independently associated with worse survival in patients with chronic heart failure. Further studies are necessary to use its effect as a marker of risk for this syndrome.

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Which formula for estimating glomerular filtration rate is the better predictor of outcomes in heart failure with preserved ejection fraction? An analysis from the I-Preserve trial

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Purpose: Low GFR is associated with poor prognosis in heart failure (HF). We compared the predictive value of Cockcroft-Gault (CG), Modification of Diet in Renal Disease Study Group (mMDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) in the I-Preserve in Patients with Heart Failure and Presence of Kidney Disease (P=0.03; 0.07 and 0.05) and 0.018). But better than sMDRD for all the endpoints (all cause mortality p = 0.017; all cause mortality compared to sMDRD p = 0.007). There was no difference between CG and sMDRD.

Conclusions: CKD-EPI was a better predictor of events in HFpEF compared with sMDRD or CG.

15 | BEDSIDE
Left ventricular global strain is a superior predictor of all-cause mortality compared to left ventricular ejection fraction in patients with severe heart failure

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Objective: Myocardial strain deformation analysis (global strain) obtained by 2D speckle tracking may be superior to left ventricular ejection fraction (LVEF) in predicting all-cause mortality in patients with severe systolic heart failure.

Methods: In this study transthoracic echocardiographic examinations were retrieved from heart failure clinic’s database of our hospital in 1061 patients. The echocardiographic images were subsequently analyzed and conventional echocardiographic parameters and strain data were obtained.

Results: During a median follow-up of 40 months 177 (16.7%) patients died. Patients who died during follow-up had significantly lower LVEF (23.7% vs. 28.2%, P < 0.001) and mean global strain (8.12% vs. 9.86%, p < 0.001). The risk of dying increased with decreasing tertile of global strain being approximately three times higher for the patients in the lowest tertile compared to patients in the highest tertile (1. tertile vs 3. tertile HR: 3.38 95% CI: 2.3 – 5.1 P < 0.001). Many of the conventional echocardiographic parameters proved to be predictors of mortality. However, global strain remained an independent predictor of mortality after adjusting for age, gender, BMI, total cholesterol, heart rate, atrial fibrillation, diabetes mellitus and conventional echocardiographic parameters (HR: 1.19 95% CI: 1.04 – 1.37, per 1% decrease, P = 0.014) while ejection fraction proved to be insignificant adjusted for aforementioned characteristics (P=0.81). In addition, global strain had a higher Harrell’s C statistics than LVEF (0.67 vs. 0.65).

Conclusion: In patients with severe systolic heart failure global strain is an independent predictor of all-cause mortality. Furthermore, global strain proved to be a superior prognosticator when compared to left ventricular ejection fraction.
Heart failure: prognostic pointers 3

16 | BEDSIDE
Left ventricular ejection fraction as a prognostic marker for all-cause mortality in HIV-infected patients

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Background: Since the advent of highly active antiretroviral treatment, cardiovascular disease prevalence by standardised non-invasive cardiovascular screening program and echocardiographic investigation in 843 HIV-infected patients from four specialised outpatient clinics in Germany between 2004 and 2011. The follow-up was 60 month. The LVEF grouped into <35%, 35-50% and >50% on the incidence of all-cause mortality was assessed using multivariate Cox regression analysis.

Results: At baseline, 84% of the 843 patients were male, 89% Caucasians, 60% aged ≤40 years. CDC categorised 41% C and 47% immunological stage 3. In mean, HIV-infection was diagnosed for 7.8±5.6 years at baseline (IQR 2.8-11.6 years). The mean age was 44±10 (IQR 37-50, Range 20-75) years and the mean measured CD4 cell counts were 505±298 (IQR 301-650, range 4-1984) cells/μl. 729 (87%) patients underwent antiretroviral treatment, of whom 74% had an HIV-RNA ≤50 copies/ml. 7/843 patients (1%) had LVEF <35% and 53/843 (6%) patients had LVEF values ranged in 35 to 50%. Subjects with low LVEF had increased frequency of death (mortality: 57% for LVEF <35%, 14% LVEF values ranged in 35 to 50% and 8% LVEF >50%). In unadjusted univariate cox model, LVEF <35% and LVEF ranged 35-50% were associated with a 3.9 [3.2-16.9]-fold and a 1.7 [1.2-2.5]-fold risk, respectively, for all-cause mortality. After further adjustment for traditional cardiovascular risk factors (age, smoking, total cholesterol, antihypertensive drugs), and HIV related variables (HIV Stadium C = AIDS) and CD4 cell count, LVEF <35% was still predictive in the model (4.8 [1.4-16.8]).

Conclusions: According to our data, reduced LVEF is an independent predictor for an increased risk for all-cause mortality in a HIV-infected population. Screening for low LVEF is of main importance in this group of patients and should be carried out in patients with suspected heart failure.

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Features and outcomes of acute myocarditis in children

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This study was to assess features and outcomes of children with acute myocarditis.

Methods: Patients <18y with acute myocarditis (proved by virology and/or MRI and/or complete recovery of myocardial function) were included. Clinical data, echocardiographic parameters and outcomes were collected and cases divided in groups I (≤2y), II (2 to 10y) and III (>10y).

Results: 72 patients were included (1983 to 2012), 30 males, aged 4.1±5.1y (med 1.5y), 43 in group I, 17 in II and 12 in III. Heart failure was present at onset in 57 cases (78%): 8 cardiac shock (12%), 30 severe HF (44%) were more frequent in groups I (56%) and II (46%) than in III (17%, p<0.001), while chest pain (15.5% of all) was more frequent in III (83%). LVEF at diagnosis was 18.4±9% (med 1.5%), 16% and 15% in groups I and II vs 30.5% in III (p<0.001). Aortic VTI was 11.4±5.8 cm (med 10): 8cm and 11 in groups I and II vs 17 in group III (p<0.05). Mitral regurgitation was present in 75.6%, pericarditis in 16.4%, thrombolytic in 3 cases (7%), arrhythmias in 7 (10%). Virus was positive in 27 cases (40%), 1 virus in 24, 1 virus in 3). Nine patients died (13%) between 2months post-diagnosis (2 days to 8.6 months), 1 was transplanted (3rd month), 2 patients (27.5%), 40 completely recovered (58%), at FU=5.5±5.6y (med 4y). Inotropic support was needed in 34 cases (47%): 51%, 59% and 16% of groups I, II and III respectively (p<0.0001). Six patients (8.3%, 1 in group II) needed mechanical circulatory support (SECMO, IABP) within days to 10 days from onset. In 5 patients (13%), 2 were weaned-off (duration of support: 4 days to 3 months). Survival was 96%, 90%, 87.5% and 86% at 1 month, 3 months, 6 months, 2y and 10y of FU. All patients in group III survived. Ten-year survival was 61.4% in group I and 88.2% in II (p=NS). LVEF improved from 18.4±8.9% (med 16%) at onset, to 24.6±10.3% (med 23.5%) at 1 month, 26.5±8.6% (med 26.5%) at 3 month, 30.7±8.6% (med 29.6%) at 6 month and 38±7% (med 37%) at last FU.

Conclusion: Acute myocarditis in children has favourable outcomes despite early myocardial dysfunction and heart failure are less frequent in patients >10 years of age. Mechanical circulatory support successfully lessens mortality. Myocardial contractility can progressively improve within the first 6 months after onset of disease.

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Left ventricular contractile function assessed by 2D strain is a simple surrogate of recruitable function and predicts the outcome after cardiac resynchronization therapy

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Purpose: Recruitable contractile function is important for a favorable response to cardiac resynchronization therapy (CRT). Ejection fraction (EF) is inferior to newer parameters that quantify myocardial deformation to study LV contractile function. We tested the hypothesis that average peak radial strain (RS) by 2D speckle tracking can be a simple surrogate of recruitable function to predict the outcome after CRT.

Methods: We prospectively studied patients undergoing CRT and followed-up over 5 years. RS was measured by speckle tracking echocardiography in 18 segments from the short axis basal, mid and apical levels. Regional RS <10% indicated scar. Lead position by fluoroscopy and its relation to scar was also assessed. Pre-specified outcome events were death, heart transplantation or LV assist device implantation. Volume response was considered as reduction in end systolic volume (ESV) >15%.

Results: Out of 107 patients (20% female, 60% ischemic) 60 were volume responders. 33 end-point events occurred over 5 years: 30 deaths, 2 heart transplants, and 1 LV assist device. Baseline average peak RS but not baseline ESV or EF, correlated with the extent of volume reduction and mechanical resynchronization after CRT (r=0.32, P=0.001 and r=0.55, P<0.001, respectively). On multivariate regression analysis including average peak RS, ESV, RS dyssynchrony, EF, and lead position in relation to scar, only the average peak RS independently predicted (P=0.003, 95% CI 0.785-0.953) reverse remodeling at 6 mo. Furthermore, average peak RS was predictive and additive with mechanical dyssynchrony for event-free survival after CRT over 5 years (Figure).

Conclusion: LV contractile function assessed by 2D average peak radial strain is a simple surrogate of recruitable function and predicts the outcome after CRT.
was no increased risk of SCD in pts with low-grade NSVT (19% vs 9%, adjusted hazard ratio (HR): 1.3 (0.41-4.4), p=0.63); however, the risk of SCD was significantly greater in pts with high-grade NSVT (36%, adjusted HR, 3.9 (1.1-13.8), p=0.04). Furthermore, pts with high-grade NSVT had the significantly increased risk of SCD, compared to those with low-grade NSVT (36% vs 19%, adjusted HR 2.5 (1.1-5.7), p=0.03).

Conclusion: NSVT lasting 8 or more beats detected by serial Holter ECG monitoring would be more strongly associated with an increased risk of SCD in patients with CHF.

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Prediction of rehospitalisation or death within 30 days after discharge among heart failure patients: roles of administrative, socio-economic, geomapping and clinical data

Purpose: Better targeting of heart failure (HF) intensive management programs may reduce readmission. However, available prediction scores are modestly effective. We hypothesised that these scores could be improved by including other factors, and aimed to develop a prediction score of 30-day rehospitalisation or death in HF, using clinical, demographic and socio-economic data.

Methods: This Statewide study included all 1499 HF patients (male 49.6%, median age 80 years) who were admitted and survived the first admission to a public hospital with HF during 2009-2012. General administrative, socio-economic and geomapping data were available for the whole cohort. Full clinical data collected before the first discharge were available from 675 patients. Prediction models were developed using logistic regression, and were validated using bootstrap validation method.

Results: 388 patients (25.9%) were rehospitalised or died within 30 days after discharge. The prediction model that was derived using general administrative, socio-economic and geomapping data had fair discrimination (C-statistic 0.65 [95% CI: 0.62, 0.68]). Using clinical data provided better discrimination (C-statistic 0.69 [95% CI: 0.64, 0.73]). Combining both sources of data best predicted risk of 30-day rehospitalisation or death (C-statistic 0.72 [95% CI: 0.67, 0.76]). The C-statistics for internal validation of the three models were 0.65, 0.69 and 0.71 respectively.

Conclusions: Clinical data are stronger predictors than administrative data, but combining both sources of data may provide the best prediction of 30-day rehospitalisation or death among HF patients.

21 | BEDSIDE
Prognostic implication of worsening renal function in acute heart failure syndrome patients with and without baseline renal failure
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Background: Dynamics changes of renal function is frequently observed in treatment course of acute heart failure syndrome (AHFS) patients, and called worsened renal function (WRF). The exact value of WRF in AHFS needs to be elucidated. Baseline chronic kidney disease (CKD: estimated glomerular filtration rate $\leq 60$ ml/min/1.73m$^2$) is the strongest predictor of WRF and one of the powerful prognostic predictors in AHFS, whether prognostic implication of WRF is different when occurred in patients with CKD and without CKD is not known.

Methods: We retrospectively included 383 consecutive AHFS patients (75.7±12.7 years, 52.0% male) from two hospitals who admitted during January 2011 to December 2012 and can discharge. They had postdischarge death or AHFS readmission rate of 27.4% during median follow-up of 1 year (139±579 days). Patients were divided into 4 groups according to had WRF or not during hospitalization and the baseline CKD at admission. Kaplan-Meier analysis and Cox regression model which was adjusted by other risk factors including eGFR at hospitalization and the baseline CKD at admission were used.

Results: Patients with CKD and no WRF (HR 3.11, 95% CI 1.54-.6.29) and with CKD and WRF (HR 2.30, 95% CI 1.01-5.25) had significantly worse prognosis in comparison with patients without CKD and without WRF (HR 1.60, 95% CI 0.74-3.46).

Conclusion: Prognostic implication of WRF is influenced by whether the baseline CKD is present or not in AHFS patients.
36 | BEDSIDE
Longitudinal 2D strain predicts severe coronary artery disease in patients with NSTEMI, normal left ventricular ejection fraction and no wall motion abnormality


Purpose: In the era of high-sensitivity troponin, many patients are diagnosed with Non-ST elevation myocardial infarction (NSTEMI), accessible bedside tools are needed for early risk stratification. Longitudinal strain provided by speckle tracking echocardiography has been proven to be very sensitive for diagnosing subclinical myocardial injuries. Our aim was to compare global and territorial longitudinal strains to the findings of coronary angiography in subjects with NSTEMI and no sign of myocardial dysfunction, to determine if the decline of the systolic longitudinal function was related to the severity of the coronary artery disease (CAD).

Methods and results: 40 patients were prospectively examined by echocardiography immediately prior to coronary angiography after a first hospitalisation for NSTEMI. Global longitudinal strain (GLS) was provided semi automatically and we calculated territorial longitudinal strains (TLS) on the basis of the perfusion areas of the 3 major coronary arteries, by averaging all segmental peaks systolic strain values within each territory. The subjects were classified into three groups depending on the extent of CAD: no significant CAD, one-vessel and two-vessel CAD (excluding left main [LM] or proximal left anterior descending [LAD] arteries), three-vessel CAD or LM and proximal LAD arteries involvement (qualified as severe CAD).

The mean GLS value for the entire cohort was -19.3 ± 2.3%. A significant worsening of GLS depending on the extent of CAD was found (21.1 ± 1.6% [no significant CAD] vs. -19.9 ± 1.8% [1 or 2- vessel disease] vs. -17.2 ± 2.2% [severe CAD] p < 0.002). To rule out the influence of acute phase reactants (CRP), we also performed a multivariate analysis in order to confirm that long-term outcomes were not explained by CRP. Conclusion: This study confirms that global longitudinal myocardial function is impaired in patients with NSTEMI depending on the extent of CAD, even if left ventricle visual assessment is normal. GLS enables rapid risk stratification and predicts severe CAD with excellent accuracy.

36 | BEDSIDE
Poststochastic shortening measured early in PCI-treated STEMI patients is a strong predictor of myocardial salvage and left ventricular recovery: a cross-modality imaging study

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Purpose: Assessment of potential recovery of myocardium at risk after reperfusion is difficult in patients with ST elevation myocardial infarction (STEMI). Previous studies have shown that poststochastic shortening (PSS) is associated with myocardial recovery in patients with non-STEMI. However, little is known about a possible association between PSS and myocardial salvage in patients with STEMI. The aim of the study was to evaluate the association between myocardial strain measured by echocardiography in the acute stage and myocardial salvage measured by repeated cardiac magnetic resonance (CMR) imaging.

Methods: The study population consisted of 100 patients with first-time PCI treated by primary PCI. Global longitudinal peak systolic strain (εSYS) and peak strain (εPEAK) were measured by two-dimensional speckle tracking echocardiography at a median of 2.4 (range 1.0 to 29.0) days after PCI. Poststochastic index (PSI) was calculated manually, PSI = [(εPEAK - εSYS) x 100] / εSYS x 100. PSI and εSYS and PSI were dichotomized into two groups and defined as, those with low negative strain values (minimum to median) and those with high negative strain values (median to maximum). Myocardial salvage index (MSI), infarct size (IS) and ejection fraction (EF) were assessed by CMR performed both in the acute stage and after 4 months.

Conclusion: This study confirms that global longitudinal myocardial function is impaired in patients with NSTEMI, normal left ventricular ejection fraction and no wall motion abnormality. Low PSI range was lower in gl than in 2 gl pts (53.2 ± 6.7 vs 56.0 ± 4.9, p < 0.01) and PSI was similar in both groups. PSI was severely impaired in patients with inferior than anterior AMI (18.9 ± 4.3 vs 23.0 ± 3.0, p < 0.001) mainly due to a significant difference in infarct size (-19.1 ± 7.0 vs -24.4 ± 4.9, p < 0.001) and lateral ε (-22.8 ± 6.8 vs 28.3 ± 5.6, p < 0.001) but not in septal ε (-14.9 ± 3.6 vs -15.4 ± 3.7, ns). At 6 months, MSI- RVEF (56.7 ± 6.9 vs 58.6 ± 6.1, ns) and PSI was similar in both groups and inferior ε was the only RV function parameter that remained significantly different among both groups (-24.5 ± 6.5 vs -27.5 ± 6.4, p < 0.03).

Among the whole population, MRI-RVEF significantly increased between V1 and V2 (54.1 ± 6.1 vs 57.8 ± 6.6, p < 0.001) as did all strain values (global ε: -20.9 ± 4.1 vs -24.5 ± 4.0, p < 0.001) and TAPSE was similar in both groups and inferior ε was the only RV function parameter that remained significantly different among both groups (-23.5 ± 6.4 vs -27.5 ± 6.4, p < 0.03).

In the era of high-sensitivity troponin, many patients are diagnosed with NSTEMI, normal left ventricular ejection fraction and no sign of myocardial dysfunction, to determine if the decline of the systolic longitudinal function was related to the severity of the coronary artery disease (CAD).
During follow-up of 420±127 days, mortality was higher among RFP+ pts (11.76% vs. 2.72%; p=0.017) and hospitalizations for heart failure were more frequent (18.75% vs. 6.07%; p=0.022), as well as major adverse cardiovascular/cerebral events (MACCE) (20.41 ± 6.46%; p=0.017).

**Conclusions:** RFP was associated with larger infarctions, poorer LV systolic function and worse long-term outcome following primary PCI for STEMI, but it was not related to ischemic times.

**EXTRACELLULAR AND INTRACELLULAR COMPONENTS OF PROTECTION AGAINST ISCHAEMIA/REPERFUSION INJURY**

**40 | BENCH**

**Circulating NOS3 affects adverse left ventricular remodeling post myocardial infarction**

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**Purpose:** Nitric oxide (NO) can protect against myocardial infarction and is constitutively produced within the endothelium and several blood cell types by the isoforms nitric oxide synthase (NOS3). Recently we demonstrated that depletion of circulating NOS3 increases the size of myocardial infarction and the severity of left ventricular dysfunction in an acute murine model. In the current study we hypothesized that circulating NOS3 also affects adverse left ventricular remodeling post myocardial infarction.

**Methods:** To analyze the role of circulating NOS3 we transplanted bone marrow of NOS3−/− and WT mice into wild type mice, producing chimeras expressing NOS3 only in vascular endothelium (BC−EC+) or in both, blood cells and vascular endothelium (BC+EC+). Both groups underwent 60 min coronary occlusion in a closed chest model of myocardial ischemia followed by 3 weeks of reperfusion. During the 3 weeks of reperfusion, functional left ventricular remodeling was serially assessed (24h, 1d, 2w and 3w) by echocardiography (Vevo 2100, Visual Sonics). At 3 weeks post ischemia, hemodynamics were obtained by pressure catheter (Millar Instruments), and infarct size and collagen content were quantified post mortem by Gomori’s One Step Trichrom staining.

**Results:** 3 weeks post ischemia BC−EC+ exhibited a significantly increased infarct size/left ventricle (19.5±1.5%; n=13; p<0.01) compared to BC+EC+ (13.8±0.7%; n=16). Functionally, BC−EC+ exhibited decreased ejection fraction (36.4±3.0%; ***p<0.001; n=5), increased end-systolic (53.2±5.9 mmHg; ***p<0.001) and end-diastolic volume (82.7±5.6 ml; p<0.05) compared to BC+EC+ (EF: 48.8±1.7%; ESV: 35.6±2.2 ml; EDV: 69.1±2.6 ml; n=8) 3 weeks post ischemia. Within the myocardial scar, BC−EC+ presented a significantly increased total collagen content (20.2±0.8%; n=13; ***p<0.001) compared to BC+EC+ (15.9±0.5; n=16). Specifically, the content of collagen type I and III was elevated in the infarcted myocardium of BC−EC+.

**Conclusion:** Our results support an important role for circulating NOS3 in modulating adverse left ventricular remodeling following myocardial infarction.

**41 | BENCH**

**Nanoparticle-mediated targeting of cyclosporine A to the mitochondria of repertused myocardium enhances cardioprotection against ischemia-reperfusion injury in preclinical models**


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**Background:** The opening of the mitochondrial permeability transition pore (mPTP) plays a critical role in myocardial ischemia-reperfusion (IR) injury. We hypothesized that nanoparticle-mediated targeting of cyclosporine A (CsA), an inhibitor of the mPTP opening, to the mitochondria would be an innovative approach for cardioprotection to enhance CsA-induced cardioprotection.

**Methods and results:** In cultured rat cardiomyocytes, mitochondrial-targeting of Poly (lactic-co-glycolic acid) (PLGA) nanoparticle was noted after the addition of hydrogen peroxide (150 μM) which represents oxidative stress during IR (Fig. A). In an in vivo murine model, intravenous administration of PLGA nanoparticles containing CsA (CsA-NPs) or a fluorescence marker FITC (FITC-NP) at the time of reperfusion yielded significantly higher FITC/CsA concentrations in the mitochondria of the IR myocardium compared with a non-ischemic myocardium (Fig. B). Importantly, treatment with CsA-NPs enhanced the cardioprotection against IR injury achieved by CsA (as indicated by the reduction in MI size at lower concentration of CsA) (Fig. C). The beneficial effects of CsA-NP treatment were blunted in mice lacking cyclophilin D (a key molecule associated with mPTP opening) (Fig. D). CsA-NP ameliorated left ventricular remodeling and fractional shortening 4 weeks after IR. The enhanced cardioprotection by CsA-NP was also noted in a conscious pig model (Fig E).

**Conclusions:** Nanoparticle-mediated targeting of CsA to the mitochondria enhanced cardioprotection against IR injury through the inhibition of mPTP opening in IR cardiomyocytes. CsA-NPs can be developed as a more effective inhibitor of mPTP opening and may protect organs from IR injury in acute MI and other clinical settings.
treatment, while that in the UT group worsened more in 4 weeks. Elevated serum level of derivatives of reactive-oxygen metabolites (d-ROM) by MI was significantly reduced by the RIC treatment (605±24 and 495±23 U.CARR, respectively). Sirius red staining revealed that RIC treatment significantly attenuated MI-induced LV interstitial fibrosis in the boundary region (P<0.01). Heat shock protein 72 (Hsp72) level in boundary region of LV was significantly increased in the UT group, compared with the non-MI control group. Interestingly, Hsp72 level in the same region of the RIC group was more increased compared with that in the UT group. The protein amount of serum exosomes in the RIC group was not changed compared the UT group (P>0.01). MicroRNA-29a, which involves the suppression of tissue fibrosis and remodeling, was highly expressed in the RIC-exosomes compared with the UT-exosomes (P<0.05). The microRNA-29a expression in boundary region of left ventricle tended to be increased in the RIC group that in the UT group.

Conclusion: Repetitive treatment of RIC reduces adverse LV remodeling and oxidative stress by MI. Exosome-mediated intercellular communication may contribute to the beneficial effect of RIC treatment. These results may have clinical implications for the treatment of patients with evolving LV dysfunction.

43 | BENCH Macrophage migration inhibitory factor is cardioprotective in ischemia-reperfusion injury by redox regulation J. Pohl1,2, U. Hendgen-Cotta1, C. Rammos1, J. Bernhagen2, M. Kelm3, T. Rassaf1,1, Division of Cardiology, Pulmology and Vascular Medicine, University Hospital Dusseldorf, Germany; 2 University Hospital Aachen, Department of Biochemistry and Molecular Cell Biology, Aachen, Germany

Purpose: Macrophage migration inhibitory factor (MIF) is cardioprotective in myocardial ischemia/reperfusion (I/R) injury. MIF’s structure shows a Cys-Xaa-Xaa-Cys (CX2C) motif with 58% identity to thioredoxin (Trx) superfamily. While the exact mechanisms of most of the other members of this family like glutaredoxin, peroxiredoxin and protein disulfide isomerase are known and form a complex redox system with regulation of the highly conserved thioredoxin system, the relevance of the structurally highly similar protein MIF in this redox system has not been elucidated. We therefore set out to test whether MIF mediates cardioprotective effects by participating in myocardial intracellular redox regulation via the glutathione system.

Methods: To assess whether MIF is able to reduce GSSG, we incubated recombinant MIF (rMIF) with GSSG, DTNB and NADPH and measured MIF dependent reduction of GSSG to GSH spectrophotometrically in an in vitro assay. Using an in vivo I/R model with 30 minutes of ischemia and 5 minutes of reperfusion, we assessed whether MIF-deficiency affects formation of glutathiolated proteins using a Western Blot technique with consecutive mass spectrometry analysis. Furthermore, we measured levels of cardiac GSSH, GSSG and GSSH/GSSG ratio in WT and MIF-deficient (Mif−/−) hearts. Infarct sizes were measured after 24 hours of reperfusion in WT and Mif−/− mice by TTC staining.

Results: MIF does not exhibit an intrinsic glutathione reductase activity, but acts catalytically on GSSG reduction when glutathione reductase and MIF are present. Using an in vivo approach, we showed that MIF-deficiency affected cellular levels of GSSG and GSSG/GSSG ratio in the mitochondrial protein oxidase (MPO) activity, which is typically found in proteins of the thioredoxin (Trx) superfamily. While the exact mechanisms of most of the other members of this family like glutaredoxin, peroxiredoxin and protein disulfide isomerase are known and form a complex redox system with regulation of the highly conserved thioredoxin system, the relevance of the structurally highly similar protein MIF in this redox system has not been elucidated. We therefore set out to test whether MIF mediates cardioprotective effects by participating in myocardial intracellular redox regulation via the glutathione system.

Conclusion: We conclude that MIF mediates cardioprotective effects in myocardial I/R injury by redox regulation.

44 | BENCH Metformin modulates IL-33/ST2 system in cardiac remodeling after myocardial infarction M.C. Asensio-Lopez1, A. Lav1, D.A. Pascual-Figal1, M.J. Fernandez-Del Palacio2, G. Santarelli1, L. Caballero1, M.T. Perez-Martinez1, I. Garrido1, M.C. Asensio-Lopez1, A. Laix1, D.A. Pascual-Figal1, M.J. Fernandez-Del Palacio2, G. Santarelli1, L. Caballero1, M.T. Perez-Martinez1, I. Garrido1, J. Sanz, P.P. Sengupta, V. Fuster, J.J. Badimon. Mount Sinai School of Medicine, Cardiovascular Institute, New York, United States of America

Purpose: Sphingosine-1 phosphate receptor agonist fingolimod increases myocardial salvage and decreases adverse post-infarction left ventricular remodeling in a porcine model of ischemia-reperfusion.

Methods: I/R was induced in pigs by 60-minute balloon occlusion of proximal LAD. Animals randomly received fingolimod or saline for controls, 15 minutes pre-reperfusion. Animals were evaluated with cardiac MRI, 3D-echocardiography, invasive hemodynamics, histology, and Western blot analysis.

Results: Fingolimod treatment significantly upregulated cardioprotective proteins and reduced myocardial apoptosis in the infarct border zone 24 hours post MI. One week post MI, despite similar myocardium at risk in both groups, fingolimod significantly improved myocardial salvage, reduced infarct size and improved LV systolic function. Importantly, these cardioprotective effects were preserved one month post MI. Additionally, fingolimod mitigated the development of adverse post-MI LV remodeling with significantly lower LV mass, reduced LV dilatation and reduced activation of the sympathetic system. Consistent with this, fingolimod pigs showed less cardiomyocyte hypertrophy and lower interstitial fibrosis. Activation of Akt and ERK1/2 was reduced in fingolimod animals supporting a reduction in compensatory hypertrophy.

Conclusions: S1P-R activation with fingolimod prior to reperfusion resulted in increased myocardial salvage, reduced infarct size, improved systolic LV function and LV mechanics, and reduced LV remodeling following MI. These data support a cardioprotective role for S1P-R agonism during myocardial ischemia.

45 | BENCH The sphenosine 1-phosphate receptor agonist fingolimod increases myocardial salvage and decreases adverse post-infarction left ventricular remodeling in a porcine model of ischemia-reperfusion C. Garcia Santos-Gallego, T. Vahl, G. Golasch, B. Picastotte, T. Arias, K. Ishikawa, J. Sanz, P.P. Sengupta, V. Fuster, J.J. Badimon. Mount Sinai School of Medicine, Cardiovascular Institute, New York, United States of America

Purpose: Sphingosine-1 phosphate (S1P) is a lysosphospholipid with antiapoptotic properties. We hypothesized that treatment with the S1P receptor (S1P-R) agonist fingolimod during cardiac ischemia inhibits apoptosis leading to increased myocardial salvage, reduced infarct size, and mitigated left ventricular (LV) remodeling in a porcine model of ischemia-reperfusion (I-R).

Methods: I/R was induced in pigs by 60-minute balloon occlusion of proximal LAD. Animals randomly received fingolimod or saline for controls, 15 minutes pre-reperfusion. Animals were evaluated with cardiac MRI, 3D-echocardiography, invasive hemodynamics, histology, and Western blot analysis.

Results: Fingolimod treatment significantly upregulated cardioprotective proteins and reduced myocardial apoptosis in the infarct border zone 24 hours post MI. One week post MI, despite similar myocardium at risk in both groups, fingolimod significantly improved myocardial salvage, reduced infarct size and improved LV systolic function. Importantly, these cardioprotective effects were preserved one month post MI. Additionally, fingolimod mitigated the development of adverse post-MI LV remodeling with significantly lower LV mass, reduced LV dilatation and reduced activation of the sympathetic system. Consistent with this, fingolimod pigs showed less cardiomyocyte hypertrophy and lower interstitial fibrosis. Activation of Akt and ERK1/2 was reduced in fingolimod animals supporting a reduction in compensatory hypertrophy.

Conclusions: S1P-R activation with fingolimod prior to reperfusion resulted in increased myocardial salvage, reduced infarct size, improved systolic LV function and LV mechanics, and reduced LV remodeling following MI. These data support a cardioprotective role for S1P-R agonism during myocardial ischemia.


Purpose: Patients with chronic kidney disease (CKD) and particularly those receiving hemodialysis (HD) are poor responders to clopidogrel. We sought to assess the functional impact of ticagrelor in CKD patients with receiving maintenance HD.

Methods: In a single-center, prospective, randomized, crossover study, seventeen patients undergoing regular maintenance HD were assigned to receive ticagrelor and clopidogrel in random order. Ticagrelor and clopidogrel were administered as 180 and 75 mg, respectively. The primary endpoint was the area under the curve (AUC) of change in platelet inhibition (PI) from baseline to 72 hours. Secondary endpoints included the time at which PI reached the target, and the number of patients achieving PI > 90% at 72 hours.

Results: Of the 17 patients enrolled, 15 completed the study. The mean (±SD) age was 60.2±13.8 years, and 11 (73.3%) were men. The mean (±SD) HD duration was 13.1±6.2 years. The mean (±SD) estimated glomerular filtration rate (eGFR) was 12.4±4.3 ml/min/1.73 m². At baseline, the mean (±SD) platelet count was 247.2±45.8 x10⁹/L. The mean (±SD) PI from baseline to 72 hours was 0.7±0.3% with ticagrelor and 0.2±0.1% with clopidogrel (P<0.001). The mean (±SD) time to achieve PI > 90% was 11.4±3.8 hours with ticagrelor and 13.9±4.7 hours with clopidogrel (P=0.008). The number of patients achieving PI > 90% at 72 hours was 15 (100%) with ticagrelor and 14 (93.3%) with clopidogrel (P=0.033).

Conclusions: Ticagrelor is more effective than clopidogrel in patients with chronic kidney disease undergoing maintenance HD, achieving higher and faster platelet inhibition. This finding is consistent with previous studies demonstrating the superiority of ticagrelor over clopidogrel in patients with CKD. Further research is needed to determine the optimal antiplatelet regimen for patients with CKD undergoing maintenance HD.
grelor (180-mg load, 90-mg BID maintenance dose) or clopidogrel (600-mg load, 75-mg/d maintenance dose) for 14 days and after 14 days of washout period, cross-over treatment assignments for another 14 days. Platelet function was evaluated before and after anti-platelet therapy with light transmittance aggregometry and with VerifyNowTM P2Y12 assay. Platelet activation markers (P2Y12, GPIb/IIIa, and P-selectin) were also assessed.

Results: Greater IPA (20 μmol/L ADP, final extent) occurred with ticagrelor than with clopidogrel at 1, 5, 48 hours after loading and at 2 weeks; by 5 hours after loading, a greater proportion of patients achieved >50% IPA (76.5% versus 17.6%, p<0.004) and >75% IPA (41.2% versus 5.9%, p=0.002) in the ticagrelor group than in the clopidogrel group, respectively. A faster offset occurred with ticagrelor than with clopidogrel (P=0.003). At 48 hours after the last dose, mean IPA was -15.8% for ticagrelor versus -154% for clopidogrel (P=0.022). By 1 hour after loading, mean PRU was 152 for ticagrelor versus 400 for clopidogrel (P<0.001).

Conclusions: Ticagrelor achieved more rapid and greater platelet inhibition than clopidogrel; this was sustained during the maintenance phase and was faster in offset after drug discontinuation.

54 | BEDSIDE
The impact of low dose aspirin on 5-year clinical outcomes in patients with coronary artery spasm as assessed by the intracoronary acetylcholine provocation test

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Background: Low dose aspirin (LDA) was known to be more frequently associated with coronary artery spasm (CAS) and ischemic symptoms, as well as severe and multivessel spasm. The aim of this study was to evaluate the impact of LDA on clinical outcomes up to 5 years in confirmed CAS patients (pts).

Methods: A total of 5,053 consecutive pts without significant coronary artery disease who underwent acetylcholine (Ach) provocation test from Nov 2004 to Oct 2010 were enrolled. Among them, a total of 3,024 pts were finally diagnosed as significant CAS. During 5 years, a total of 1,072 pts were followed, and patients were divided into two groups depending on the use of LDA: LDA group (n=43 pts per year) and no LDA group (n=1,029 pts).

Results: The baseline clinical characteristics showed that the prevalence of old age, diabetes mellitus, hypertension, and hyperlipidemia were higher in LDA group. During the Ach test, the incidence of multivessel spasm and the response rate to lower Ach doses were higher in LDA group (P<0.043). The incidence of repeated CAS and MACCE were higher in LDA group (Table). Multivariate analysis showed that LDA was a strong predictor of repeated CAS due to recurrent chest pain (OR: 2.6, 95% CI: 1.4-5.0, p-value=0.004).

Table. Clinical outcomes up to 5 years between LDA group and No LDA group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>LDA (n=43)</th>
<th>No LDA (n=1,029)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1 (2.3%)</td>
<td>14 (1.4%)</td>
<td>0.900</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>0 (0.0%)</td>
<td>5 (0.5%)</td>
<td>0.005</td>
</tr>
<tr>
<td>De novo percutaneous coronary intervention (PCI)</td>
<td>3 (7.0%)</td>
<td>18 (1.7%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Myocardial infarction (MI)</td>
<td>0 (0.0%)</td>
<td>10 (1.0%)</td>
<td>0.130</td>
</tr>
<tr>
<td>Cerebrovascular accidents (CVA)</td>
<td>1 (2.3%)</td>
<td>7 (0.7%)</td>
<td>0.210</td>
</tr>
<tr>
<td>Repeat coronary angiography (CAG)</td>
<td>16 (37.2%)</td>
<td>109 (10.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>MACCE (Mortality, PCI, MI)</td>
<td>4 (9.3%)</td>
<td>31 (3.0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>MACCE (Mortality, PCI, MI, CVA, Repeat CAG)</td>
<td>17 (39.5%)</td>
<td>182 (17.2%)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Conclusion: In this study, the CAS patients with use of LDA was related to higher incidence of 5-year clinical outcomes and LDA was a strong predictor of repeated CAS due to recurrent chest pain during 5 years, requiring more intensive medical therapy and close clinical follow up.

55 | BEDSIDE
POCT for determination of basic pharmacogenetic profile for individualization of antiplatelet therapy: pilot study

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“Spartan RX CYP2C19 Assay” is a POCT (Point Of Care Testing) technology intended to determine three selected single nucleotide polymorphisms (SNPs) of cytochrome P450 gene (CYP2C19 *2, *3, *17), which have been proposed for genotyping in individualization of antiplatelet treatment. In comparison with existing techniques, that use DNA isolated from whole blood and provide results within 36 to 72 hours after the sample collection, this POCT technology yields results already in 1 hour. The purpose of the study was to determine the success rate of the POCT genotyping and compare the results with those obtained using our standard genotyping technology - MassArray® (Sequenom®).

Method: Buccal swabs were collected from patients undergoing acute coronary angioplasty with stent implantation for ACS into the reagent tubes; 3 tubes in total, each detecting one SNP. Obtained samples were tested by Spartan RX AnalyserTM according to the operator’s manual. Simultaneously, patients’ blood was sampled for DNA isolation and subsequent genotyping of CYP2C19 polymorphisms performed using MassArray® technology.

Results: Altogether, 50 patients were tested by both methods. Using Spartan RX, all three tested polymorphisms were successfully determined in 37 (74%) patients. In the remaining 13 (26%) patients, CYP2C19 polymorphisms could not be determined by POCT. Genotypes assigned by the Spartan RX CYP2C19 Assay were in 100% compliance with the genotypes identified using MassArray® technology, which reliably identified genotypes of CYP2C19 SNPs in all 50 patients.

Conclusion: The results of our pilot study show that the evaluated POCT technology is very fast, but is not able to determine all three selected CYP2C19 polymorphisms in every tested subject. Despite this lower “success”, the POCT technology enabled accurate determination of the basic pharmacogenetic profile in the three quarters of patients already in 1 hour after a simple non-invasive buccal swab collection. Knowledge of a pharmacogenetic profile at very early stage of patient care may represent an advantage for individualization of antiplatelet therapy and preventative measures.

Support: GA JU LF 2014_012, CZ.1.05/2.1.00/01.0003.

56 | BEDSIDE
Prevalence of functional dyspepsia in patients under antithrombotic therapy and efficacy of esomeprazole: a single center large-scale trial in Japan

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Background: Functional dyspepsia (FD) is increasing because of aging of the population, stressed society, lack of exercise, and Western dietary habit in Japan. FD receives attention as a cause of impairing QOL of patients not only with a physical symptom but also by affecting a psychological symptom such as depression or anxiety.

In Cardiovascular Field, bleeding complications such as bleeding stomach ulcer in patients of a long term antithrombotic therapy are to be well known, whereas FD is not generally recognized yet. Recently, with the growing significance of antithrombotic therapy in patients with atrial fibrillation, there are growing concerns about increase of FD with antithrombotic drugs.

Some studies reported that esomeprazole (EPZ) is effective for improving symptoms of FD. We evaluated the prevalence of EPZ under antithrombotic therapy and investigated the effect of EPZ.

Methods: This large-scale trial included 1,201 consecutive patients (Male: 852, Female: 349, mean age: 62±12) under antithrombotic therapy to manage myocardial ischemia, atrial fibrillation, or thrombotic disease. We conducted a questionnaire investigation about their physical condition during the last week using The GI Symptom Questionnaire (GSQ). The symptoms of FD were scored from 0 to 4; 0: no symptom, 1: mild symptom, 2: moderate symptom, 3: severe symptom, 4: very severe symptom.

If any of Q1-Q5 got a score of 3 and above, we diagnosed as having symptoms of FD. We grouped oral medicines with antithrombotic effect, then examined differences in the prevalence of FD in patients receiving each oral medicine.

When FD was observed, we prescribed the proton-pump inhibitor (PPI), EPZ, according to the patients’ will and re-evaluated the FD after 8 to 12 weeks.

Results: Of all patients, 233 (19.4%) had symptomatic FD. The patients given dabigatran had a significantly higher rate of FD (29.95%: 30.5%); 83/451 (18.4%) with warfarin and 143/801 (17.9%) with antiplatelet drugs. In patients with any of PPI, out of 742 patients, 148 (19.4%) had FD symptoms. In patients with any of H2 blockers, 12 out of 96 patients (12.5%), and in patients without gastric mucosa protector agent, 66 out of 129 patients (50.4%).

Conclusion: The prevalence of FD under antithrombotic therapy is increased; however, the significances of FD increase with dabigatran use. Further, the effectiveness of EPZ was evaluated.
Conclusion: This study demonstrated the relationship between the administration of anticoagulants, particularly dabigatran, rather than antiplatelets, and FD. The administration of EPZ significantly improved symptomatic FD.

57 | BEDSIDE
C34T P2Y12 ADP receptor polymorphism and smoking status: effects on cardiovascular outcome in patients with coronary artery disease receiving clopidogrel
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Purpose: The clinical benefit of clopidogrel has been attributed to its inhibition of platelet activation and aggregation. We tested the combined impact of smoking status and C34T polymorphism of P2Y12 adenosine diphosphate (ADP) receptor on cardiovascular outcome in patients with coronary artery disease (CAD) after percutaneous coronary intervention (PCI) receiving clopidogrel.

Methods: We consecutively enrolled 229 patients with CAD, receiving clopido- grel regimen (75mg/d), one month after PCI. C34T genotyping was performed by real-time polymerase chain reaction. Patients were followed for a mean time of 19 (range 3 to 40) months. The primary composite endpoint was death from cardiovascular causes, nonfatal myocardial infarction and hospitalization for unstable angina or stroke. Subjects smoking at least one cigarette per day were categorized as smokers and the rest as non-smokers.

Results: The mean age of the participants was 62±10 years and 23% were active smokers. In the total study population, 124 patients (54%) were carriers of at least one C34T reduced-function allele and 105 patients (46%) were non carriers. The primary end point occurred in 21% of the non smokers and 40% of smokers and the hazard ratio (HR) for smokers compared to non smokers was (HR=2.4, 95%CI: 1.05 to 5.60, p=0.03). In order to investigate time dependency of smoking habits in the occurrence of primary endpoint we conducted stratified to C34T polymorphism Cox regression analysis after adjustment for age and sex. Interestingly in carriers of at least one C34T allele, smoking was significantly associated with the occurrence of primary end point (for smokers HR=+95%CI: 1.05 to 6.11, p=0.04) while in subjects without a C34T allele smoking was not associated with the occurrence of primary end point (HR=0.87, 95%CI: 0.21 to 3.65, p=0.86).

Conclusion: Smoking is associated with adverse cardiovascular outcome in CAD patients after PCI receiving clopidogrel, especially in carriers of at least one C34T reduced-function allele. These findings highlight the possible interplay between polymorphisms affecting the P2Y12 ADP receptors activity and smoking in CAD patients under clopidogrel treatment.

58 | BEDSIDE
Characterization of dabigatran effects on platelet function
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Purpose: The impact of novel anticoagulants on platelet function is largely unknown and may have clinical relevance. We characterized the effects of dabiga- tran (D) on platelet function.

Methods: With in vitro increasing concentrations of D (50, 150 and 250 ng/mL) added to platelet rich plasma from 10 donors, we assessed light transmittance platelet aggregation by 2 and 5 μM ADP, 5 and 10 μM TRAP, 1.5, 3 and 6 ng/mL human γ-thrombin. With the same concentrations of D in whole blood, we also quantified protease-activated receptors (PAR)-1 and P-selectin (CD62E) expression by flow-cytometry.

Results: We found a complete inhibition of γ-thrombin-induced aggregation with all plasma concentrations of D compared with control without drug. ADP- and TRAP-induced aggregation was not modified by the addition of D. PAR-1 expression (mean fluorescence intensity, MFI ratio) was significantly higher as a function of increasing D blood concentration (Fig. 1). Expressed as mean±SE, MFI ratio was 33±8 for control, 53±6 for D 50 ng/mL (P<0.05 vs control), 82±15 for D 150 ng/mL (P<0.05 vs D 50 ng/mL), 84±20 for D 250 ng/mL (P<0.05 vs D 150 ng/mL), CD62E expression was not modified by the addition of D.

Conclusions: The complete inhibition of γ-thrombin-induced platelet aggregation by dabigatran was also accompanied by a concentration-dependent increase of PAR-1 expression, in the absence of platelet activation, as indicated by unmodified CD62E expression. This may suggest an upregulation of PAR-1 in a setting of reduced thrombin availability for PAR-1 occupancy. The increased expression of these receptors may induce a recovery or an upregulation of platelet aggrega- tion by thrombin in the presence of inadequate dabigatran concentrations. Further studies need to confirm these findings in a clinical setting.

63 | BEDSIDE
Thrombolysis for intermediate-risk pulmonary embolism: 6-month follow-up of the PEITHO trial
S.V. Konstantinides1, G. Meyer2, T. Danays3, E. Vicaut4 on behalf of the PEITHO investigators. 1University Medical Center of Mainz, Center for Thrombosis and Hemostasis, Mainz, Germany; 2University Paris-Descartes, Hopital European Georges-Pompidou, Paris, France; 4Kleinherr Ingelheim, Reims, France

Purpose: Normotensive patients with intermediate-risk pulmonary embolism (PE), indicated by the presence of acute right ventricular (RV) dysfunction and myocardial infarction, have an elevated risk of adverse outcome. It remains unclear whether fibrinolysis can improve the long-term prognosis of intermediate-risk PE.

Methods and results: The Pulmonary Embolism Thrombolysis trial (PEITHO) was an investigator-initiated, academic-sponsor, prospective, multicenter, interna- tional, randomized (1:1), double-blind comparison of thrombolytic therapy with weight-adapted i.v. bolus tenecteplase versus placebo in normotensive patients with confirmed acute PE. Patients had RV dysfunction on echocardiogram or computed tomography, plus a positive troponin I or T test. Both treatment groups received standard anticoagulation. The primary efficacy outcome was death from any cause or haemodynamic collapse within 7 days of randomization. A total of 1006 patients were enrolled at 76 sites in 13 countries. The results regarding the primary outcome have been presented. Briefly, thrombolytic therapy reduced (from 5.6% to 2.6%; P=0.015) the primary endpoint at the cost of an increased risk of major haemorrhage, particularly haemorrhagic stroke (2.4% ver- sus 0.2%; P<0.003). Death rates at 30 days were 2.4% and 3.2% respectively. Six-month (180-day) follow-up data were available for 498 patients (98.4%) of the tenecteplase and 478 (98.1%) of the placebo group (P=0.566). Six-month death rates for patients who survived the first 30 days after randomization were 4.7% and 3.3% respectively (P=0.152). Most deaths occurring within the first 30 days resulted from acute PE or the complications of treatment; between day 30 and day 180, 16/23 (70%) of deaths in the tenecteplase and 474 (98.1%) of the placebo (heparin-only) arm. During this period, a total of 35 patients (7.0%) in the tenecteplase and 30 (6.1%) in the placebo group died (P=0.566). Complications of treatment; between day 30 and day 180, 16/23 (70%) of deaths in the tenecteplase and 12/14 (86%) in the placebo arm were due to the underly- ing underlying particular cancer. Residual dyspnea at 6 months was assessed in 71.2% of the patients, 45.2%, 20.4%, 4.8% and 0.6% were in NYHA stage I, II, III and IV, respectively, without difference between the groups. In 51% of the pa- tients, follow-up echocardiography was performed without significant differences in the rates of residual pulmonary dysfunction or RV dysfunction.

Conclusions: In a large randomized trial of patients with intermediate-risk PE, thrombolytic treatment did not affect 6-month mortality, residual dyspnea and RV function. In patients who survive the first 30 days after acute PE, late deaths are primarily due to underlying disease.

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Predictors of hospitalization during extended treatment of venous thromboembolism in the AMPLIFY-EXT trial
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Purpose: Apixaban after the Initial Management of Pulmonary Embolism and Deep Vein Thrombosis with First-Line Therapy-Extended Treatment (AMPLIFY- EXT) trial demonstrated that two doses of apixaban (2.5 mg, 5 mg twice daily) vs. placebo significantly reduced symptomatic recurrent venous thromboembolism (VTE) or all-cause death without increasing the rate of major bleed- ing. The trial also demonstrated that both doses of apixaban vs. placebo signifi- cantly reduced all-cause hospitalization, a critical factor in healthcare resource assessment. This analysis examined baseline predictors of hospitalization during the AMPLIFY-EXT trial.

Methods: AMPLIFY-EXT was a double-blind placebo-controlled trial with 12 months of treatment plus 1 month follow-up in patients with VTE who had completed 6-12 months of anticoagulation therapy. A total of 2,486 patients were enrolled and randomised at 328 sites in 28 countries. All-cause hospitalizations during the trial were captured by dedicated case report forms. Patients were cen-
sored at either death, loss to follow-up, or end of study, whichever came first. Baseline clinical and demographic predictors of hospitalization were examined using stepwise Cox proportional hazards regression models. Variables with a significant level < 0.20 were entered into the model.

Results: Of the 2,482 patients included in the intention-to-treat analyses, 840 were assigned to receive axiaban 2.5 mg BID, 813 to receive axiaban 5 mg BID, and 829 to receive placebo. During the trial, 138 patients were hospitalized at least once, 62 (7.5%/year) in the placebo group, 42 (4.8%/year) in the axiaban 2.5 mg group, and 34 (4.0%/year) in the axiaban 5 mg group. The following significant clinical predictors of hospitalization during the trial: axiaban 5 mg vs. placebo (HR = 0.54, 95% CI = 0.36–0.83), axiaban 2.5 mg vs. placebo (HR = 0.65, 95% CI = 0.43–0.96), DVT vs. PE (HR = 0.72, 95% CI = 0.51–1.01), severe or moderate renal function impairment vs. normal renal function (HR = 2.27, 95% CI = 1.30–3.95). Sex, age, and baseline body weight did not significantly predict hospitalization.

Conclusions: During extended treatment of venous thromboembolism in the AMPLIFY-EXT trial, baseline renal function impairment and PE significantly predicted all-cause hospitalization, while axiaban treatment significantly reduced risk of hospitalization, which should impact healthcare resource utilization.

66 | BEDSIDE
Anticoagulant therapy does not influence long-term outcomes in patients with pulmonary arterial hypertension (PAH): insights from the randomised controlled SERAPHIN trial of macitentan

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Purpose: In the 12-wk PATENT-1 study, riociguat, a novel soluble guanylate cyclase stimulator, improved 6MWD and several secondary endpoints in PAH patients (pts). This subgroup analysis of the PATENT-2 LITE investigated safety and efficacy of riociguat in treatment-naïve and pretreated pts at 1 yr.

Methods: Treatment-naïve or pretreated (with ERAs or prostanoids) PAH pts entered PATENT-2 after completing PATENT-1 without ongoing riociguat-related serious AES. All pts received riociguat adjusted up to 2.5 mg tid. The primary endpoint was safety and tolerability; secondary endpoints included 6MWD and WHO functional class (FC).

Results: Of the 405 pts completing PATENT-1, 98% entered PATENT-2. Of these, 50% were treatment-naïve and 50% pretreated. At the Mar 2013 cut-off, 85% and 83%, respectively, had received ≥1 yr of riociguat treatment (mean treatment duration: 98 and 92 wks, respectively). Riociguat was well tolerated; 15% of treatment-naïve and 22% of pretreated pts withdrew, 6% and 11%, respectively, due to AES. At 1 yr, 89% of treatment-naïve pts remained on riociguat therapy, while 3% of pretreated pts had transitioned to riociguat monotherapy, Changes in 6MWD and FC are shown in Table 1. At 1 yr, after censoring pts who had not reached 1 yr of treatment or who withdrew without experiencing an AE, 87% of treatment-naïve and 89% of pretreated pts were free from clinical survival. Survival was 97% in both subgroups.

Conclusions: This subgroup analysis shows that long-term riociguat therapy, either as monotherapy or in combination with ERAs or prostanoids, is well tolerated in PAH and suggests sustained improvements in 6MWD and FC.

67 | BEDSIDE
Oral targeted therapies in the treatment of pulmonary arterial hypertension: a meta-analysis of clinical trials

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Background: Oral targeted therapies have been widely used in the treatment of pulmonary arterial hypertension (PAH). Many new oral agents emerge for PAH in recent years. Thus, we performed a meta-analysis to evaluate the efficacy and safety of oral targeted therapies in PAH, focusing on overall survival improvement.

Methods: Trials were searched in the Cochrane Library, EMBASE, and PUBMED...
Abstract 67 – Table 1. Meta-analyses based on drug classes

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Mortality</th>
<th>RR (95% CI)</th>
<th>p</th>
<th>Clinical worsening</th>
<th>RR (95% CI)</th>
<th>p</th>
<th>WHO-FC</th>
<th>EMWD</th>
<th>Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERAs</td>
<td>0.82 (0.52-1.30)</td>
<td>0.396</td>
<td>0.40 (0.22-0.73)</td>
<td>0.003</td>
<td>1.44 (1.17-1.78)</td>
<td>0.001</td>
<td>35.16 (22.58-47.73)</td>
<td>0.000</td>
<td>0.92 (0.66-1.28)</td>
</tr>
<tr>
<td>PDE-5</td>
<td>0.22 (0.07-0.71)</td>
<td>0.011</td>
<td>0.42 (0.28-0.64)</td>
<td>0.004</td>
<td>4.88 (2.21-10.78)</td>
<td>0.005</td>
<td>38.89 (22.59-55.18)</td>
<td>0.000</td>
<td>0.64 (0.39-1.04)</td>
</tr>
<tr>
<td>Prostanoids</td>
<td>0.91 (0.46-1.79)</td>
<td>0.377</td>
<td>0.78 (0.55-1.11)</td>
<td>0.167</td>
<td>1.26 (0.87-1.82)</td>
<td>0.222</td>
<td>19.88 (10.12-39.64)</td>
<td>0.000</td>
<td>0.34 (0.26-5.63)</td>
</tr>
<tr>
<td>sGCS</td>
<td>0.40 (0.08-1.94)</td>
<td>0.254</td>
<td>0.25 (0.08-0.74)</td>
<td>0.013</td>
<td>1.50 (0.92-2.42)</td>
<td>0.095</td>
<td>36.00 (20.00-52.00)</td>
<td>0.000</td>
<td>0.51 (0.19-1.34)</td>
</tr>
</tbody>
</table>

ERAs: bosentan (five studies) or ambrisentan (two studies) or macitentan (one study); PDE-5s: sildenafil (two studies) or tadalafil (one study) or vardenafil (one study); Prostanoids: beraprost (two studies) or treprostinil (three studies); sGCS: riociguat (one study); RR: relative risk; CI: confidence interval.

Conclusions: The results of this meta-analysis suggest a consistent and statistically significant reduction in the incidence of CW in pts with PAH treated with combination therapy compared with monotherapy. A significant reduction in mortality was not observed.

BIORESOVABLE STENTS IN COMPLEX LESIONS

73 | BEDSIDE

Multimodality assessment of the outcome 12 months after implantation of bioreosorbable scaffold for the treatment of acute coronary syndromes

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Introduction: We previously reported on the periprocedural and short-term outcome after implantation of bioreosorbable scaffold for the treatment of acute coronary syndromes. We describe here the 12-months clinical, anatomic and function outcomes.

Methods: 35 Patients (62.1±13 years old, 32 males, 2 diabetics) underwent coronary angiography at 12 months after BVS implantation for acute coronary syndromes (8 unstable angina, 13 NSTEMI, 15 STEMI). OCT was performed in all vessels; endothelial function (intracoronary infusions of three different doses of acetylcarnine) and endothelium-independent vasodilation (intracoronary nitroglycerin, 200mcg) were tested in 28 patients.

Results: The culprit lesion was classified in all cases with OCT. The minimum thickness of the fibrous cap covering the lesion was 0 to 550 micrometer (mean 220±114 microm). Incomplete BVS expansion was evidenced in 7 cases and malapposition in 8. The minimum lumen area was 2 to 11 mm². There were 3 cases of in-BVS restenosis, all due to incomplete BVS expansion, all treated with re-PTCA and implantation of a metallic stent. At least one dose of acetylcarnine (Table 1) caused vasodilation >3% in 17 lesions, and vasoconstriction in 10. Nitroglycerin caused vasodilation in 15 lesions. A combination of fibrous cap thickness >150 micrometers associated with acetylcarnine-induced vasodilation was seen in 8 lesions.

Table 1

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Ach 1</th>
<th>Ach 2</th>
<th>Ach 3</th>
<th>Nitroglycerin</th>
</tr>
</thead>
<tbody>
<tr>
<td>% change in diameter</td>
<td>0.7±6.1</td>
<td>1.3±6.2</td>
<td>0.2±7.3</td>
<td>4.6±6.9</td>
</tr>
<tr>
<td>(mm-max)</td>
<td>−10.2 to 13.6%</td>
<td>−12 to 18%</td>
<td>−11 to 27%</td>
<td>−6 to 26%</td>
</tr>
</tbody>
</table>

Discussion: 12 months after BVS implantation, the majority of lesions was sealed by a fibrotic cap. There was relatively high incidence of malapposition. Physiological endothelium-dependent vasodilation was observed in about half of the cases. A combination of full neointima coverage and endothelium-dependent vasodilation, demonstrating a structural and functional normalization of previously unstable plaques, was seen however in a minority of cases.

74 | BEDSIDE

Assessment of endothelization and late apposition of the 15mm-eluting bioreosorbable scaffold implanted in the ST-segment elevation myocardial infarction setting - PRAVIG 19 OCT substudy

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Background: Incomplete strut/scaffold apposition (ISA) and uncovered struts are related to higher risk of scaffold thrombosis. No data exist about the process of endothelization and late apposition status of the bioreosorbable vascular scaffold (BVS) when implanted in the highly thrombogenic setting of the ST-elevation acute myocardial infarction setting.

Aim: The aim of this study is to assess the serial changes in strut apposition and early coverage of the BVS with optical coherence tomography (OCT) in selected patients enrolled in the PRAVIG-19 study.

Methods and results: Intracoronary OCT imaging using the frequency domain main C7 system with a Dragonfly catheter (St. Jude Medical, St. Paul, MN, USA) was performed in 25 patients at the end of primary PCI. Repeated OCT of the indexed segment with BVS was performed in 6 patients who had the clinical indication for PCI of a non-infarct vessel during follow-up (after 4 weeks in 4 patients, in 2 patients after 6 months). Cross-sections were analysed at each 1 mm interval within the stented segment and 5 mm proximal and distal. Scaffold area, scaffold mean diameter, and ISA were compared at baseline and control OCT.

Furthermore, strut coverage was assessed during the control OCT. Mean scaffold area and diameter from baseline to control OCT did not significantly change (8.1 vs 8.8 mm²; p=0.19 and 3.2 vs 3.3mm; p=0.20, respectively). During the control OCT, 145 frames and 1440 struts were analysed. No changes were observed in ISA between baseline and control OCT (1.1% vs 0.8%; NS). We have observed 79% covered struts in 4 patients in whom control OCT was performed 4 weeks after BVS implantation and 100% covered struts in 2 patients 6 months
after BVS implantation. Minimal intraluminal masses were seen only in 2 frames (1.4%).

Conclusion: Good and persistent strut apposition and early endothelization was observed after biodegradable vascular scaffold implantation in patients with acute ST-elevation myocardial infarction.

75 | BEDSIDE
Immediate and mid-term follow-up of floating bioabsorbable vascular scaffold technique for the ostial lesions of the left anterior descending and left circumflex coronary arteries

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Introduction: Floating stent technique has been proved to be feasible and effective for the treatment of ostial lesions in the left anterior descending artery (LAD), with a good outcome at long term follow-up. There is no information regarding the role of the bioabsorbable vascular scaffold (BVS) in this type of lesions, although concern exists over the possibility of migration of the floating scaffold.

Aim: The purpose of this study is to evaluate the safety of the floating BVS technique for the treatment of the ostial lesions of the LAD and left circumflex (LCx) coronary arteries.

Material and methods: From August 2012 to January 2014, 155 out of 394 lesions treated with BVS in our hospitals were bifurcated ostial coronary lesions. Fifteen of these lesions (0.1, 0 or 0,1 according to the Medina’s classification) were treated with a scaffold floating strategy. Thirteen out of 15 patients (81%) were monitored by intravascular ultrasound (IVUS) or by optical coherence tomography (OCT) at baseline condition and after BVS implantation. Anglo-CT scan was scheduled at 6 months follow-up.

Results: Mean age was 62 years old, most of them were male (87%) and 62% of the patients were admitted in unstable clinical condition. Left ventricular ejection fraction was normal (71.6%). The vessel involved was the ostial LAD in 10 patients (67%) and the ostial LCx in 5 patients (33%). In terms of QCA, main vessel reference diameter was 3.10±0.61 mm, minimal lumen diameter was 1.09±0.50 mm and the percentage of stenosis was 73±15%. Primary success was obtained in all cases. Direct BVS implantation was performed in 13 lesions (87%). In the two remaining cases, predilation was needed. BVS diameter was 3.28±0.26 mm, BVS length was 17.12±3.93 mm and the mean inflation pressure was 16 atm. According to the endovascular images information, no further manipulation at the level of the bifurcation was done. IVUS after implantation showed a minimal BVS area of 7.04±1.5 mm² and a residual stenosis of 10±6%. The degree of BVS protrusion in the carinal area measuring by IVUS/OCT was 2.16±0.82 mm. After a 9 months follow-up, no adverse cardiac events have been documented, being the global MACCE 0%. Anglo-CT was performed in all patients with no restenosis. No evidence of the proximal marker of the BVS was found.

Conclusions: BVS floating technique is feasible, safe and effective, with no adverse cardiac events at mid-term follow-up. Long term follow-up is needed to confirm these results.

76 | SPOTLIGHT
Mid-term clinical outcomes with multi-imaging assessment of bioresorbable everolimus-eluting vascular scaffold for Chronic Total Occlusions

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Purpose: This is the first prospective, pilot study assessing the safety, performance and efficacy of the BVS, in percutaneous CTO recanalization, under guidance of multi-imaging techniques.

Methods and results: In 2013, 33 true CTOs lesions treated with BVS were included in this prospective registry. Target lesions were scaffold after mandatory predilation with IVUS analysis. Patients were followed clinically at 1, 6, 12, 18, and 24 months, optical coherence tomography (OCT) was performed after BVS implantation and at 12 months. A computed tomography (CT) was performed at 7 and 18 months. The mean age was 61±9.2 years old. 19.4% were diabetic 32% with a large profile, lower deliverability, lower radial support and concerns about possible recoil and restenosis. Till date no large data is available for the use of BVS in calcified lesions.

Conclusions: Gentle low pressure balloon dilation of the SB normally preserves the BVS integrity. However, minor BVS rupture after 2.5 mm lateral balloon dilation may occur, but it is infrequent. Prolonged balloon inflation of main vessel may restore the geometry of BVS.
Methods: Our Real Absorb Registry is a single centre prospective database of all BVS implanted in real life patients since its approval for unrestricted clinical use in December 2012 onwards. A total of 480 lesions in 365 patients were treated with 542 BVS. Of this 82 calcified lesions in 76 patients were treated with 89 BVS. Calcified lesions were assessed angiographically and classified as Moderate (n=56) and Severe (n=20). Preparation of vascular bed was performed in all patients and it was achieved using Rotational atherectomy in 26% (n=20). Cutting balloon in 7% (n=6) and optimal sized non compliant balloon with extreme high pressure dilatation (>20 atm) in 67% (n=50). Failure to deliver the BVS to the lesion in the first attempt occurred in 9 lesions (10%) 4 were overcome by using Mother and child catheter (Guideliner) to deliver the BVS, while in the remaining 5 use of buddy wire and/or support wires with further high pressure balloon dilatations achieved successful delivery. The device success was thus 100%. All BVS were post dilated with non compliant balloon to greater than 22 atmosphere. OCT imaging for optimization was performed in 9 cases. There were no in hospital complications. At a median clinical follow up of 170 days (range 27-213 days), 1 patient (1.3%) had diffuse intima restenosis and there has been one scaffold thrombosis (1.3%) at 3 months. Remaining patients remained asymptomatic and well.

Conclusion: Our experience in real world patients demonstrate that BVS can be used in calcified coronary lesion with high device and procedural success rate with low complication rates and MACE rates in short and mid term clinical follow up. Tricks to preempt or overcome failure of deliverability and meticulous vascular bed preparation and implantation techniques is the key to favourable results.

MAKING CLINICAL SENSE OF BIOMARKERS

83 | BEDSIDE
Plasma kidney injury molecule (KIM-1) and endothelin-1 (ET-1) are associated with worsening renal function in heart failure patients

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Purpose: Renal dysfunction is a significant comorbidity in patients with heart failure (HF). Traditional blood markers for the diagnosis of renal dysfunction are insensitive, nonspecific, and may only present late in the injury process. Elevations of urinary Kidney Injury Molecule-1 (KIM-1), represent renal tubule epithelial damage; however, there are no reports of its utility in plasma. Endothelin-1 (ET-1) is a low-abundance plasma biomarker of endothelial function that has been proposed to increase in the setting of renal dysfunction. The aim of this study was to assess the potential for KIM-1 and ET-1 to be novel biomarkers of renal dysfunction in HF.

Methods: We performed a cross sectional study among 200 HF patients (distributions of urinary Kidney Injury Molecule-1 (KIM-1), represent renal tubule epithelial damage; however, there are no reports of its utility in plasma. Endothelin-1 (ET-1) is a low-abundance plasma biomarker of endothelial function that has been proposed to increase in the setting of renal dysfunction. The aim of this study was to assess the potential for KIM-1 and ET-1 to be novel biomarkers of renal dysfunction in HF.

Results: The median age of our population was 55 years (42% female). The high sensitivity assays allowed for both a single and a score in the setting of all patients. Both plasma KIM-1 and ET-1 values increased with decreasing eGFR. In a fully adjusted linear regression model (adjusted for age, sex, HF classification, plasma BNP, and either KIM-1 or ET-1), the β-regression coefficient for every one unit log-transformed KIM-1 incremental increase, eGFR decreased by 11.9 ml/min (p<0.006). The β-regression coefficient for every one unit log-transformed increase in ET-1, eGFR decreased by 19.3 ml/min (p=0.0125).

Conclusions: This is the first study to demonstrate that KIM-1 is measurable in plasma. Plasma KIM-1 and ET-1 are independently associated with worsening renal function in HF patients. These findings introduce the potential for using low abundance biomarkers to detect renal dysfunction and to further refine HF disease severity.

84 | BEDSIDE
Circulating microRNAs and outcome in patients with acute heart failure

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Purpose: Circulating microRNAs (miRNAs) have been extensively studied for their potential biomarker value in patients with acute coronary syndromes. However, the association between miRNAs and the diagnostic and prognostic in patients with acute heart failure (AHF) has received less attention.

Methods: 294 patients with acute dyspnea (236 AHF and 58 non-AHF), and 44 patients with stable chronic heart failure (CHF), were included in this prospective, single-center case-control study. This study was set up in the emergency department and in the 10-bed cardiac intensive care unit of an academic hospital. Circulating levels of miR-1/21/23-252-3p were assessed by quantitative PCR in plasma samples obtained at admission and after 5 days.

Results: At admission, levels of miR-21 and miR-23 were comparable among AHF, non-AHF and CHF patients. Levels of miR-1 were lower in AHF and stable CHF patients compared to non-AHF patients (p=0.0016). Levels of miR-126 and miR-423-5p were lower in AHF and in non-AHF patients compared to stable CHF patients (both p<0.001). All miRNAs had a poor diagnostic value for AHF. During the 5 days post admission, miRNA levels were stable in AHF patients. In non-AHF patients, levels of miR-23, miR-126 and miR-423-5p decreased over the same period. Interestingly, admission levels of miR-423-5p were lower in patients who were re-admitted to the hospital, mostly for cardiovascular disease, in the year following the index hospitalization compared to patients who were not (p=0.0001). Adjusted odds ratios [95% confidence interval] for one-year readmission was 0.70 [0.53-0.93] for miR-423-5p (p=0.01). Admission levels of the five miRNAs were not associated with one-year mortality.

Conclusion: In AHF patients, low circulating levels of miR-423-5p at presentation are associated with hospital readmission. This study supports the value of miR-423-5p as prognostic biomarker of AHF.

85 | SPOTLIGHT
Decreased cerebral blood flow and BDNF levels are associated with depression and memory impairment in patients with heart failure

-Brain Assessment and Investigation in Heart Failure Trial (B-HeFT)

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Purpose: Depression and cognitive impairment are commonly observed in patients with heart failure (HF). Recent studies suggest that blood brain-derived derived brain-derived neurotrophic factor (BDNF) and cerebral blood flow (CBF) are linked to depression and memory function. To date, the interaction between brain and heart in HF patients remains to be fully elucidated. We thus tested the hypothesis that cerebral blood flow (CBF) in the hippocampus and/or plasma BDNF level are associated with depressive symptoms and memory impairment in patients with HF by the prospective study of “Brain Assessment and Investigation in Heart Failure Trial” (B-HeFT) (UMIN000008584).

Results: We recruited 40 patients of HF Stage B (65.0±1.7 yrs) who have structural heart disease without symptomatic HF, and 40 patients of HF Stage C (66.8±1.4yrs) who have structural heart disease with previous or current symptomatic HF. The primary endpoint of B-HeFT is CBF, which was measured in 4 anterior-posterior segments of the hippocampus using magnetic resonance imaging (MRI). Depressive symptoms, memory impairment and plasma BDNF level were assessed using geriatric depression scale (GDS), Wechsler Memory Scale-Revised (WMS-R) and blood sampling respectively. Correlations between CBF in the 4 hippocampal segments or plasma BDNF level and GDS or WMS-R score were examined in each Stage B or C group.

Spearman rank correlation was achieved by the significant CBF decrease in the most posterior segment of the hippocampus in Stage C group compared to Stage B group (Stage B, 39.4±3.8 ml/100g/min vs Stage C, 37.4±3.8 ml/100g/min, P=0.022). GDS score was significantly decreased in Stage C group compared to Stage B groups (Stage B, 4.0±0.3 vs stage C, 4.4±0.4, P=0.025). WMS-R score was smaller but were not statistically significant in Stage C group compared to Stage B groups (Stage B, 18.4±1.3 vs Stage B, 17.4±1.2, P=0.187). Plasma BDNF level was significantly increased compared to Stage C group compared to Stage B group (Stage B, 406±83 pg/ml vs Stage C, 212±28 pg/ml, P=0.004) and positively correlated with WMS-R score (R=0.375, P=0.017). CBF in the most posterior hippocampal segment negatively correlated with GDS score (R=−0.522, P=0.001) and positively correlated with WMS-R score (R=−0.417, P=0.007).

Conclusion: The present study demonstrates for the first time that CBF in the hippocampus and/or plasma BDNF level are associated with depressive symptoms and memory impairment in patients with HF, suggesting the involvement of the brain and the heart connection in the pathogenesis of HF-associated symptoms.
for all). In age-, sex-adjusted Cox proportional hazards regression models, higher observed a gradient of increasing biomarker levels across the HF stages (p < 0.05). When patients where divided into 3 subgroups according to eGFR (≥ 60 ml/min/1.73 m² [n=218], 30–60 ml/min/1.73 m² [n=243], and < 30 ml/min/1.73 m² [n=224]), Galectin-3 levels significantly increased as eGFR worsened (12.3 [10.4-15.6] vs. 16.1 [13-19.8] vs. 24.5 [20-33.8] ng/mL, respectively; p for trend < 0.001) irrespective of NYHA functional class (both I-II and III-IV) and LVEF (both < 45% and ≥ 45%) (all p < 0.001).

Conclusion: Galectin-3 serum concentrations in HF patients were highly associated with clinical status beyond NYHA functional class and LVEF. Interpretation of Galectin-3 levels should be done carefully in presence of renal insufficiency; it is unclear whether galectin-3 is a marker or a mediator of renal insufficiency, thus also reflecting renal fibrosis.

87 | SPOTLIGHT
Prevalence, neurohumoral correlates and prognosis of heart failure stages in the community

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Objective: To assess the association between Galectin-3 and renal function (using estimated glomerular filtration rate [eGFR] by CKD-EPI equation) in a cohort of ambulatory HF patients.

Methods: We evaluated 6800 participants (mean age 51 yrs; 54% women) from the Framingham Study second and third generation cohorts attending routine examinations sectionally, and describe the prognosis of the stages prospectively in the community.

Results: 876 patients were studied (median age 70.2 years, main etiology of HF: ischemic heart disease [52.2%], median LVEF 34%). Serum Galectin-3 concentration highly correlated with eGFR (Rho 0.64, p < 0.001). This correlation remained high after adjustment by age, sex, NYHA functional class, LVEF and etiology of HF (ischemic vs non-ischemic) (Rho=0.64, p<0.001). When patients where divided into 3 subgroups according to eGFR (≥ 60 ml/min/1.73 m² [n=218], 30–60 ml/min/1.73 m² [n=243], and < 30 ml/min/1.73 m² [n=224]), Galectin-3 levels significantly increased as eGFR worsened (12.3 [10.4-15.6] vs. 16.1 [13-19.8] vs. 24.5 [20-33.8] ng/mL, respectively; p for trend < 0.001) irrespective of NYHA functional class (both I-II and III-IV) and LVEF (both < 45% and ≥ 45%) (all p < 0.001).

Conclusion: Galectin-3 serum concentrations in HF patients were highly associated with clinical status beyond NYHA functional class and LVEF. Interpretation of Galectin-3 levels should be done carefully in presence of renal insufficiency; it is unclear whether galectin-3 is a marker or a mediator of renal insufficiency, thus also reflecting renal fibrosis.
94 | SPOTLIGHT
Is high quality CPR achievable by mass training?
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Pavia nel Cuore, IRC-COM Training Center. Pavia, Italy; 2Robbi nel Cuore, IRC-COM Training Center, Robbio, Italy; 3Luigi Sacco Hospital, Intensive Care Unit, Milan, Italy.

Purpose: The importance of High Quality CPR to improve survival in cardiac arrest is stressed by ILCOR 2010 Guidelines, but it is also essential to train as many people as possible to increase the frequency of bystander CPR. With this study we wanted to assess the quality of chest compressions after Mass Training in comparison to classic BLS training.

Methods: We enrolled 190 CPR-untrained lay people (18-35 years) onto one of two courses: course A (55 people) and course B (135 people). Course A was Mass Training characterized by 30-mins of theory and 45-mins of practice performed on a personal low-budget inflatable manikin with an instructor:attendee ratio of 1:15:15. Course B was a classic BLS course consisting of 1-hour of theory and 4-hours of practice on a classic BLS manikin with an instructor:attendee ratio of 1:5:1. At the end of both courses and for each participant we evaluated 1-min compression-only CPR using a wireless skill evaluator manikin. We measured the following parameters: compressions per minute (C/min), percentage of adequate compression depth (target 5 cm, max 6 cm) (Cdepth%), and percentage of correctly released compressions (target 0 cm) (Crel%).

Results: There was no significant difference (calculated with Mann-Whitney test) between course A and course B regarding Crel% (96% [95%CI, 86.4-100] vs 94% [95%CI, 89.9-98], p=0.36) and Cdepth% (89.1% [95%CI, 69.3-99] vs 76.7% [95%CI, 51.9-93], p=0.54), whilst there was a significant difference in Cmin (115 [95%CI, 110-119] vs 120 [IQR, 118-121], p=0.009) with a better result in course A.

Conclusions: Results show that Mass Training is at least as effective as classic BLS Training according to all parameters analyzed. Mass Training attendees reached the target of compressions per minute more often than those on BLSD. This could be due to the continuous use of a personal manikin instead of the interrupted training on a shared manikin. Therefore Mass Training achieves the goal of increasing the amount of people trained in high Quality CPR.

95 | SPOTLIGHT
Out-of-hospital cardiac arrests in children and adolescents: incidences, outcome, household income and parental education

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Background: There is insufficient knowledge of out-of-hospital cardiac arrest (OHCA) in the very young. We conducted a nationwide study in Denmark. Methods: All OHCA patients in Denmark, ≤21 years of age, were identified from 2001 to 2010. The population was divided into infants (<1 year); pre-school children (2-5 years); school children (6-15 years); and high school adolescents / young adults (16-21 years). Multivariate logistic regression analyses were used to investigate associations between prehospital factors and study endpoints: bystander CPR, return of spontaneous circulation and survival.

Results: A total of 459 individuals were included. The overall incidence of OHCA was 3.3 per 100,000 inhabitants per year. The incidence rates for infants, pre-school children, school children and high school adolescents were 11.5, 3.5, 1.3 and 5.3 per 100,000 inhabitants. The overall bystander CPR rate was 48.8%, and the rates for the four age groups were 55.4%, 41.2%, 44.9% and 63.0%, respectively. The overall 30-day survival rate was 8.1%, and the rates for the four groups were 1.4%, 4.5%, 16.1% and 9.3%, respectively. Significant crude difference in survival (OR 3.18, CI 1.12-8.34) between high household incomes vs. low household incomes was found, but the difference was not significant when adjusted for age and sex (OR 0.40, CI 0.08-2.63). High income was found to be associated with improved survival after OHCA, also when adjusted for age and sex (OR 3.48, CI 1.27-9.41).

Conclusion: OHCA incidences and survival rates varied significantly between age groups. High parental education was found to be associated with improved survival after OHCA.

96 | BEDSIDE
Ambient temperature at the onset of out-of-hospital cardiac arrest affects neurological outcome after one month
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1Kyorin University, Emergency Medicine, Mitaka, Japan; 2Toho University, Tokyo, Japan; 3National Center of Neurology and Psychiatry, Kodaira, Japan; 4Nihon University, Tokyo, Japan.

Purpose: Therapeutic hypothermia in resuscitated out-of-hospital cardiac arrest (OHCA) gets favorable reviews in the guidelines, but we have no conclusive evidence supporting a benefit. On the other hand, it has been reported the association between body temperature at the time of OHCA and the seasonal variability of outside temperature. We hypothesized that ambient temperature affects outcome after cardiopulmonary resuscitation (CPR).

Methods: We extracted the data of all patients, 18 years old or older, who had witnessed OHCA from the database of the nationwide, population-based Ustein-style registry, collected from January 2005 through December 2010 in Japan. The primary endpoint was favorable neurological outcome one month after OHCA, defined as Cerebral Performance Category (CPC) 1 or 2. Hourly ambient temperature, atmospheric pressure, humidity, and daylight length of the day of each OHCA, at the capital city of the prefecture where the OHCA was witnessed, were obtained from the database at the Meteorological Agency. To determine the influence of ambient temperature, atmospheric pressure, humidity, and daylight length on neurological outcome, we performed multiple logistic regression analysis, adjusting for factors known to potentially affect the outcome, such as age, gender, etiology of cardiac arrest, and the presence or absence of bystander CPR.

Results: Among the 245,258 witnessed adult OHCA patients, survival with favorable neurological status increased with a rise in ambient temperature in Celsius (adjusted OR 1.007, 95% CI 1.004-1.010). In contrast, we found no significant influence of atmospheric pressure (adjusted OR 1.001; 95% CI 0.998-1.003), humidity (adjusted OR 1.001; 95% CI 0.998-1.003), and daylight length (adjusted OR 0.996; 95% CI 0.989-1.003) on neurological outcome.

Conclusions: Among adult patients with OHCA, an increase in ambient temperature significantly affects neurological outcome after one month. To determine mechanisms how ambient temperature influences on body temperature and neurological recovery of cardiac arrest survivors, further, prospectively designed studies are needed.

97 | BEDSIDE
Increased arginine levels contribute to impaired microvascular perfusion after cardiopulmonary resuscitation

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Objectives: The post cardiac arrest syndrome occurs after global hypoxia leading to microcirculatory impairment. Nitric oxide (NO) is a key molecule regulating microvascular function by regulating NO metabolism. Therefore we investigated whether arginine levels increase following global hypoxia and in the setting of resuscitation and tested whether arginine inhibition ameliorates disorders in the microcirculation in patients that have been successfully resuscitated.

Methods: To determine the effect of global hypoxia on circulating arginine levels, fourteen healthy subjects were exposed to hypoxia in an air-conditioned normobaric hypoxia chamber (height of 5500m, oxygen concentration, FiO2=9.9%) lasting 130 minutes, fourteen healthy subjects were characterized clinically and arginase 1 was measured on day 1 and day 3.

Results: Among the 245,258 witnessed adult OHCA patients, survival with favorable neurological status increased with a rise in ambient temperature in Celsius (adjusted OR 1.007, 95% CI 1.004-1.010). In contrast, we found no significant influence of atmospheric pressure (adjusted OR 1.001; 95% CI 0.998-1.003), humidity (adjusted OR 1.001; 95% CI 0.998-1.003), and daylight length (adjusted OR 0.996; 95% CI 0.989-1.003) on neurological outcome.

Conclusions: Among adult patients with OHCA, an increase in ambient temperature significantly affects neurological outcome after one month. To determine mechanisms how ambient temperature influences on body temperature and neurological recovery of cardiac arrest survivors, further, prospectively designed studies are needed.

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global hypoxia in the hypoxic chamber (p<0.01). In addition, arginase 1 levels were higher on day 1 (69.1±83.3 ng/ml) and on day 3 (44.2±65.6 ng/ml) after resuscitation than in control subjects (p<0.001). Neuronal specific enolase and arginase 1 correlated significantly to each other on day 1 (p<0.026, R=0.40). Incubation of the sublingual mucosa with nor-NOHA increased microcirculatory perfusion (p<0.001). This effect was inhibited by co-incubation with L-NMMA.

Conclusions: Circulating 1 levels are increased following exposure to global hypoxia and in patients that have been successfully resuscitated after cardiac arrest. Topical arginase inhibition improves microcirculatory perfusion following resuscitation. This is of potential therapeutic importance for the post-cardiac arrest syndrome.

98 | BENCH Prognostic importance of interleukin-6 in post-cardiac arrest patients treated with targeted temperature management at 33°C or 36°C J. Bro-Jeppesen1, C. Hassager1, M. Wanscher2, M. Bjere3, J. Kjaergaard1. 1Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; 2Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Anaesthesia, Copenhagen, Denmark; 3Aarhus University, Medical Research Laboratory, Aarhus, Denmark

Purpose: A systemic inflammatory response is a part of post-cardiac arrest syndrome (PCAS), but whether level of inflammation is associated with adverse outcome is not known. We investigated the prognostic importance of level of inflammation by interleukin-6 (IL-6), a potent mediator of the immune response and the acute phase response, in a single centre sub-study of the Target Temperature Management study (NEJM 2013).

Methods: In a single centre study of 171 consecutive comatose patients, randomly assigned to targeted temperature management at 33°C or 36°C (TTM33) or 36°C (TTM36) for 24 h, IL-6 was analyzed at 0, 24, 48 and 72 h after cardiac arrest. Seventy cytokines were assessed including IL-1β, IL-10 and TNF-α, but IL-6 had the most pronounced prognostic influence. For outcome analysis, patients were stratified by median value of IL-6 at each time point to a high or low IL-6 group.

Results: Levels of IL-6 increased significantly from baseline and peaked at 24 h (87 (43-213) vs. 132 (54-261) pg/ml, p=0.03) with no difference between the two TTM-groups (p=0.50). At 24 h, the 30-day mortality rate in patients with high IL-6 levels (>123 pg/ml) was 37% compared to 19% in patients with low IL-6 levels, p=0.02 (Figure), corresponding to an unadjusted hazard ratio of 2.0 (95%CI: 1.1-3.8), p=0.02. When adjusting for pre-hospital prognostic factors the hazard ratio for IL-6 >123 pg/ml at 24 h was 1.9 (95%CI: 1.0-3.6), p=0.05, with no significant interaction between level of IL-6 and TTM-group, p=0.26.

Conclusions: Level of inflammation assessed by IL-6, peaked at day 2 after cardiac arrest and IL-6 >123 pg/ml at 24 h of TTM was independently associated with increased mortality with no interaction of targeted temperature management at 33°C or 36°C.

HOT TOPICS IN RISK PREDICTION

103 | BENCH Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome C. Bonanad Lozano, V. Ruiz, J. Fernandez, S. Garcia-Blas, L. Mainair, E. Nunez, J. Nunez, J. Sanchis. University Hospital Clinic, Department of Cardiology, Valencia, Spain

Background: Geriatric conditions may predict outcomes beyond age and standard risk factors. Our aim was to investigate a wide spectrum of geriatric conditions in survivors after an acute coronary syndrome

Methods: A total of 342 patients older than 65 years were included. At hospital discharge, 5 geriatric conditions were evaluated: Frailty (Fried and Green scores), physical disability (Barthel index), instrumental disability (Lawton-Brody test), cognitive impairment (Pfeiffer test) and comorbidity (Charlson and simple comorbidity index). The outcomes were mortality and the composite of death/myocardial infarction during 30 month median follow-up.

Results: Seventy-four (22%) patients died and 105 (31%) suffered the composite endpoint. By univariable analysis, all individual geriatric conditions were associated to outcomes, mainly mortality. From all of them, frailty using the Green score had the strongest discriminative accuracy (area under the curve for mortality, AUC=0.76). After full adjustment including clinical data and geriatric status, the Green score was the only predictive geriatric condition (per point; mortality; HR=1.23, 95% CI 1.09-1.24, p<0.0001; composite endpoint; HR=1.16, 95% CI 1.09-1.24, p<0.0001). Regarding mortality, the addition of the Green score to the clinical model improved discrimination (AUC– 0.823 versus 0.840) and significantly reclassified patients (integrated discrimination improvement 4.1, 95% CI 0.8-10.5; continuous net reclassification improvement 53.7, 95% CI 24.9-82.3).

Conclusions: Geriatric conditions predict worse outcome after an acute coronary syndrome. Frailty assessed using the Green score captures most of the prognostic information provided by the geriatric conditions.

104 | BENCH Predictors of 1-year mortality at hospital discharge after acute coronary syndromes: a new risk score from the EPICOR study S.J. Pocock1, H. Bueno2, M. Liaaen3, L. Green4, N. Dannenhoffer5, Y. Huo6, F. Van De Werf4, 1London School of Hygiene and Tropical Medicine, London, United Kingdom; 2University Hospital Gregorio Maranon, Madrid, Spain; 3AstraZeneca France, Medical Department, Rue-Valmalmson, France; 4AstraZeneca Observational Research, Madrid, Spain; 5CHU Interuniversity Centre for Health Economics Research UGent, Ghent, Belgium; 6Hospital Espanol Georges Pompidou, & Rene Descartes University, Paris, France; 7Peking University First Hospital, Beijing, China, People’s Republic of; 8University Hospitals (UZ) Leuven, Leuven, Belgium

Purpose: At hospital discharge after an ACS event, patients vary markedly in their prognosis. There is a need for a reliable prediction tool to identify patients with high mortality risk at discharge.

Methods: EPICOR (NCT01711404) is a prospective cohort study of 10568 consecutive hospital survivors after an ACS event (4933 STEMI, 5625 NSTE-ACS), enrolled October 2010–March 2011. 65.1% underwent PCI and 25.9% CABG. Post-discharge mortality was recorded up to 12 months. From over 50 potential predictor variables a new risk score for 1 year mortality was developed using forward Cox regression, and examined for goodness-of-fit and discriminatory power.

Results: 407 patients (3.9%) died within 1 year of discharge. We identified 12 highly significant independent predictors of mortality (in order of predictive strength): age, lower ejection fraction, poorer EQ-SD quality of life, elevated serum creatinine, in-hospital cardiac complications, COPD, elevated blood glucose, male gender, no PCI or CABG after NSTE-ACS, low haemoglobin, PAD, on diuretics at discharge. When combined into a new risk score excellent discrimination was achieved (c-statistic = 0.81), validated on a large similar patient cohort of 9907 patients from Asia (c=0.78). For both STEMI and NSTE-ACS there was a steep gradient in 1-year mortality, from 0.5% in the lowest quintile to 18.5% in the highest decile (Fig. 1). NSTE-ACS contributed over twice as many high-risk patients as STEMI.

Conclusions: Post-discharge mortality for ACS patients remains of concern. Our new user-friendly risk score can readily identify who is at high risk.

105 | BENCH Modelling the potential impact of diet & lifestyle changes on a CVD risk communication tool: heart age M. Dotsch1, R. Newson1, M. Haseli-Mashhadi2, M.R. Cobain2.
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Purpose: To improve the understanding of the general population of CVD risk the Heart Age tool was developed. This online tool helps to communicate risk in simple terms, by showing your “heart age”, the age for which the individual’s reported risk factors would be considered “normal”. This tool is effective in increasing the understanding of CVD risk, however motivating people to lower their risk remains a challenge. Demonstrating the effect of small lifestyle changes on heart age may
be a useful avenue towards increasing motivation to modify risk. As such, we conducted a modelling study to determine the effects of reducing heart age through specific lifestyle modifications.

**Methods:** Scenarios were developed to model the impact of improving cardiovascular risk factors via the following lifestyle modifications: DASH diet, weight loss, increased physical activity, and smoking cessation. For the scenario analyses we used data from the 2007/2008 NHANES 2007/2008. Subjects included were: free from CVD, aged between 20-80 years and had complete measures for heart age risk factors (n=4,029). For each subject heart age was calculated before and after application of the different scenarios (virtual interventions). The effect of changes on the risk factors included in the heart age algorithm were based on effects of interventions.

**Results:** In people with hypertension, adherence to the DASH diet could lower heart age by 2-6 years, reducing the gap between heart age and the actual age with an average 15-45%. In overweight or obese people, a 5-kilogram weight loss could reduce heart age by 2-4 years (18-32% reduction of the gap with actual age). In sedentary subjects being more physically active could reduce heart age by 0-3 years (0-20% reduction of the gap with actual age). Smoking cessation could reduce heart age with on average 13 years (30% reduction of the gap with actual age). In hypercholesterolemia, starting use of statins could reduce heart age with 3 to 6 years (13-25% reduction of the gap with actual age). In hypertensive people, starting to take anti-hypertensives has a similar effect with a reduction in heart age of 3-5 years, reducing the initial gap between heart age and actual age with 12-20%.

**Conclusions:** Relatively small changes in diet and lifestyle could considerably lower heart age in people with elevated heart ages. Moreover, changes in diet or lifestyle could lead to even larger effects on heart age than starting drug usage. This modelling study supports that demonstrations of the effect of small lifestyle changes on heart age could be a useful motivator to modify lifestyle.

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**106 | BEDSIDE**

The CHA2DS2-VASc score is useful to stratify risk of death and ischemic stroke in patients after acute myocardial infarction and with no history of atrial fibrillation.

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**Purpose:** The aim of the study was to assess whether the CHA2DS2-VASc score might be useful to indentify patients at high risk of ischemic stroke and death among subjects after acute myocardial infarction (AMI) and with no history of atrial fibrillation (AF).

**Methods:** We analyzed 2,980 consecutive AMI-patients admitted to our center between 2003 and 2009. Finally, 2647 subjects were included into analysis, as 333 were excluded because of AF and/or use of oral anticoagulants. On the basis of the CHA2DS2-VASc score 4 groups were distinguished: low-risk (1 point; n=534), intermediate-risk (2-3 points; n=1261), high-risk (4-5 points; n=688) and very high-risk (≥5 points; n=164). Data on long-term follow-up were screened to identify patients who experienced stroke or died during remote observation.

**Results:** Among 2,647 sinus rhythm patients ischemic stroke occurred in 71 (2.7%) patients, CV death in 205 (7.8%) and AMI reinfarction in 19 (0.7%) patients. The incidence of stroke and death among subjects after acute myocardial infarction and with no history of atrial fibrillation was 4-fold increased in the intermediate-risk group (Table 1). Every point in CHA2DS2-VASc scale was independently associated with 41% increase in stroke risk and 23% increase in mortality rate (for both p<0.001) during long-term observation.

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Population, n</th>
<th>Stroke, n (%)</th>
<th>Death, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (1 point)</td>
<td>534</td>
<td>6 (1.12)</td>
<td>33 (6.18)</td>
</tr>
<tr>
<td>Intermediate (2-3 points)</td>
<td>1261</td>
<td>23 (1.82)</td>
<td>163 (12.93)*</td>
</tr>
<tr>
<td>High (4-5 points)</td>
<td>688</td>
<td>31 (4.51)*</td>
<td>179 (26.02)*</td>
</tr>
<tr>
<td>Very high (≥5 points)</td>
<td>164</td>
<td>11 (6.71)*</td>
<td>64 (39.02)*</td>
</tr>
</tbody>
</table>

**p<0.001 vs Low-risk group.**

**Conclusions:** The mortality rate and risk of stroke were strongly associated with the CHA2DS2-VASc score. Hence this scoring system could be useful to identify high risk patients with no AF history, in whom additional preventive measures might be beneficial to improve the outcome.

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**107 | BEDSIDE**

Serious underestimation of the overall risk of cardiovascular events if extrapolated from cardiovascular mortality: observations from the EPIC-Norfolk prospective population study

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**Purpose:** The European prevention guideline suggests that total (fatal and non-fatal) cardiovascular disease (CVD) risk can be calculated from the risk of fatal CVD using a fixed multiplier (3x) in individuals with a SCORE of ≥5%. However, the relationship between total CVD and fatal CVD in the general population is unclear, and the suggested fixed multiplier has not been validated. We therefore investigated the ratio of total CVD to fatal CVD in a large, population-based cohort.

**Methods:** Fatal CVD and total CVD (fatal plus non-fatal CVD events requiring hospitalization) were analyzed using Kaplan-Meier estimates in 15,171 men and women aged 39-65 without baseline CVD or diabetes mellitus. CVD outcomes included death and hospitalizations for ischemic heart disease, heart failure, cerebrovascular disease, peripheral artery disease, and aortic aneurysm. The main outcome was the ratio of 10-year total CVD to 10-year fatal CVD stratified by sex and SCORE.

**Results:** In individuals with SCORE ≥5% (n=880) 10-year fatal CVD was 7.3%; rate-of-total CVD was 41.2%, yielding an overall multiplier of 5.6 (men 5.4, women 16.4). In individuals with SCORE ≤5% (n=14,491), this ratio was markedly higher, with an overall ratio of 12.5 (men 10.4, women 15.9) (Figure).

**Conclusion:** The relationship between 10-year total CVD and fatal CVD cannot be estimated using fixed multipliers, regardless of SCORE. The proposed multiplier in the current guideline leads to an underestimation of risk, particularly in men and individuals with a low SCORE. These findings have important implications for individual decision-making on preventive therapy and for future guidelines.

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**108 | BEDSIDE**

The brand new AHA/ACC 2013 cardiovascular risk calculator: will it keep up with the European standards?

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**Purpose:** The recently published ACC/AHA cardiovascular (CV) risk calculator, that evaluates the atherosclerotic cardiovascular disease (ASCVD) risk in ten years, has been criticised for risk overestimation. We aimed to compare this system with Systematic Coronary Risk Evaluation (SCORE) in a Southern European cohort.

**Methods:** We prospectively included 446 CV events-naïve patients treated at a Lipidology Clinic (1994-2007). The main outcomes followed-up up to ten years were cerebrovascular events, non-fatal coronary events, AMI, stroke and CV death. The cohort was divided in four groups according to SCORE and ASCVD calculated risks (cut points: ASCVD -5%, 7.5%, 10%; SCORE -1%, 5%, 10%); the median expected event rate was compared with the observed one. We built receiver operating characteristic (ROC) curves according to specific definitions. Afterwards, the same composite endpoint of AMI, stroke and CV death was tested for both risk calculators in order to compare ROC curves. Hosmer and Lemeshow test was used for calibration analysis.

**Results:** The mean age of our population was 48.9±14.4 years, with a mean arterial systolic pressure of 134.0±20.6 mmHg and a mean total cholesterol of 276.4±77.6 mg/dL. There were 58.3% males, 21.1% smokers, 24.8% type 2 diabetics and 53.5% under antihypertensive drug treatment. The 10-year incidence rate of AMI, stroke and CV death was respectively 3.4%, 2.4% and 1.5%. The median calculated SCORE risk was 0.95% (P25-75: 0.2-3.1). The low-risk patients (SCORE ≤1%) experienced no events; in the other groups the expected event rate was slightly superior to the real one. The median calculated ASCVD risk was 8.46% (P25-75: 2.7-19.1). There were no events when ASCVD risk was under 7.5%; the observed event rate was superior to the expected in the next risk group, whereas in the ≥10% group the predicted event rate nearly doubled the real one. The area under ROC curve (AUC) for SCORE was 0.92 (p<0.01) and 0.76 for ASCVD (p<0.001). The scores were positively correlated (spearman coefficient 0.82, p<0.001). There was no difference between SCORE (AUC 0.72) and ASCVD (AUC 0.76) ROC curves for the same composite CV endpoint (p=0.34). Both calculators showed good calibration.

**Conclusion:** In a prospective ‘real-life’ European cohort, the SCORE system and the ASCVD risk calculator are strongly correlated, well calibrated and show similar discriminative power for CV risk prediction. Overall, the SCORE system slightly overestimates CV risk. The ASCVD calculator overestimates CV risk in low-risk individuals, however the 7.5% suggested cut-off is extremely effective in discriminating high-risk subjects.
INNOVATIONS IN THE MANAGEMENT OF SUDDEN CARDIAC DEATH

119 | BEDSIDE
Public access defibrillators location strategy in major urban aeras using geographic optimization, is there an optimal number?
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Purpose: In major cities, optimal distribution of automatic external defibrillators (AED) has long been debated. International guidelines recommended placing AED where at least an out-of-hospital cardiac arrest (OHCA) occurs every 2 years. However, bystander awareness of AED location is often limited. The aim of the study was to determine a potential strategic AED placement policy.

Methods: We included all OHCA managed in Paris by Emergency Medical Services between 2000 and 2010. First, we worked on different scenarios of regular AED placement according to several deployment distances (from 200 meters to 2000 meters), then we analyzed median distance between these AED potential placements and included OHCA. Second, we identified different types of public facilities in Paris and we calculated the median distance according to each type of public facilities. We evaluated the number needed of AED in each case.

Results: Among the 4176 OHCA of presumed cardiac etiology, 1415 (34%) occurred out-of-home and 1355 were eventually geocoded (Figure). Median distances between OHCA and district councils (n=20), post offices (n=195), subway stations (n=302), bike sharing stations (n=957) and pharmacies (n=1466) were 1052, 324, 239, 137 and 142 meters respectively.

Conclusion: Increasing number of AED following a regular distribution on the territory decreases drastically the median distance between AED potential placement and OHCA until a certain number (350 AED for Paris). Additional AED placement benefit becomes less apparent. AED public facilities coverage strategy may help to optimize AED placement. The choice of the best public facility should be based on its number and repartition on the territory and its proximity to OHCA.

120 | BEDSIDE
Effect of electrical therapy in the 2010 CPR guidelines for patients with out-of-hospital cardiac arrest due to ventricular fibrillation
T. Yagi, K. Nagao, E. Tachibana, N. Yonemoto, S. Shiira, M. Takayama, H. Nonoghi, T. Kimura, A. Hirayama, on behalf of the Japanese Circulation Society with Resuscitation Science Study (JCS-ReSS) Group, Kawaguchi Municipal Medical Center, Kawaguchi, Japan; 2 Surugadai Nihon University Hospital, Tokyo, Japan; 3 National Center of Neurology and Psychiatry, Tokyo, Japan; 4 Kokura Memorial Hospital, Kitakyushu, Japan; 5 Shikakbara Heart Institute, Department of Cardiology, Tokyo, Japan; 6 Shizuoka General Hospital, Shizuoka, Japan; 7 Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; 8 Nihon University, School of Medicine, Department of Internal Medicine, Division of Cardiology, Tokyo, Japan

Background: The 2005 guidelines for cardiopulmonary resuscitation (CPR) with electrical therapy recommended a single shock instead of 3-shock sequences recommended in the 2000 guidelines. The 2010 guidelines stressed that it is necessary to improve CPR quality. We compared the effects of electrical therapy based on the three guidelines.

Methods: From the data of the All-Japan Ustsein Registry, a prospective, nationwide, population-based registry of out-of-hospital cardiac arrest (OHCA), we included adult patients who had OHCA due to cardiac etiology and in whom shockable arrest was recorded as an initial rhythm. Study patients were divided into three groups based on the different CPR guidelines: 3-shock protocol in the 2000 guidelines (2000G), 1-shock protocol in the 2005 guidelines (2005G), and 1-shock protocol in the 2010 guidelines (2010G). The primary endpoint, favorable neurological outcome at 30 days after OHCA, was compared among the three groups with or without bystander CPR.

Results: Of the 4176 OHCA of presumed cardiac etiology, 1415 (34%) occurred out-of-home and 1355 were eventually geocoded (Figure). Median distances between OHCA and district councils (n=20), post offices (n=195), subway stations (n=302), bike sharing stations (n=957) and pharmacies (n=1466) were 1052, 324, 239, 137 and 142 meters respectively.

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118 | SPOTLIGHT
The FirstAED project - incorporates emergency dispatch, global positioning system technology, first responders with distinct roles, smartphones and an automatic external defibrillator network
F.L. Henriksen, H. Schakow, M.L. Larsen, Odense University Hospital, Cardiology, Odense, Denmark

Purpose: FirstAED is meant as a supplement to the existing emergency response systems. The purpose is to shorten the first responder response times at emergency calls to below 5 minutes on an island characterized by 13,000 inhabitants, long ambulance response times, and long distances to the nearest hospitals.
The FirstAED project defines a new way to dispatch the nearby first responders and organize their roles in the hope of reducing response times and improving survival rates.

Methods: First aid and cardiopulmonary resuscitation is provided by 215 trained volunteer first responders who use their rescuer smartphone. The population purchased 95 automated external defibrillators (AEDs) which are available around 500 meters, then we worked on different scenarios of regular AED placement according to several deployment distances (from 200 meters to 2000 meters), then we analyzed median distance between these AED potential placements and included OHCA. We included all OHCA managed in Paris by Emergency Medical Services between 2000 and 2010. First, we worked on different scenarios of regular AED placement according to several deployment distances (from 200 meters to 2000 meters), then we analyzed median distance between these AED potential placements and included OHCA. Second, we identified different types of public facilities in Paris and we calculated the median distance according to each type of public facilities. We evaluated the number needed of AED in each case.

Results: Among the 4176 OHCA of presumed cardiac etiology, 1415 (34%) occurred out-of-home and 1355 were eventually geocoded (Figure). Median distances between OHCA and district councils (n=20), post offices (n=195), subway stations (n=302), bike sharing stations (n=957) and pharmacies (n=1466) were 1052, 324, 239, 137 and 142 meters respectively.

Conclusion: Increasing number of AED following a regular distribution on the territory decreases drastically the median distance between AED potential placement and OHCA until a certain number (350 AED for Paris). Additional AED placement benefit becomes less apparent. AED public facilities coverage strategy may help to optimize AED placement. The choice of the best public facility should be based on its number and repartition on the territory and its proximity to OHCA.
CATHETER ABLATION BEYOND ATRIAL FIBRILLATION

P127 | SPOTLIGHT
Zerofluoroscopic catheter ablation of supraventricular arrhythmias
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Background: Conventional catheter ablation of cardiac arrhythmias is associated with radiation risks for patients and laboratory personnel. Widespread use of zerofluoroscopic catheter ablation is limited by safety concerns. This study investigated the feasibility of zerofluoroscopic catheter ablation using 3-D-Mappingystem and optional catheter contact force technology.

Methods and results: 100 patients including 27 pediatric patients received a zero fluoroscopic EP-study using the EnSiteNavX system with real time visualization of all electrodes. Inclusion criteria were symptomatic suspected atrioventricular nodal reentrant tachycardia, typical atrial flutter, atrioventricular reentrant tachycardia, and focal atrial tachycardia. In one patient no arrhythmia could be induced and one patient ablation was not attempted due to a parahissian pathway. Thus, in 98 patients zero-fluoroscopy catheter ablation of right-sided ($n=77$) and left sided atrial arrhythmias ($n=21$) was attempted. For left atrial arrhythmia an irrigated-tip catheter with integrated contact force sensor was used in order to avoid perforation by keeping the maximum contact force below 100g and during ablation below 50g. Transseptal access if necessary was achieved under transesophageal echocardiography for ablation of left-sided arrhythmias. In 55 patients an AVRN was diagnosed. 27 patient received slow-pathway-modulation by cryotechnique and 28 by radiofrequency. In 25 patients a WPW-syndrome was diagnosed (17 left sided, 8 right sided). In all patients ablation was successfully performed in the presence of zero fluoroscopy and without fluoroscopy was achieved in 97 of 98 patients (98.9%). No severe complications occurred besides a delayed AV-block more than three days after the procedure.

Conclusion: Nonfluoroscopic catheter ablation is generally feasible in right-sided cardiac arrhythmias. Safety concerns regarding zerofluoroscopic ablation of left atrial substrates can be overcome with real-time contact force measurement.
Age and gender-related symptoms recurrence after AV node re-entrant tachycardia


Purpose of study: To evaluate the factors correlated with the recurrence of symptoms after radiofrequency (RF) ablation of slow pathway for ativoentricu-

lar AVRT. Recurrence of AVNRT (AVNRT). RF ablation currently is used to treat

patients with AVNRT. Methods: 881 patients 264 males, 547 females were consecutively referred for ablation of AVNRT. They were aged from 13 to 87 years (mean 52±18). AVNRT was typically (n=730) or atypical (n=88). AVNRT: the study control state or after isoproterenol. Ablation used RF energy, 65±40 watts, delivered on slow pathway potentiak, until that AVNRT was not induced after 20 minutes following application. Results: 90 patients were excluded because AVNRT remained inducible or ab-

lation of atrial tachycardia was stopped for atrial fibrillation/tachycardia (AF) (n=30). Success was obtained in 791 patients. During follow-up (mean 2.5±2.2 years), 128 patients (16%) had recurrence of symptoms. After non-invasive studies and another electr

physiological study, symptoms were attributed to another tachycardia (n=61) (group I) (AF/atrial flutter 4B, ventricular tachycardia 3), a recurrence of AVNRT (n=30) (group II) or a sinusal tachycardia (n=38) (group III); 663 patients were asymptomatic (group IV). Patients of group I were older (60±13 years) than group II (53±20; III (34±16; IV (52±18; <0.001), more frequently males (51%) than group II (61.5%); III (16%) or IV (33%) <0.001) and had more frequently atypical AVNRT (16%) than group II (10%); III (5% or IV (6%) <0.006). Clinical and electrophysiological data of group II and IV were in group II (p<0.001) and the higher frequency of women (p<0.02). Associated syncope and need of isoproterenol to induce AVNRT did not differ significantly between each group. Conclusions: The rate of initial success of AVNRT ablation is dependent on the mechanisms of tachycardia with a higher success in typical AVNRT than in atypi-

cal AVRT. Recurrence of symptoms after successful ablation is frequent (16%), but true recurrence of AVNRT is only present in 5% of patients. Old patients of

cardiac AVNRT. Recurrence of symptoms after successful ablation is frequent (16%), but true recurrence of AVNRT is only present in 5% of patients. We conclude that empirical SPM improved clinical symp-

oms (p=0.13). Regression analysis showed that surgically corrected CHD was signifi-

cantly different between MBC and Lasso (448±19; 424±154; p=0.56), but the mapping time was significantly shorter with MBC than with Lasso (314±134sec vs 515±153sec; p<0.001).

P131 | BEDSIDE Atrial tachycardia following persistent atrial fibrillation ablation: Number of atrial tachycardias predicts the outcome of the ablation procedure

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Purpose: The aim of this study was to identify predictive factors for arrhythmia recurrence after ablation of atrial tachycardias (AT) following ablation of persistent atrial fibrillation (AF). Patients and methods: A population consisted of 117 consecutive patients (mean age 66±9 years, mean LA diameter 47±6mm) who underwent catheter ablation of AT following ablation of persistent AF. The first procedure consisted of a pulmonary vein isolation, followed by an ablation of complex fractionated atrial electrograms and linear lesions. Using entrainment and activation mapping, a total of 203 ATs were identified in the 117 pts (1.8±1 [1-6] per pt). AT mechanism was macroreentry in 63 patients (54%), localized reentery in 23 patients (20%) and both in patients (26%). More than one AT was identified in 54 (48%) patients. Macroreentries occurred around the mitral valve (n=57, 49%), around the tricus-
pidal valve (n=15, 13%) or involved the LA roof (n=55, 47%). The most frequent locations for localized reentries were the anterior LA and left atrial appendage (n=21, 18%), the posterior LA (n=17, 14.5%) and the septum (n=15, 13%). AT was due to a gap in a previously deployed line in 4236% patients). Following ablation, patients were seen every 3 months with repeated 7-days Holter ECGs. The study endpoint was freedom from any arrhythmia recurrence without antiarrhythmic drugs at 12 months. Results: At 12 months, 50% of patients reached the study endpoint. AT mecha-
nism did not significantly influence the outcome of the procedure with a freedom from recurrence of 51% (macroreentry), 40% (localized reentry) or 54% (both mechanisms) (p=n.s).

Conclusions: The rapid mapping for atrial tachycardia using multi-electrode basket catheter

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Background: The mechanisms of atrial tachycardia (AT) are often difficult to iden-
tify because AT could easily be terminated during mapping and could not always be induced reproducibly. Recently, a new multi-electrode basket catheter (MBC) became available. We supposed the MBC could be utilized for the diagnosis of AT circuit.

Method: This study consisted of 32 consecutive patients with clinically docu-
mented right-sided AT who underwent catheter ablation for AT. Using a 3-D mapping system (Ensite NavX), two activation maps of the AT were generated respectively with both a conventional ring catheter (Lasso, 10 poles, 15mm) and a MBC (PV3200, 31 poles, 32mm) consisted of six flexible, self-
expanding splines. The time required to complete the activation map and the points acquired with both mapping catheters were compared. Results: In all 40 ATs, both maps of the AT created by MBC and Lasso were completely identical to each other. Of those 28 ATs were CTI dependent, the remaining 12 ATs consisted of incisonal (n=7), crista related (n=3), and focal (n=2) ATs.

Conclusions: The number of points acquired to complete the activation map was not signifi-
cantly different between MBC and Lasso (448±19 vs 424±154; p=0.56), but the mapping time was significantly shorter with MBC than with Lasso (314±134sec vs 515±153sec; p<0.001).
EMBRACING COMORBIDITY IN HEART FAILURE

P134 | BEDSIDE
Clinical predictors of obstructive sleep apnoea (OSA) and central sleep apnoea (CSA) in patients with heart failure with reduced left ventricular ejection fraction (HFREF)

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Purpose: Sleep-disordered breathing (SDB) is very common in patients with heart failure (HF). There are two main types of SDB: OSA and CSA with Cheyne-Stokes respiration (CSA/CSR). Since different types of SDB may lead to different treatment strategies, this study investigated clinical predictors for predominant OSA or CSA in patients with HFREF.

Methods: Patients enrolled in the SchlaHF registry who had HFREF (left ventricular ejection fraction [LVEF] <45%) and showed moderate-to-severe SDB on polysomnography were eligible for this analysis, which was performed using a logistic regression model.

Results: A total of 1808 patients, 1570 male and 238 female, were included. Predominant OSA was significantly less common in males (odds ratio [OR] 0.49, 95% confidence intervals [CI] 0.31-0.78; p<0.002), and in the presence of atrial fibrillation (OR 0.66, 95% CI 0.53, 0.87; p<0.001) or an ischaemic HF etiology (OR 0.53, 95% CI 0.30, 0.92; p<0.024). A 5-unit increase in body mass index (BMI) significantly increased the risk of OSA (OR 1.38; 95% CI 1.25, 1.53; p<0.001). Conversely, each 5% decrease in LVEF was associated with a decrease in the risk for OSA (OR 0.88, 95% CI 0.83, 0.94; p<0.001). The combination of male gender and ischaemic aetiology markedly increased the risk of OSA (OR 2.07, 95% CI 1.14, 3.74; p<0.017). Significant predictors of predominant CSA were male gender (OR 2.03, 95% CI 1.28, 3.21; p<0.002), a 5% decrease in LVEF (OR 1.14, 95% CI 1.07, 1.21; p<0.001), and having ischaemic aetiology (OR 1.90, 95% CI 1.09, 3.31; p<0.024) or atrial fibrillation (OR 1.52, 95% CI 1.23, 1.89; p<0.001). Male gender and older age combined to a significant increase in CSA (OR 1.49 [male gender and 10-year increase in age], 95% CI 1.11, 2.01; p=0.008). A lower risk for CSA was significantly associated with each 5-unit increase in BMI (OR 0.72, 95% CI 0.65, 0.80; p<0.001) and with the combination of male gender and ischaemic aetiology (OR 0.48, 95% CI 0.27, 0.88; p=0.017). Neither age nor NYHA class >II were significantly associated with the predominance of either OSA or CSA.

Conclusions: The results of the SchlaHF registry data suggest that although OSA and CSA are both types of SDB, each entity features different clinical predictors. Better understanding of the factors associated with OSA and CSA in HFREF may assist in their differential diagnosis and management.

P135 | BEDSIDE
Vitamin B12 and folate deficiency: prevalence, clinical correlates and outcome in chronic heart failure (HF)

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Purpose: To determine the prevalence, clinical correlates, and the effects on outcome of vitamin B12 and folate acid levels in chronic Heart Failure (HF).

Methods: We studied an international pooled cohort comprising 610 patients with chronic HF. The main outcome measure was all-cause mortality.

Results: Mean age was 68±12 years, mean left ventricular ejection fraction was 33±13%, and median serum NT-proBNP level was 1801 pg/mL (IQR: 705-4335). Vitamin B12 deficiency (serum level <200 pg/mL) folate deficiency (<4 ng/mL), and iron deficiency (serum ferritin level <100 μg/L, or 100-299 μg/L with a transferrin saturation <20%) were present in 5%, 4%, and 58% of all patients, respectively. Vitamin B12 levels were positively associated with higher NT-proBNP and...
ferritin levels (p<0.001), whereas clinical associates of folic acid included systolic blood pressure, hemoglobin, transferrin saturation, renal function, and atrial fibrillation. No significant correlation between mean corpuscular volume (MCV) and vitamin B12, folic acid or ferritin levels was observed. Lower folic acid levels were associated with an impaired quality of life (p<0.0003). In multivariate Cox proportional hazard regression models, serum vitamin B12 and ferritin and folic acid were not significantly associated with all-cause mortality.

Conclusions: Vitamin B12 and folate deficiency are relatively rare in patients with chronic HF, in contrast to iron deficiency. No significant correlation was found between MCV and serum levels of vitamin B12 and folic acid, making MCV an unreliable screening marker for hematinic deficiencies in patients with chronic HF. In contrast to iron deficiency, folic acid and vitamin B12 were not related to prognosis.

P136 | BEDSIDE
The incidence, clinical significance and treatment effects of depression in patients undergoing cardiac resynchronization therapy
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Purpose: The aim of the study was to assess the incidence, clinical impact of depression and effectiveness of treatment of this syndrome in cardiac resynchronization therapy (CRT)-dependent patients.

Methods: The prospective, single-center, intervention, non-randomized trial included 260 consecutive CHF-patients who were implanted with CRT-D. All patients completed the Beck Depression Inventory (BDI-II) and underwent a psychiatric examination at the time of implantation. The assessment of psychiatric status was repeated at 3, 6 and 12 months after implantation. 129 (49.6%) patients with depression at baseline (Depression Group) were included into further analysis. Among this group 51 (39.5%) subjects received antidepressants (Treated Group), whereas 78 (60.5%) patients, who refused to take antidepressants, were included into non-Treated Group. Data on long-term follow-up were screened to identify patients who developed a composite endpoint defined as death or hospitalization for depressed heart failure.

Results: Considering whole depressive group, significant reduction in the incidence of depression was observed 6 and 12 months after a CRT-D implantation (32.5% and 34.1%, respectively; p<0.05). Depression remission after 6 months was achieved in 40 (78.4%) patients from Treated Group and in 30 (38.5%) subjects not taking antidepressants (p<0.05). During 12-month observation period, patients with depression at baseline had a significantly higher risk for the development of a composite endpoint than CRT-D population free of this disorder: 34.0% vs 14.4% (p<0.05). Additionally, depression was found to be the independent predictor for a composite endpoint in CRT-D population (HR 2.55).

Conclusions: Depression is a common morbid symptom in patients with severe CHF, affecting half of the CRT candidates. Resynchronization therapy reduces significantly the incidence of this syndrome, also in patients not taking antidepressants. Nevertheless, the remission-rates are 2-fold higher in patients taking antidepressant drugs. Depression at baseline is the independent predictor of unfavorable outcomes in CRT-D population.

P137 | BEDSIDE
The impact of chronic obstructive pulmonary disease on readmission and survival of heart failure patients
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Background: The association between chronic obstructive pulmonary disease (COPD) and heart failure (HF) has been investigated in randomized studies of patients with reduced ejection fraction (HFREF). This post hoc analyses showed inconsistent association between COPD and mortality. Recently, we found that COPD is associated with worse outcome among hospitalized elderly male HF patients, in whom significant diastolic dysfunction was also more prevalent. As compared to COPD patients, we sought to investigate whether the impact of COPD on outcome of HF patients is related to echocardiographic measures, type and severity of HF.

Methods: In this retrospective analysis we analyzed clinical and echocardiographic data from all HF patients, 16 years of age or older, who were hospitalized in a Medical Center between January 1st 2000 and December 31st 2009, who did not undergo heart valve replacement.

Results: Data were available for 9,335 HF patients, among them 1,826 (20%) had COPD. HF patients with COPD as compared to those without COPD were more prevalent (64% vs. 54%, p<0.0001), had more chronic renal failure (42% vs. 34%, p<0.0001), atrial fibrillation (45% vs. 40%, p<0.0001), obesity (18% vs. 10%, p<0.0001) and less history of past myocardial infarction (14% vs. 17%, p<0.0001). HF patients with COPD had more left ventricular hypertrophy (LHV) (38% vs. 31%; p=0.03) and right ventricular dysfunction or enlargement (23% vs. 19%, p<0.0001), but did not differ from those without COPD with respect to the prevalence of systolic or diastolic dysfunction, significant valvular abnormalities and pulmonary hypertension. Subgroup analysis by HF type showed that patients with HFREF and COPD had significantly higher LV end-systolic and end-diastolic diameters as compared to HFREF patients without COPD (p<0.016 and p=0.005), while HFPEF patients with COPD had significantly higher rates of RV dysfunction or enlargement (20% vs. 15%, p<0.0001). Readmissions within 30 days were more frequent among HF patients with COPD of (35% vs. 24%, p=0.001). Kaplan Meier analysis showed that both HFREF and HFPEF patients with COPD had significantly reduced survival, as compared to those without COPD.

Conclusions: Among hospitalized HF patients, the presence of COPD is associated with higher all-cause and CV mortality, as well as with frequent readmission rates and reduced long-term survival.

P138 | BEDSIDE
Interactive impact of atrial fibrillation and heart failure on mortality in community-dwelling older adults: insights from a prospective population study
N.S. Bajaj1, V. Bhatia1, P. Deedwania1, N. Prabhu1, N. Nanda1, C. Morgan1, C. Adamopoulos2, W. Aronow4, G. Fonarow5, R. Morgan1, A. Rosengren1. 1University of Alabama Birmingham, Cardiology, Birmingham, United States of America; 2UCSF, Fresno, United States of America; 3Hospital Papageorgiou, Thessaloniki, Greece; 4New York Medical College, Valhalla, United States of America; 5University of California Los Angeles, Los Angeles, United States of America

Background: Atrial fibrillation (AF) and heart failure (HF), both common in older adults, are associated with poor outcomes. However, little is known about their interactive impact on outcomes among community-dwelling older adults.

Methods: We studied 5795 Medicare-eligible community-dwelling adults aged ≥65 years in the Cardiovascular Health Study (CHS). Baseline AF was diagnosed by ECG and baseline HF was adjudicated by a central events committee. We excluded 156 AF and 180 HF patients with history of AF but without ECG evidence of AF. Of the remaining 5673 participants, 219 had HF only, 116 had AF only, 39 had both and 5263 had neither. Cox-proportional hazards model were used to estimate age-sex-rate-adjusted HR (95% CI) for all-cause, cardiovascular (CV) and non-CV mortality during 13 years of follow-up, associated with HF, AF and both (vs. neither).

Results: Participants had a mean age 73 (±6) years, 58% were women and 15% were African American. All-cause mortality occurred in 43%, 66%, 74% and 85% of those with neither, AF only, HF only, and both, respectively. Compared to those with neither condition, age-sex-rate-adjusted HRs (95% CIs) for all-cause mortality for those with AF only, HF only, and both were 1.36 (1.08–1.72), 2.31 (1.97–2.71) and 3.04 (2.15–4.29), respectively (Fig. 1). Both AF and HF increased the risk of age-sex-rate-adjusted mortality; however, only HF (HR,1.72) was associated with higher non-CV mortality.

Conclusions: Among community-dwelling older adults, both AF and HF were associated with higher all-cause and CV mortality; however, only HF was associated with non-CV mortality.
P140 | BEDSIDE

Right ventricular strain and dysynchrony assessment in arrhythmogenic right ventricular cardiomyopathy: a cardiac magnetic resonance feature-tracking study


Purpose: Cardiac magnetic resonance imaging (cMRI) represents the gold-standard non-invasive imaging technique for assessment of right ventricular (RV) function; however, analysis of regional dysfunction in arrhythmogenic right ventricular cardiomyopathy (ARVC) may be inadequate due to the complex contraction pattern of the RV. Aim of the present study was to determine the utility of RV strain and dysynchrony assessment using a novel feature-tracking MR software system and its incremental value over conventional cMRI.

Methods: 32 consecutive patients with ARVC diagnosed according to the 2010 Task force criteria (45±13 years, 69% males) referred to cMRI were included. 32 patients with idiopathic right ventricular outflow tract (RVOT) arrhythmias and 32 control subjects, matched for age and gender to the ARVC group, were included for comparison purpose. cMRI using a 1.5 T esla scanner was performed to assess biventricular function; feature-tracking analysis was applied to assess regional and global RV strain and RV dysynchrony from the 4-chamber cine MR images, longitudinal systolic strain (SS) from basal, mid and apical RV free wall segments was measured and averaged as a measure of global RV function (global longitudinal strain, GLS). Standard deviation (SD) of time-to-peak strain (TPS) was calculated as a parameter of mechanical dispersion, using a 6 RV segment model (3 RV free wall and 3 septal segments).

Results: SS at RV basal (-22.1±1% vs. -35.1±15%; p<0.001), mid (-15.8% vs. -22.1±12% vs. -26.1±11%; p<0.001) and apical level (-14.1% vs. -22.1±12% vs. -25.1±11%; p<0.001) and RV GLS (-17.5% vs. -22.6±6% vs.-29.6±6%; p<0.001) were significantly lower and RV SD-TPS (145±90ms vs. 88±47ms vs. 50.2±33ms; p<0.001) was significantly higher among ARVC patients compared to RVOT patients and controls. Except for RV basilar free wall SS, differences remained significant even when considering only ARVC patients with RV ejection fraction (EF) ≥ 50% or without wall motion abnormalities. At ROC curve analysis, RV GLS ≥ -23.19% and RV SD-TPS ≥ -113.13ms had the highest sensitivity and specificity for identification of patients with ARVC (91% and 75% and 95% and 95%, respectively). When these cut-off values were assessed, RV GLS and RV SD-TPS allowed correct identification of 14 out of 17 (82%) and 11 out of 17 (65%) ARVC patients with RV ejection fraction <50% respectively.

Conclusion: Strain analysis by feature-tracking MR helps to objectively quantify global and regional RV dysfunction and RV dysynchrony in ARVC patients and provides incremental value over conventional cMRI.

P141 | BEDSIDE

Clinically isolated cardiac sarcoidosis

R. Kendall, J. Lehtonen, M. Kupari. Helsinki University Central Hospital, Department of Medicine, Division of Cardiology, Helsinki, Finland

Purpose: Sarcoidosis is a systemic disease, which can be clinically confined to the heart. The aim of this study was to evaluate the differences between clinically isolated cardiac sarcoidosis (CS) and CS associated with manifest extracardiac disease.

Methods: Our study involves 110 patients (age 51±9 years, 65% females) with histologically confirmed CS identified between 1988 and 2013. Their clinical characteristics and co-morbidities were determined. Clinical cardiac events during follow-up (median, 61 months) were analyzed in retrospect.

Results: At presentation, 71 of 110 patients (65%) had clinically isolated CS defined as cardiac involvement with neither past history nor any signs or symptoms of extracardiac sarcoidosis by clinical examination, routine blood tests and plain chest x-rays. The remaining 39 patients (35%) had CS associated with previously diagnosed or clinically manifest extracardiac sarcoidosis. Patients with isolated CS presented more often with atrioventricular block (48% vs 36%) and ventricular arrhythmias (38% vs 23%). The proportion of females was higher in isolated CS (75% vs 46%, p<0.003) but there was no age difference. Isolated CS was also associated with more extensive left ventricular involvement as evidenced by more frequent systolic dysfunction (ejection fraction <50%) at echocardiography (55% vs 33%, p<0.003) and more late enhancement at magnetic resonance imaging (95% vs 62%, p<0.002). Circulating concentrations of angiotensin converting enzyme and lysozyme were lower in isolated CS (p=0.005 and p=0.016, respectively) as was urinary calcium excretion (p=0.029). More patients with isolated CS were diagnosed only at autopsies or transplantation (77% vs 1/3). Survival from first heart failure event for patients free of transplanted organ was 97% in isolated CS vs in CS associated with manifest extracardiac disease (log rank p<0.009).

Conclusions: In clinical practice, CS manifests as a disease isolated to the heart in two thirds of patients. This phenotype is more common in women and associated with more extensive myocardial involvement at diagnosis. Isolated CS may escape detection until death or transplantation and is therefore associated with poorer outcome from symptom onset.

CARDIOMYOPATHIES: GENETICS, ARRHYTHMIA AND RISK STRATIFICATION

P140 | BEDSIDE

Right ventricular strain and dysynchrony assessment in arrhythmogenic right ventricular cardiomyopathy: a cardiac magnetic resonance feature-tracking study


Purpose: Cardiac magnetic resonance imaging (cMRI) represents the gold-standard non-invasive imaging technique for assessment of right ventricular (RV) function; however, analysis of regional dysfunction in arrhythmogenic right ventricular cardiomyopathy (ARVC) may be inadequate due to the complex contraction pattern of the RV. Aim of the present study was to determine the utility of RV strain and dysynchrony assessment using a novel feature-tracking MR software system and its incremental value over conventional cMRI.

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Results: SS at RV basal (-22.1±1% vs. -35.1±15%; p<0.001), mid (-15.8% vs. -22.1±12% vs. -26.1±11%; p<0.001) and apical level (-14.1% vs. -22.1±12% vs. -25.1±11%; p<0.001) and RV GLS (-17.5% vs. -22.6±6% vs.-29.6±6%; p<0.001) were significantly lower and RV SD-TPS (145±90ms vs. 88±47ms vs. 50.2±33ms; p<0.001) was significantly higher among ARVC patients compared to RVOT patients and controls. Except for RV basilar free wall SS, differences remained significant even when considering only ARVC patients with RV ejection fraction (EF) ≥ 50% or without wall motion abnormalities. At ROC curve analysis, RV GLS ≥ -23.19% and RV SD-TPS ≥ -113.13ms had the highest sensitivity and specificity for identification of patients with ARVC (91% and 75% and 95% and 95%, respectively). When these cut-off values were assessed, RV GLS and RV SD-TPS allowed correct identification of 14 out of 17 (82%) and 11 out of 17 (65%) ARVC patients with RV ejection fraction <50% respectively.

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P141 | BEDSIDE

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R. Kendall, J. Lehtonen, M. Kupari. Helsinki University Central Hospital, Department of Medicine, Division of Cardiology, Helsinki, Finland

Purpose: Sarcoidosis is a systemic disease, which can be clinically confined to the heart. The aim of this study was to evaluate the differences between clinically isolated cardiac sarcoidosis (CS) and CS associated with manifest extracardiac disease.

Methods: Our study involves 110 patients (age 51±9 years, 65% females) with histologically confirmed CS identified between 1988 and 2013. Their clinical characteristics and co-morbidities were determined. Clinical cardiac events during follow-up (median, 61 months) were analyzed in retrospect.

Results: At presentation, 71 of 110 patients (65%) had clinically isolated CS defined as cardiac involvement with neither past history nor any signs or symptoms of extracardiac sarcoidosis by clinical examination, routine blood tests and plain chest x-rays. The remaining 39 patients (35%) had CS associated with previously diagnosed or clinically manifest extracardiac sarcoidosis. Patients with isolated CS presented more often with atrioventricular block (48% vs 36%) and ventricular arrhythmias (38% vs 23%). The proportion of females was higher in isolated CS (75% vs 46%, p<0.003) but there was no age difference. Isolated CS was also associated with more extensive left ventricular involvement as evidenced by more frequent systolic dysfunction (ejection fraction <50%) at echocardiography (55% vs 33%, p<0.003) and more late enhancement at magnetic resonance imaging (95% vs 62%, p<0.002). Circulating concentrations of angiotensin converting enzyme and lysozyme were lower in isolated CS (p=0.005 and p=0.016, respectively) as was urinary calcium excretion (p=0.029). More patients with isolated CS were diagnosed only at autopsies or transplantation (77% vs 1/3). Survival from first heart failure event for patients free of transplanted organ was 97% in isolated CS vs in CS associated with manifest extracardiac disease (log rank p<0.009).

Conclusions: In clinical practice, CS manifests as a disease isolated to the heart in two thirds of patients. This phenotype is more common in women and associated with more extensive myocardial involvement at diagnosis. Isolated CS may escape detection until death or transplantation and is therefore associated with poorer outcome from symptom onset.
P143 | BEDSIDE
Preclinical identification of TTR-related amyloidosis (hereditary and wild type) with 99mTc-DPD scintigraphy: a cohort study of 12400 subjects
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Purpose: We have previously shown that 99mTc-3,3-diphenyl-1,2,3-propionic acid (99mTc-DPD) scintigraphy has a high affinity for TTR-infiltrated myocardium, allowing an accurate diagnosis of both mutant and wild-type cardiac amyloidosis. The potential role of this method as a preclinical screening tool has not yet been evaluated. This study aimed to evaluate prevalence and phenotypic characteristics of myocardial uptake among patients who underwent scintigraphy for oncologic or rheumatologic reasons.

Methods: We retrospectively analysed all DPD scintigraphies performed between 2008 and May 2013 in outpatients referred to our Nuclear Medicine Unit for oncologic or rheumatologic reasons and assessed clinical and instrumental details of patients with incidental myocardial tracer uptake.

Results: Incidental myocardial uptake was detected in 45 subjects (0.36%): 28 males (62%), median age 81 [77-84] prevalence. was higher among men and increased progressively with age: age <60, 0 patients; age 61-70, 4 men and 4 women; age 71-80, 18% of men and women 16%. Fourteen of the 45 patients agreed to undergo a cardiological evaluation. Among these, 11 (79%) were males with a median age of 82 [70 – 88] years. Four were symptomatic for dyspnea (NYHA II). One patient had a pace-maker. Cardiac gene had been previously diagnosed in 3 cases. None of them had overt neurologic symptoms. ECG was abnormal in all cases, showing atrial fibrillation in 4 patients, left anterior hemiblock in 2, isolated ST-T abnormalities in 4, abnormal Q waves in 3 and low QRS voltage in 1 case. Echocardiographically, increased left ventricular (LV) wall thickness was detected in all patients (LV wall thickness 14 [1Q 13-15] mm). LV “hypertrophy” was completely unexplained by hypertension or valvular heart disease in 10 cases and was out of proportion in the remaining 4. Genetic analysis was performed in 6 cases and documented an increased TTR mutation in a single patient. Endomyocardial biopsy was performed in the 5 patients in which no mutation was found and detected TTR-related myocardial amyloid infiltration in all. These patients received a final diagnosis of wild-type TTR-related amyloidotic cardiomyopathy (Senile Systemic Amyloidosis, SSM).

Conclusions: DPD scintigraphy appears to be specific for a preclinical identification of patients affected by TTR-related amyloidotic cardiomyopathy (mainly the form related to the deposition of wild-type TTR) and can be useful for a non-invasive screening of subjects at risk for this disease.

P144 | BENCH
Gene-specific increase in energetic cost of contraction in hypertrophic cardiomyopathy caused by thick filament mutations: in vitro and in vivo assessment of cardiac efficiency
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Purpose: Disease mechanisms regarding hypertrophic cardiomyopathy (HCM) are largely unknown and disease onset varies. Sarcromere mutations may induce energy depletion for which until now there is no direct evidence at sarcomere level in human HCM. This study investigated if mutations in genes encoding myosin binding protein C (MYBPC3) and myosin heavy chain (MYH7) underlie changes in energetic cost of contraction in human HCM disease development.

Methods: Energetic cost of contraction was studied in vitro by measurements of force development and ATP utilization in cardiac muscle strips from 26 matched HCM patients (11 MYBPC3mut, 9 MYH7mut, 6 sarcomere mutation-negative, MVA).

Results: Energetic cost of contraction was significantly lower in MYH7mut and MYBPC3mut carriers compared to controls, while MVO2 did not differ. As a result, MEE was significantly lower in MYH7mut and MYBPC3mut carriers compared to controls, showing the lowest efficiency in MYH7mut carriers (30±5 versus 37±7 versus 49±6%, respectively; p<0.05, MYH7mut vs other groups)

Conclusion: This study provides direct evidence that sarcromere mutations perturb energetic cost of cardiac contraction. Gene-specific severity of cardiac abnormalities may underlie differences in disease onset and suggests that early initiation of metabolic treatment may be beneficial in particular in MYH7mut carriers.

P145 | BEDSIDE
Risk stratification for prophylactic implantation of implantable cardiac defibrillator in non-compaction cardiomyopathy. Single centre experience
Purpose: ACC/AHA/HRS 2012 guidelines recommended ICD implantation (class Ib-C) for patients (pts) with Non-Compaction Cardiomyopathy (NCC) to reduce the risk of sudden cardiac death (SCD). NCC has a wide spectrum of presentation and variable outcomes. Therefore, it seems inappropriate to issue a general recommendation for primary prevention of SCD. The aim of the study was to describe the outcome of pts with NCC according to some selected risk-stratification criteria to decide ICD primary prevention (PP) implantation.

Methods: From November 1997 to January 2014, 100 pts with NCC and without any previous SCD or VT/VF were analyzed. Mean age was 43±17 years (64% symptomatic). Eighty pts had LVEF<30%, 36% had LVEF<30% and NYHA class II-II or >2 of the following risk factors: family history of SCD (FH-SCD), syncope and NSVT were considered high risk factors. Pts without heart failure (HF) or >2 risk factors were considered de low risk group.

Results: I. High Risk Group (58 pts): Forty pts (69%) received an ICD: Mean age was 48±16 years (28 men), mean LVEF was 31±11%, 28 pts (70%) had LVEF<30%, 5 (12.5%) LVEF<35% + NYHA FC II-II, 7 pts (17.5%) had >2 risk factors (4 FH-SCD, 2 Syncope+NSVT and 1 FH-SCD+Syncope). During a mean follow-up of 62.1±33 months no pts had SCD, 2 pts (5%) died due to sepsis and 1 (2.5%) underwent heart transplant (HT). Eight pts (20%) had appropriate ICD therapies. Eighteen pts who fulfilled the risk stratification criteria did not receive an ICD due to end-stage HF (7 pts with mean LVEF 21±11 and NYHA FC III-IV underwent HT and 5 with mean LVEF 15±5 and NYHA FC IV died due to progressive HF waiting HT) or comorbidities (6 pts had severe renal dysfunction). II. Low Risk Group (42 pts): No pts were implanted with an ICD. Mean age was 40±15 years (29 men). Mean LVEF was 53±10%, 41 pts (97.6%) had NYHA FC I, 1 pts NYHA FC II, 2 NSVT and 2 syncope. During a mean follow up of 28±25 months, there was no death or HT.

Conclusions: According to the selected risk-stratification criteria to decide ICD PP implantation, in our single centre experience, the low risk group showed a good outcome with no arrhythmic death. The high risk group with ICD had a similar rate of appropriate therapies that those reported in trials about ischemic or non-ischemic cardiomyopathy. This registry suggests that pts with NCC might be stratified for prophylactic implantation of ICD.

P146 | BEDSIDE
Clinical, instrumental and prognostic characterization of arrhythmogenic dilated cardiomyopathy
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Background: Arrhythmogenic Dilated Cardiomyopathy (dCM) is a variant of Dilated Cardiomyopathy (DCM) characterized by a particular arrhythmogenic profile, with frequent ventricular arrhythmias, often malignant and life threatening. The purpose of this study was to set specific diagnostic criteria of dCM and describe its prevalence, phenotype and natural history as compared to DCM and to identify its prognostic role on sudden death (SD) and major ventricular arrhythmias (MVA).

Methods: From February 1979 to November 2012, we studied 324 out of 469 DCM patients enrolled in the Familial Cardiomyopathy Registry with available data for evaluation of dCM. Criteria for dCM were, alternatively, history of documented arrhythmic death (excluding SCD)/heart transplant respectively. A subgroup of patients was tested for DCM genes (LMNA, MYH6, MYH7, MYBPC3, TNN1, TTN, SCN5A). Primary and secondary endpoints were SD/MVA and death (excluding SCD or VT/VF) (primary endpoint), VT/VF (secondary endpoint). A group of patients was followed for mean age 43±17 years (64% symptomatic). Presence of syncope or NSVT and were appropriate therapies. Eighteen pts who fulfilled the risk stratification criteria did not receive an ICD due to end-stage HF (7 pts with mean LVEF 21±11 and NYHA FC III-IV underwent HT and 5 with mean LVEF 15±5 and NYHA FC IV died due to progressive HF waiting HT) or comorbidities (6 pts had severe renal dysfunction). Eighty pts had LVEF<30%, 36% had LVEF<30% + NYHA FC II-II, 7 pts (17.5%) had >2 risk factors (4 FH-SCD, 2 Syncope+NSVT and 1 FH-SCD+Syncope). During a mean follow-up of 28±25 months, there was no death or HT.

Conclusions: According to the selected risk-stratification criteria to decide ICD PP implantation, in our single centre experience, the low risk group showed a good outcome with no arrhythmic death. The high risk group with ICD had a similar rate of appropriate therapies that those reported in trials about ischemic or non-ischemic cardiomyopathy. This registry suggests that pts with NCC might be stratified for prophylactic implantation of ICD.
ANTIPLATELET THERAPY AND CLINICAL OUTCOMES

P147 | BEDSIDE
Dual antiplatelet therapy discontinuation after coronary stenting and the risk of short-term cardiac adverse events: observation from CREDO-Kyoto 2 investigators.

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Purpose: To evaluate the short-term risk of antiplatelet therapy discontinuation after coronary stenting.

Methods: CREDO-Kyoto Registry Cohort-2 is a multicenter registry in Japan enrolling consecutive 15939 patients undergoing first coronary revascularization procedures from January 2005 to December 2007. Among them, 3315 patients who underwent coronary stenting implantation were eligible to evaluate the first discontinuation of dual antiplatelet therapy. End point of this study was major adverse cardiac event (MACE) including cardiac death, definite or probable stent thrombosis and spontaneous myocardial infarction within 30 days after drug discontinuation. The risk difference related with timing, drug pattern, situation or alternative heparin use was analyzed by Cox proportional hazard model. Situation of discontinuation was categorized into 7 groups as follows; planned and doctor-indicated, operation or invasive examination, bleeding, drug side effect, problematic compliance, other cause and unknown reason.

Results: 25 patients (0.75%) faced MACE within 30 days after drug discontinuation. Compared with discontinuation beyond 1 year, discontinuation within 1 month was significantly hazardous (HR 4.68, 95%CI 1.72-12.73, P=0.003) but discontinuation between 1 month and 6 month was not (HR 1.03, 95%CI 0.31-3.10, P=0.955). Compared with discontinuation of ticagrelor only, discontinuation of both acetylsalicylic acid and ticagrelor was significantly hazardous (HR 13.331, 95%CI 5.04-45.83, P<0.001). Compared with planned discontinuation, discontinuation related with operation or invasive examination (HR 6.96, 95%CI 1.68-46.68, P<0.007) and with other cause (HR 111.1, 29.82-717.94, P<0.001) were significantly hazardous. The majority of the other cause was difficulty of taking oral medication or drug discontinuation related with severe or end-stage comorbidities. Alternative hepatic use was not related with significant effect (HR 0.68, 95%CI 0.43-9.03, P=0.243). Multivariate cox regression model showed significantly higher HR in discontinuation within 1 month, discontinuation of both acetylsalicylic acid and ticagrelor and discontinuation for severe comorbidities even after adjustment of some clinical or procedural backgrounds.

Conclusions: Early discontinuation of dual antiplatelet therapy or discontinuation of both drugs is significantly harmful. Hazard of discontinuation for other treatment is not independent and strongly influenced by severe comorbidities.

P148 | BEDSIDE
Incidence and predictors of haemorrhagic stroke in a cohort of patients receiving acetylsalicylic acid for secondary prevention of cardiovascular events

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Purpose: Antithrombotic drugs have been reported to increase the risk of haemorrhagic stroke (HS). Here, we report data from a retrospective study assessing the incidence and predictors of HS in a cohort of patients receiving low-dose acetylsalicylic acid (ASA) for secondary prevention of cardiovascular (CV) events.

Methods: The Health Improvement Network (THIN), a UK primary care database, was used to identify a cohort (N=36,775) of first-time users (aged 50–84 years) of low-dose ASA (75–300 mg/day) for secondary prevention of CV events (cerebrovascular disease, n=11,764; ischaemic heart disease [IHD], n=15,506; myocardial infarction [MI], n=8790; unstable angina, n=715) during 2000–2007. Patients were followed up from the date of first ASA prescription (start date) until the occurrence of HS, cancer or alcohol abuse, reaching 85 years of age, or date of last data collection, or study end (30 June 2011). The incidence of HS was calculated, and stratified by ASA use and by a retrospective case-control analysis that included only current ASA users (77 HS cases; 760 controls) was performed to determine risk factors for HS during ASA use. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated using unconditional logistic regression with full model analysis.

Results: In total, 117 cases of HS were identified, resulting in a crude incidence rate of 5.7 cases per 10,000 person-years of follow-up. The overall incidence among current ASA users was 4.9 cases per 10,000 person-years, and 7.6, 3.2 and 2.7 cases per 10,000 person-years for the ASA indications of cerebrovascular disease, IHD and MI, respectively. There was an increased risk of HS among current ASA users with: a history of HS (OR: 4.84; 95%CI: 1.48–15.88); a body mass index >20 (OR: 6.84; 95%CI: 2.53–18.50); a history of blood dyscrasia (OR: 13.22; 95%CI: 1.94–90.86); atrial fibrillation (AF) when starting ASA (OR: 4.03; 95%CI: 1.53–10.62); exposure to warfarin (OR: 23.42; 95%CI: 4.89–112.10); and hypertensive/antihypertensive drug use (OR: 2.67; 95%CI: 1.17–6.05). Patients taking ASA for cerebrovascular conditions had more than double the risk of HS (OR: 2.70; 95%CI: 1.45–5.04), compared with those treated for IHD. Patients taking ASA for cerebrovascular conditions had double the risk of HS compared with those treated for IHD. Predictors of HS in this patient cohort included a history of HS, AF, warfarin use and hypertensive/antihypertensive drug use.

P149 | BEDSIDE
Bleeding rates in patients with acute coronary syndromes: safety profile of prasugrel and clopidogrel in the prospective swiss acs cohort

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Purpose: To assess 30-days bleeding and major adverse cardiovascular event (MACE) rates associated with prasugrel and clopidogrel use in a cohort of consecutive patients with acute coronary syndromes (ACS).

Methods and results: Between 2009 and 2012, 2286 patients invasively managed for ACS were enrolled in the multicenter Swiss ACS Cohort comprising patients in the Swiss National Fund Special Programme University Medicine SPUM-ACS trial (clinical trial number NCT01000701) and patients enrolled at the Swiss Centers in the COMFORTABLE AMI trial (clinical trial number NCT00962416). Among these, 2148 patients received either prasugrel or clopidogrel according to current guidelines. Patients with ST-elevation myocardial infarction preferably received prasugrel, while those with a history of stroke or transient ischaemic attack [TIA], age >75 years, or weight <60 kg received clopidogrel or reduced dose of prasugrel to comply with the prasugrel label. Overall bleeding at 30 days (adjudicated events as of 11/2013) was less common in patients receiving prasugrel compared with clopidogrel (adjusted HR 0.50, 95% CI 0.28-0.87, p=0.015). This was associated with multiple potential confounding factors assessed by the TIMI, GUSTO and BARC classifications. Clinically relevant bleedings at 30 days, defined as the composite of BARC type 3, 4 or 5 bleeding events, occurred in 2.4% of patients (18/756) on prasugrel and in 3.8% of patients (53/1392) on clopidogrel (adjusted HR 0.67, 95% CI 0.36-1.27, p=0.221). Stratified analyses in low- and high-risk patients yielded similar risk ratios. After adjusting for baseline variables, no differences in major adverse cardiovascular events were detectable between patients receiving prasugrel or clopidogrel.

Conclusions: In this prospective cohort of consecutive patients with ACS, the use of prasugrel according to current guidelines, i.e. in patients without cerebrovascular disease, old age or overweight, appears to be a safe alternative to clopidogrel.

P150 | BEDSIDE
Discontinuation of dual antiplatelet therapy over 12 months after acute coronary syndromes increases risk for adverse events in patients treated with pci: systematic review and meta-analysis

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Introduction: Duration of dual anti-platelet therapy (DAPT) following Acute Coronary Syndrome (ACS) hospitalization remains to be defined, both for patients...
treated medically and for those undergoing Percutaneous Coronary Intervention (PTCA).

**Methods:** PubMed, Cochrane and Google Scholar were systematically searched for studies including patients presenting with ACS, and treated either with DAPT longer than or shorter than 12 months. Multivariable-adjusted risk estimates for death and recurrent ACS with stopping DAPT after 12 months (odds ratios [OR] 95% confidence intervals [CI]) were pooled after logarithmic transformation according to random-effect models with inverse-variance weighting.

**Results:** 5 studies with 49,586 patients were included. Median age was 68 (64-75) years, 60% (57-75) of males. Myocardial infarction (MI) represented the admission diagnosis for 88% (60-100) of the patients, and 66% (50-74) were treated with stenting. After a follow up of 2.1 years (1.5-2.7), 40% (35-46) still on DAPT after 12 months and the rates of death or recurrent ACS were 16.8 (14.5-17.0). Risk of adverse events for patients stopping DAPT after 1 year was significantly increased (OR=1.19 [1.07-1.32]) for those receiving stents, but not for patients managed medically (OR=1.13 [0.95-1.35]). The increased risk did not vary according to age, gender, myocardial infarction as admission diagnosis and kind of stent.

**Conclusion:** Interruption of DAPT over 12 months after ACS increases the risk of adverse events for patients treated with PTCA, but not for those managed conservatively, independently from baseline features and admission diagnosis. This hypothesis generating finding should be tested in randomized controlled trials.

P151 | BEDSIDE
Impact of chronic kidney disease on long-term cardiovascular outcomes in medically managed patients with acute coronary syndromes: insights from the TRILOGYACS trial

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**Purpose:** Chronic kidney disease (CKD) is associated with increased risk of ischemic and bleeding events in ACS patients, but the relationship of CKD stages with long-term cardiovascular outcomes in medically managed ACS patients and the influence of more potent antiplatelet therapies on ischemic and bleeding risks remain unclear.

**Methods:** Of 98,536 medically managed ACS patients enrolled in TRILOGY ACS, 8953 had baseline serum creatinine levels to estimate creatinine clearance (CrCl) (Cockcroft-Gault). Patients were classed by CKD stage: CKD 1-2 (CrCl ≥60mL/min), CKD 3 (CrCl 30-60 mL/min), or CKD 4-5 (CrCl <30 mL/min). Kaplan-Meier (KM) event rates at 30 mos were evaluated for the primary composite (cardiovascular death/MI/stroke), individual component endpoints, and TIMI major bleeding by CKD stage and treatment allocation within each stage. Adjusted HRs (95% CI) for CKD 3 and for CKD 4-5 vs CKD 1-2 were estimated.

**Results:** The majority of patients were CKD stage 1-2 (n=6029), followed by CKD 3 (n=2569) and CKD 4-5 (n=339). Patients in more severe CKD stages were older, more often female, had lower body weight, and had higher baseline risk features. KM event rates (95% CI) increased sharply with CKD stage for all ischemic and bleeding endpoints; no significant differences were observed with prasugrel vs clopidogrel (Table). Risk of the primary composite remained significantly higher in more severe CKD stages after adjustment (CKD 3 vs CKD 1-2: HR=1.26 [95% CI, 1.09-1.46]; CKD 4-5 vs CKD 1-2: HR=1.60 [95% CI, 1.25-2.04]).

**Conclusions:** CKD is associated with markedly increased long-term risks of ischemic and bleeding complications in medically managed ACS patients, with minimal differences in event rates between treatment groups within CKD stages. Novel strategies are needed to mitigate the high risks of ischemic and bleeding complications associated with CKD.

P152 | BEDSIDE
The net clinical benefit of personalized antiplatelet therapy in patients undergoing percutaneous coronary intervention

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**Background and objective:** We aimed to investigate whether personalized antiplatelet treatment in patients with high on-treatment platelet reactivity (HTPR) improves clinical outcome.

**Methods:** This was a prospective study comparing personalized and non-personalized treatment with P2Y12 receptor blockers during a 12-month follow-up. Platelet reactivity was assessed by adenosine diphosphate induced aggregation using a multiple electrode aggregometry in 798 patients with coronary artery disease undergoing percutaneous coronary intervention. Patients with HTPR received or not up to four repeated loading doses of clopidogrel or prasugrel in the personalized treatment group (n=403), while no change in the treatment strategy was undertaken in patients in HTPR in the non-personalized treatment group (n=395).

**Results:** There were fewer major adverse cardiac events (MACE) in the personalized treatment group than in the non- personalized treatment group (7.4% vs. 15.3%; respectively; p<0.001). The multivariable Cox regression analysis showed that the relative risk to develop MACE was 51% lower in the personalized treatment group as compared to the non-personalized treatment group (OR=0.49; 95%CI: 0.31-0.77; p<0.001). Similarly, there was a clear net benefit of the personalized antiplatelet treatment over the non-personalized treatment (rate of ischemic and bleeding events: 8.2% vs. 18.1%; respectively; OR=0.46; 95% CI: 0.29-0.70; p<0.001). Further analysis indicated that patients with aggregation values within the therapeutic window (21-49U) experienced the lowest event rates (stent thrombosis and major bleeding: 2.5%) as compared to poor responders (<50U: 5.4% or <10U: 15.2%).

**Conclusion:** Personalized antiplatelet treatment improved patients outcome without increasing bleeding complications compared to the non-personalized treatment during a 12-month follow-up.

P153 | BEDSIDE
Impact of new P2Y12 blockers on platelet reactivity and clinical outcomes after acute coronary syndrome: Insight from a large single center registry

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**Purpose:** We retrospectively studied the impact of new P2Y12 inhibitors (Prasugrel, Ticagrelor) introduction on platelet reactivity and clinical outcomes after Acute Coronary Syndrome (ACS) from a large single center registry.

**Methods:** Consecutive patients admitted for ACS since 2007 and discharged on dual antiplatelet therapy were enrolled. Biological response was assessed one month after discharge by PRI VASP and ADP-induced aggregation (%ADP). Patients were classified according to PRI VASP as Very low on-treatment platelet reactivity (VLTPR) (PRI VASP<10%), low on-treatment platelet reactivity (LTPR) (PRI VASP:20%-50%) and high on-treatment platelet reactivity HTPR (PRI VASP>50%). Ischemic and bleeding complications were reported.

**Results:** 1999 patients were analyzed, 605 before (March 2007-February 2010) and 1394 after introduction of new P2Y12 blockers (February 2010-August 2013). After introduction, we reported a significant lower PRI VASP values (38%±0.53 vs. 42%±0.81 p<0.001), %ADP aggregation (52%±4.0 vs. 54%±6.0 p=0.03) and HTPR incidence (22% versus 34% OR [95%CI]: 0.65 [0.53–0.80]; p<0.001). Conversely, incidence of VLTPR and LTPR were significantly higher after new P2Y12 inhibitors introduction: 6% versus 3% [OR [95%CI]: 2.0 [1.2–3.3]; p<0.01] and 19% versus 8% [OR [95%CI]: 2.8 [2.0–3.9]; p<0.001] respectively. Clinical follow-up confirmed biological findings with higher incidence of bleeding 10% versus 5% [OR [95%CI]: 2.1 [1.4–3.2]; p<0.01] and lower incidence of stent thrombosis 1.3% versus 3.3% [OR [95%CI]: 0.39 [0.20–0.73]; p<0.01] with new P2Y12 blockers.

**Conclusion:** New P2Y12 inhibitors introduction modified both platelet reactivity and clinical outcome of ACS patients, with higher rate of hyper responders and bleedings, and lower rate of non responders and thrombotic events.

**Figure 1.** Stent thrombosis and bleeding complications comparison before and after introduction of new P2Y12 inhibitors.
P154 | BENCH

Development and characterization of a long-term proliferation model for restenosis research

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Purpose: To produce a new in vitro test platform for restenosis research, suitable for long-term proliferation and migration studies in stented vessels.

Methods: Freshly, surgically excised segments of porcine coronary arteries were obtained for decellularization and then were reseeded with human coronary artery endothelial (HCAEC) and human coronary artery smooth muscle (HCASMC) cells for three months. Subsequently, bare metal stents (BMS, 4 mm diameter) and drug eluting stents (DES, 4 mm diameter), respectively, were implanted and the segments were reseeded with HCAEC and HCASMC for additionally up to three months. The stented segments were examined after 0 h, 2, 4, 6, 8 and 12 weeks, respectively, by histochemical (HE and EVG staining) and immunohistochemical characterization and the reseeded area before and after stent implantation were measured.

Results: By reseeding, cells formed a multiple of layers in the first three months. After stent implantation for 2, 4, 6, 8 and 12 weeks, respectively, the proliferation area was significantly smaller in the drug eluting stents, compared to bare metal stents (Fig. 1). Thereby, a maximum inhibition of cell growth could be observed in the first six weeks in the DES (70% ± 3.5%), whereas only a slightly cell decrease could be observed in the BMS over the whole time period (17% ± 2.3%). Detection with CD31 and alpha smooth muscle actin specific antibodies revealed that both, HCAEC and HCASMC proliferation were reduced in comparatively amounts in DES and BMS, respectively.

Conclusion: A new in vitro vessel model has been developed, which enables the quantification of cell type specific stent proliferation and therefore is suitable for long-term proliferation studies in stented vessels.

P155 | BEDSIDE

Non-focal restenosis and slow flow phenomenon after reintervention are not infrequent over 5 years after sirolimus-eluting stent implantation

S. Nishino1, N. Kuriyama1, Y. Koba1, T. Kimura1, H. Koiwaya1, S. Sagara1, N. Kuriyama2, T. Nakama1, K. Ashikaga1, A. Matsuyama1, Y. Shibata2, 1Miayzaki Medical Association Hospital, Miayzaki, Japan; 2Chiba University Graduate School of Medicine, Chiba, Japan

Purpose: This serial angiographic study evaluated angiographic patterns of restenosis after sirolimus-eluting stent (SES) implantation and the incidence of slow flow phenomenon during reintervention for SES restenosis.

Methods: Between May 2004 and October 2010, 2,657 patients with 3,832 lesions underwent SES implantation. Serial follow-up coronary angiographies were performed at 8-month, 2-year, and 5-year after the procedure. Restenosis were divided into 3 groups: early (<1 year), late (1 to 5 years), and very late (>5 years).

Results: See Table 1.

Conclusions: Focal restenosis is predominant <5 years after SES implantation. However, half of restenosis ≥5 years after SES implantation are non-focal. Further, slow flow phenomenon may be observed more frequently when reintervention for restenosis ≥5 years after SES implantation is performed.

Table 1. SES follow up data

<table>
<thead>
<tr>
<th>Follow up, n</th>
<th>Early</th>
<th>Late</th>
<th>Very Late</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow up, n</td>
<td>3147</td>
<td>2267</td>
<td>698</td>
<td></td>
</tr>
<tr>
<td>Restenosis, n</td>
<td>254 (7.1%)</td>
<td>336 (14.8%)</td>
<td>96 (13.8%)</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>167 (74.6%)</td>
<td>251 (74.7%)</td>
<td>49 (51.0%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>II</td>
<td>13 (5.8%)</td>
<td>31 (9.2%)</td>
<td>10 (10.4%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>18 (8.0%)</td>
<td>24 (7.1%)</td>
<td>26 (27.1%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>26 (11.6%)</td>
<td>30 (8.9%)</td>
<td>11 (11.5%)</td>
<td></td>
</tr>
<tr>
<td>TLR, n</td>
<td>129 (4.1%)</td>
<td>259 (11.4%)</td>
<td>55 (7.9%)</td>
<td></td>
</tr>
<tr>
<td>Reintervention, n</td>
<td>123 (3.9%)</td>
<td>299 (10.5%)</td>
<td>69 (9.9%)</td>
<td></td>
</tr>
<tr>
<td>Slow flow, n</td>
<td>6 (4.6%)</td>
<td>4 (1.7%)</td>
<td>5 (10.4%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

P156 | BEDSIDE

Optical coherence tomography characterization of in-stent restenosis: comparison between generations of drug eluting stent


Purpose: Characterization of neo-intimal tissue is essential to understand the pathophysiology of in-stent restenosis (ISR) after drug eluting stent (DES) implantation. Using optical coherence tomography (OCT), we compared the morphologic characteristics of ISR between first and second generation DES.

Methods: OCT was performed in 66 DES-ISR, defined as >50% angiographic diameter stenosis within the stented segment. Patients with ISR of first generation sirolimus-eluting stents (SES), paclitaxel eluting stents (PES) and second generation zotarolimus-eluting stents (ZES), everolimus-eluting stents (EES) and biolimus-eluting stents (BES) were enrolled. Quantitative and qualitative ISR tissue analysis was performed at 1-mm intervals along the entire stent, and categorized as homogeneous, heterogeneous and neoatherosclerosis. The presence of microvessels and peri-strut low intensity area (PSLIA) was determined in all ISR. Neoahterosclerosis was identified by lipid, calcium and thin-cap fibroatheroma (TCFA) like lesions. We compared the two DES generations at both early (-<1 year) and late (->1 year) follow-up.

Results: In second generation DES a heterogeneous pattern was prevalent both before than after 1 year (57.1% and 58.6% respectively). Neo-atherosclerosis was more common in the early period in first generation DES (19.4% vs 11.7%, p<0.01), but after one year was more prevalent in second generation DES (7.0% vs 19.3%, p<0.01). Similar prevalence of TCFAs were observed in both groups in all comparisons.

Conclusions: When ISR restenosis occurs in second generation DES, the current data suggest a different time course and different morphological characteristics from first generation. Future prospective studies should evaluate the relationship between ISR morphology, time course and clinical events.

P157 | BEDSIDE

Impact of neo-intimal hemorrhage on neoatherosclerotic change and development of neo-intimal formation after drug-eluting stent implantation


Purpose: Intraplaque hemorrhage has been associated with progression of atherosclerotic lesions and plaque destabilization in coronary artery. However, it is unclear whether neo-intimal hemorrhage is related to the degree and morphologic characteristics of neo-intimal formation after drug-eluting stent (DES) implantation.

Methods: Thirty-four histological cross-sections of 14 stented coronary segments (10 sirolimus-, 2 paclitaxel-, and 2 everolimus-eluting stents) from autopsy hearts were reviewed and analyzed. Neo-intimal hemorrhage was defined as extravasated red blood cells outside the vasculature within the in-stent neointima. The neo-intimal thickness (NIH) was measured at the site with maximum distance of neo-intima in each histological section. The presence of cholesterol clefs was evaluated as an index of neoatherosclerotic change. According to the duration of stent implantation, all histological sections were divided into two groups: early group (<3years, n=15) and late group (>3years, n=19).

Results: The incidence of neo-intimal hemorrhage was significantly higher in the late group as compared with the early group (68% vs. 27%, p<0.05). The aggregate of cholesterol clefs was also frequently identified in the late group than in
the early group (16% vs. 7%). Moreover, the NIH was significantly greater in the late group compared to the early group (253±1 vs. 449±203 μm, p < 0.05).

Conclusions: The higher prevalence of neointimal hemorrhage and cholesterol clefts aggregation, and the greater NIH were observed at the late phase after DES implantation as compared to the early phase. The neointimal hemorrhage and the cholesterol clefts may contribute to stimulate the development of atherosclerotic neointimal formation at the late phase after DES deployment.

P158 | BEDSIDE
The relationship of endothelial shear stress after stent implantation with subsequent in-stent neointimal hyperplasia and clinical outcomes due to in-stent restenosis
K. Shishido1, A. Antoniadi, S. Takahashi2, M. Tsuda3, M. Papafaklis4, I. Andreu5, A. Coskun6, S. Saito7, C. Feldman8, P. Stone9 on behalf of the PREDICTION Study. 1 Brigham and Women's Hospital, Cardiovascular Division, Vascular Profiling Laboratory, Boston, United States of America; 2 Shonan Kamakura General Hospital, Kamakura, Japan; 3 Hokkaido University, Sapporo, Japan; University of Ioannina, Ioannina, Greece

Purpose: Neointimal in-stent hyperplasia (ISH) occurs after percutaneous coronary interventions (PCI), and may cause in-stent restenosis (ISR) and adverse clinical events. ISH may develop in regions of low endothelial shear stress (ESS), but the relationship between low ESS and subsequent clinical events arising from ISR is unknown. In patients undergoing PCI at baseline, we assessed the association of immediate post-PCI ESS with the anatomic and clinical natural history outcomes.

Methods: We investigated the PREDICTION Study database with focus on stent outcomes: 3D coronary reconstruction by angiography & intravascular ultrasound was performed in 374 patients at baseline (BL) & 6-10 months later (FU). Each stented segment was divided into 10-mm segments, where we calculated the development post-PCI ESS at BL with computational fluid dynamics. At FU, we assessed ISH area as well as the occurrence of a clinically indicated subsequent PCI in the same stent locations.

Results: A total of 243 stents were analyzed: of these, 99 (40.7%) were bare-metal stents (BMS), 103 (42.4%) sirolimus-eluting stents (SES) and 41 (16.9%) everolimus-eluting stents (EES). Angiographic follow-up was performed in 374 patients at baseline (BL) & 6-10 months later (FU). Each stented segment was divided into 10-mm segments, where we calculated the development post-PCI ESS at BL with computational fluid dynamics. At FU, we assessed ISH area as well as the occurrence of a clinically indicated subsequent PCI in the same stent locations.

Conclusions: The magnitude of ISH after stent implantation is associated with preceding local low ESS in all stent types. Low ESS independently predicts subsequent PCI for ISR in BMS and SES, but not in ESS. ESS is a critical feature of stented lesions with high propensity to exhibit severe ISH and trigger symptoms requiring a repeat intervention.

P159 | BEDSIDE
Characterization of coronary restenotic lesions following everolimus bioabsorbable vascular scaffolding
1Hospital Universitario Dr. Negrin, Las Palmas de Gran Canaria, Spain; 2Hospital Universitario Reina Sofia, Cordoba, Spain

Purpose: Coronary restenosis after bioabsorbable vascular scaffold implantation (BVS) is becoming rare and there is little information on the characteristics of this type of lesion. This study evaluates the follow-up angiographic, 64-slices cardiac computed tomography and intracoronary image features of restenosis in lesions previously treated with BVS.

Methods: We studied 306 patients with coronary artery disease, who received 470 BVS to cover 394 lesions. The mean covered length was 23±11mm and the final minimal luminal diameter after BVS implantation was 2.8±1.1mm. Patients were followed by clinical and CT studies. After a mean follow up of 7±5 months, 10 patients were angiographically studied to treat restenosis in 11 lesions. The restenosis per lesion rate was 3%. The treated segment of these restenotic lesions was scanned either by IVUS (n=5) or by OCT (n=4), and several slices were obtained to analyze the restenosis pattern.

Results: The restenosis was located in the LAD in 8 patients (73%) and in the RCA in 2 patients (18%). In 10 out of 11 lesions the restenosis did not reproduce the morphology of the original lesion. The restenosis was focal (mean length 5.1±2.64 mm) in 9 instances, and diffuse (mean length 18±2.82 mm) in 2 lesions. The proximal border was affected in 5 cases and the distal border was never involved. Geometry of the remaining scaffold was always preserved and no evidence of fractures or recoil were detected. The intracoronary analysis of restenosis showed tissue growth as the main mechanism of restenosis, although when located at the border, it was a mixture of hyperplasia and vessel shrinking at this level. The mean percent of angiographic restenosis was 76±19% and the minimal lumen diameter was 0.69±0.28 mm. Restenosis was treated with a new BVS in two patients, with a DES in 7 patients and with balloon angioplasty in 2 patients.

Conclusions: Restenosis after BVS is rare (3%) and mainly produced by focal (81%) or diffuse (19%) hyperplasia. Proximal border is the preferred location of restenosis, which combines hyperplasia and adverse remodeling.

P160 | BEDSIDE
Prognostic role of restenosis in 10,004 patients undergoing routine control angiography after coronary stenting
S. Cassese1, R. Byrne1, S. Schulz1, P. Hoppman2, T. Ibrahim3, I. Ott1, M. Fusaro1, H. Schunkert1, K.-L. Laugwitz1, A. Kastrati1. 1German Heart Center of Munich, Cardiology, Munich, Germany; 2Hospital Rechts der Isar, Munich, Germany

Purpose: Routine control angiography is a valuable tool with high-sensitivity in detecting restenosis after coronary stenting. However, the prognostic role of restenosis is still controversial. We investigated the impact of restenosis on 4-year mortality in patients undergoing routine control angiography after coronary stenting.

Methods: All patients undergoing successful implantation of coronary stents for de novo lesions from 1998 to 2009 and follow-up angiography after 6 to 8 months at 2 centres were studied. Restenosis was defined as diameter stenosis >50% in the in-segment area at follow-up angiography. The primary outcome was 4-year mortality.

Results: This study included 10,004 patients with 15,004 treated lesions. Restenosis was detected in 2,643 (26.4%) patients. Overall, there were 702 deaths during follow-up. Of them, 218 deaths occurred among patients with restenosis and 484 deaths occurred among patients without restenosis (hazard ratio: 1.19, 95% confidence interval: 1.20 to 1.21; p=0.03). The Cox proportional hazards model adjusting for other variables identified the restenosis as an independent correlate of 4-year mortality (adjusted hazard ratio: 1.23, 95% confidence interval: 1.03 to 1.46; p=0.02).

Conclusions: In this large cohort of patients with routine control angiography after coronary stenting we demonstrated that restenosis is a strong predictor of 4-year mortality.

IMPROVING RISK PREDICTION MODELS

P161 | SPOTLIGHT
Laboratory-based versus non-laboratory-based model in prediction of cardiovascular disease risk in elderly subjects
K. Dhana, M.A. Ikram, A. Hofman, O.H. Franco, M. Kavousi. Erasmus Medical Center, Department of Epidemiology, Rotterdam, Netherlands

Background: Non-laboratory-based models replacing lipids with body mass index (BMI), have been proposed to predict cardiovascular disease (CVD) as accurately as laboratory-based models. In elderly, the ability of BMI as a predictor of CVD mortality among non-laboratory-based model and to compare the performance of this model to the laboratory-based model in our elderly population.

Methods: The study included 4983 subjects between 55-79 years free of CVD at baseline (BL) and 6-10 months later (FU). Each stented segment was divided into 10-mm segments, where we calculated the development post-PCI ESS at BL with computational fluid dynamics. At FU, we assessed ISH area as well as the occurrence of a clinically indicated subsequent PCI in the same stent locations.

Conclusions: The magnitude of ISH after stent implantation is associated with preceding local low ESS in all stent types. Low ESS independently predicts subsequent PCI for ISR in BMS and SES, but not in ESS. ESS is a critical feature of stented lesions with high propensity to exhibit severe ISH and trigger symptoms requiring a repeat intervention.

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most informative anthropometric eigenvectors. The performance of two models was evaluated by studying the discrimination, calibration, correlation, and risk agreement (proportion of the population equivalently characterized by both models as “high” or “low” risk).

Results: Over a median follow-up of 9.9 years, there were 288 and 265 ASCVD events among men and women respectively. In men, ABSI and WHR were significantly associated with the risk of ASCVD in the multivariable adjusted models, with ABSI being more informative than WHR. We therefore used ABSI to construct the non-laboratory-based model for men. Among men: discrimination of the laboratory-based model was better than the non-laboratory-based model (the c-statistic was 0.677 vs. 0.675); both models were on average well calibrated (14% observed ASCVD risk vs 15.4% and 15.2% predicted ASCVD risks by the laboratory- and non-laboratory-based models, respectively); correlation coefficient for the laboratory-based with the non-laboratory-based model was 0.87; and using the new threshold of 7.5% for 10-year ASCVD risk, 90.3% of men were equivalently characterized as “high” or “low” risk by both models. Among women, none of the anthropometric measurements were associated with risk of ASCVD in the multivariable adjusted models.

Conclusion: In an elderly population where the ability of BMI to predict CVD declines, a non-laboratory-based model, using ABSI instead of cholesterol measurements, could predict the risk of ASCVD as accurately as the laboratory-based model among men.

P162 | BEDSIDE
Predictive accuracy of the ESC SCORE in French general population
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Purpose: The assessment of cardiovascular risk is uniformly recommended as a decision-support for therapies aimed at preventing cardiovascular diseases. The aim of this study was to assess the predictive accuracy of the ESC SCORE in French general population.

Methods: Our analysis was based on the Third French MONICA Cross-sectional population-based survey (from South-Western, North-Eastern and Northern France), on cardiovascular risk factors (1995-1996) and on subjects consecutively referred for cardiovascular check-up to a Department of Preventive Cardiology (DPC) in a South-Western French University Hospital since 1995. Vital status was obtained 10 years after inclusion. The 10-year predicted risk of cardiovascular (CV) death was calculated using the SCORE equation for low-risk countries (algorithm with total cholesterol) and was compared to the 10-year observed risk of CV death.

Results: SCORE equation was applied in 6915 participants (n=3225 from MONICA-Central, n = 3690 from DPC) aged 35-64 (56% were men) and 56 CV deaths were obtained 10 years after inclusion. The 10-year predicted risk of cardiovascular CV death was calculated using the SCORE equation for low-risk countries (algorithm with total cholesterol) and was compared to the 10-year observed risk of CV death.

P163 | SPOTLIGHT
Excessive body weight can predict mortality from ischemic heart disease equally well as cholesterol: evidence from the prospective European EPIC study
M. Taghavi Azar Sharabani1, T.P. Debray2, E. Riboli3, M.R. Jarvelin1, P. Vines3 on behalf of the EPIC consortium. 1Imperial College London, London, United Kingdom; 2Julius Health Center - Julius Gezondheidscentra, Utrecht, Netherlands

Purpose: To develop and evaluate the predictive value of a Laboratory-Independent Risk Score (LIRS) for Ischemic Heart Disease (IHD) mortality. Although cholesterol, as a strong predictor, is commonly included in IHD risk models, LIRS, such as the World Health Organizations’ proposed risk chart for the Mediterranean Region, could be a practical and cost-effective screening approach in large populations.

Methods: We used the data from 7 centres of the European Prospective Investigation into Cancer (EPIC) cohort. We divided the study population temporally into two mutually exclusive sub-cohorts, including 105,161 subjects recruited before 1997 used for model development and 43,306 subjects recruited between 1997 and 2000, used for model validation. We employed multivariable Cox models to develop basic models with sex, age, smoking history, blood pressure, and diabetes. Subsequently, cholesterol and/or BMI and/or waist circumference were added to the basic model in order to compare their prognostic contributions. A comparison was also made between our models and the European Systematic Coronary Risk Evaluation (SCORE).

Results: The median follow-up for IHD mortality was 12 years. The discrimination (Harrell’s C-index) of cholesterol-inclusive models and LIRS were 0.84 vs. 0.85, respectively. LIRS also provided a better calibration and reclassification statistics (NRI=0.023) vs. (NRI=-0.027). The SCORE model yielded a C-index of 0.82 and a relatively poor calibration; however, the over-estimation of the risk by the SCORE (developed back in 2003) was expectedly consistent with the falling trend of IHD mortality in Western Europe.

Conclusions: Our population-based study of 148,467 subjects suggests that the risk of mortality from IHD can be safely measured by replacing cholesterol with anthropometry. Epidemiological, patho-physiological, and causal links between obesity and IHD explain significant prognostic contribution of anthropometry. The modern view recommends the reliance on the overall IHD risk and multiple risk factor assessment rather than hypercholesterolemia alone as a trigger for initiating therapy. Thus, clinical implications of our results are consistent with the modern view and demonstrate the adequacy of laboratory-independent risk assessment. Therefore, LIRS can be used not only as a cost-effective tool for IHD risk assessment in countries with very limited resources, but also in high-income countries as a preliminary mass screening tool to identify individuals at high risk of IHD who are suitable candidates for cholesterol measurement.

Table 1. HR stratified by sex, C-index, IDI and NRI

<table>
<thead>
<tr>
<th><em>Major ECG findings</em></th>
<th><em>Cox regression (HR) (95% CI)</em></th>
<th><em>Log(hsCRP)</em></th>
<th><em>Major ECG + Log(hsCRP)</em></th>
<th><em>SCORE + Log(Fibrinogen)</em></th>
<th><em>SCORE + Log(hsCRP)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Men</em></td>
<td>1.55 (1.72–0.075)</td>
<td>0.002</td>
<td>1.44 (1.11–1.86)</td>
<td>0.005</td>
<td>1.93 (1.93–1.93)</td>
</tr>
<tr>
<td><em>Women</em></td>
<td>1.51 (1.68–1.82)</td>
<td>0.001</td>
<td>1.44 (1.11–1.86)</td>
<td>0.005</td>
<td>1.93 (1.93–1.93)</td>
</tr>
</tbody>
</table>

**P-values**.
findings, heart rate and the two inflammatory risk markers, high sensitive CRP (hsCRP) and fibrinogen.

Method: We followed 8,463 healthy individuals without prior history of CVD from the Copenhagen City Heart Study. During a median follow-up period of 18 years, 292 men and 371 women died of CVD. Major abnormal ECG findings were coded according to the Minnesota Code and were defined as any of the following: Q-QS wave abnormalities; left ventricular hypertrophy; Wolff-Parkinson White syndrome; complete bundle branch block or intraventricular block; atrial fibrillation or atrial flutter and major S-T changes. hsCRP and fibrinogen were log transformed.

Results: In sex-stratified Cox regression model with age as the underlying time scale including the traditional SCORE variables, major abnormal ECG findings, heart rate, hsCRP and fibrinogen predicted CVD in both men and women (Table 1). With respect to the corresponding C-indices, Integrated Discrimination Improvement (IDI) and Net Reclassification Index (NRI) using 10-years absolute risk of CVD death. Cut-off at 5% and 10% defined traditional SCORE risk groups.

Conclusions: Our results indicate that major abnormal ECG findings, heart rate, hsCRP and fibrinogen were all independently associated with CVD death. ECG-findings, hsCRP and fibrinogen all slightly improved IDI while heart rate slightly worsened IDI. All the investigated risk factors failed to improve NRI; however hsCRP improved the C-index.

P165 | BEDSIDE
Predictive value of different indices of blood pressure variability on cardiovascular mortality: data from the PAMELA study
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Introduction: Whether and to what extent blood pressure variability may provide information on cardiovascular prognosis and organ damage remains controversial. This may depend, among other factors, on the different variability indices used in the studies published so far. The present study was aimed at providing a vis-a-vis comparison of the value of different variability indices in predicting cardiovascular events as well as development of target organ damage.

Methods: In the PAMELA study was evaluated the variability (standard deviation, SD) among systolic blood pressure values measured during a single visit (IT), between visits (IF) and between home measurements (H). Weighted SD of 24-hour blood pressure (wSD) was also evaluated. These indices were then related with cardiovascular (CV) and all-cause mortality as well as with new-onset cardiac organ damage (LVH), diabetes mellitus (DM) and hypertension.

Results: With the exception of IT all the indices were associated with a greater risk of CV mortality (HR=1.036, P<0.01; HH=1.029, P=0.01; wSD:HR=1.229, P<0.001). After adjustment for age and gender, however, only wSD remained a significant predictor of CV mortality (HR=1.005, P<0.05). Similar results were observed for all-cause mortality. The multivariable analysis performed by stepwise selection showed that CV mortality was independently predicted by age, gender (males) and systolic office blood pressure, while all-cause mortality by age, gender (males) and wSD. After adjustment for confounders, the increase of wSD significantly augmented the 10-year risk of developing DM (HR=1.088, P=0.01) and all-cause death (hazard ratio = 1.45 per 10%BW decrease; 95% confidence interval: 1.16-1.81, P<0.001). Patients with 35.0-44.9%BW, 25.0-34.9%BW and <25.0%BW quadriceps strength had a 2.98-fold, 5.59-fold and 14.93-fold higher cardiovascular mortality risk, respectively, as compared with those with >50%BW (see Fig. 1).

Conclusion: A quadriceps strength of <45%BW is associated with a poor prognosis in patients with CAD.

P167 | BEDSIDE
Respiratory sinus arrhythmia as an outcome predictor in survivors of myocardial infarction
D. Simmerer, M. Dormasch, A. Mueller, K.L. Laugwitz, P. Barthel, G. Schmidt, Technical University of Munich, Klinikum rechts der Isar, I. Medical Department, Munich, Germany

Purpose: Respiratory sinus arrhythmia (RSA) is caused by the modulation of the sinoatrial node discharge frequency by the autonomic nervous system. Impaired autonomic function is associated with adverse outcome in cardiac patients. This study prospectively tested the association of respiratory sinus arrhythmia and mortality in survivors of acute myocardial infarction.

Methods: Consecutive patients (n=941, mean age 61 years, 19% female) presenting with acute myocardial infarction and sinus rhythm were enrolled between May 2000 and March 2005 and followed up until August 2010. The main study outcome was 5-year all-cause mortality. Patients underwent non-invasive 30-minute recordings of ECG and respiratory chest excursions. An analytical signal was constructed from the respiratory signal, ranging from -pi (beginning of inspiration) to +pi (end of expiration). The influence of expiration on RR intervals (RRI) was assessed by bivariate phase-rectified signal averaging (PRSA). Normal beats in recordings of ECG and respiratory chest excursions were used as anchor points. RSA_PRSA was quantified by Haar wavelet analysis. RSA_PRSA <0 was defined as abnormal.

Results: During the follow-up, 72 patients died. RSA_PRSA was normal in 621 (62%) and abnormal in 301 patients. Five-year mortality rates in these groups were 4.2% and 14.4%, respectively. Under univariable analysis, RSA_PRSA was a significant predictor of death (p<0.001) as were GRACE score (p<0.001), LVEF (p<0.001) and all-cause death (hazard ratio = 1.96 per 10%BW decrease; 95% confidence interval: 1.16-1.81, P<0.001). Patients with 50.0-59.9%BW, 40.0-49.9%BW and <40.0%BW quadriceps strength had a 2.98-fold, 5.59-fold and 14.93-fold higher cardiovascular mortality risk, respectively, as compared with those with >50%BW (see Fig. 1).

Conclusion: Respiratory sinus arrhythmia, quantified by bivariate PRSA from simultaneous ECG and respiration recordings, is an independent risk predictor in post-infarction patients.

AMBULATORY BLOOD PRESSURE MONITORING

P168 | BENCH
Outcome based threshold values for increased blood pressure variability. Data from dublin outcome study
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Background: Blood pressure (BP) variability (V) has independent prognostic relevance but outcome-based BPV thresholds for risk stratification are lacking. Aim of this analysis of Dublin Outcome Study data was to propose such thresholds for
several measures of short-term (24 hour) BPV, including new indices, devoid of interference from circadian BP variation.

Methods: The study included 10,500 untreated subjects (age 45.4±14.3, 47% male) assessed for hypertension and, in whom 24th ABPM was obtained at baseline. Threshold values for different BPV indices were defined with Youden method in relation to cardiovascular (CV) mortality (mean follow-up 8 years). Only diastolic BPV indices independently predicted outcome in this population and were thus considered: daytime standard deviation (daySD), weighted 24 h SD (wSD, time-weighted average of day and night BP SD), average real variability (AVR, mean of absolute differences between consecutive BP measures) and residual BPV (rBPV, i.e. BPV unexplained by two principal circadian cyclic components).

Results: All variables had similar areas under ROC curves for CV mortality (0.61-0.63). Optimal threshold values for daySD, wSD, ARV and rBPV were 9.43, 9.86, 9.02, and 7.72 mmHg, respectively. We propose, as more convenient, a cut-off of 10 mmHg for daySD and wSD, 9 mmHg for ARV and 8 mmHg for rBPV (roughly corresponding to 75th percentiles of distribution in study population). Figure shows Kaplan-Mayer curves for CV survival and hazard ratios associated with the above thresholds for day SD and wSD (unadjusted and adjusted for major confounders, including average BP).

Conclusions: We propose outcome-based threshold values for diastolic BPV estimates. Further studies are needed in order to validate these thresholds in other populations.

P169 | BEDSIDE
Correlates of isolated nocturnal hypertension and target organ damage in untreated hypertension

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Purpose: The correlation of nocturnal hypertension (NH) with subclinical target organ damage has not been clarified yet. The purpose of this study was to compare nocturnal hypertensive with normotensive subjects regarding preclinical indices of target organ damage in hypertension.

Methods: The study population consisted of 302 untreated essential hypertensives. In all participants, carotid-fermal pulse wave velocity (cf-PWV), flow mediated dilatation (FMD), intima-media thickness of carotid arteries (CIMT), augmentation index and ankle-brachial index were evaluated. Also, left ventricular mass index (LVMi) and E/A (the mean ratio of early and late diastolic tissue velocities) were assessed by echocardiography. We also assessed creatinine clearance by Cockroft-Gault formula, while serum cystatin-C levels were measured by ELISA.

Results: Based on the presence of NH (>120/70 mmHg), the population was divided into two groups: nocturnal normotensive (n=150) and nocturnal hypertensive (n=152), who did not differ in classical risk factors. Patients with NH were characterised by increased arterial cf-PWV (9.1±1.7 vs 8.4±1.5 m/sec, p<0.0001) and marginally decreased FMD values (5.1±3.4 vs 4.1±2.6, p=0.066). In addition, this group showed increased CIMT (0.77±0.18 vs 0.69±0.15 mm, p=0.016) compared to normotensive subjects, whereas no other significant differences were observed, regarding other vascular indices (p=NS for both). Notably, they also exhibited higher values of LVMi (88.1±22.9 vs 82.8±16.6 gr/m², p=0.043) and E/A (0.90±0.26 vs 0.88±0.43, p=0.030), respectively. However, the two groups did not differ with respect to renal function, based on creatinine clearance (p=0.689) and cystatin-C levels (p=0.283).

Conclusions: According to this study, the presence of nocturnal hypertension is accompanied by subclinical atherosclerosis, as well as structural and functional abnormalities of the left ventricle, without significant impairment of renal function in untreated hypertension.

P170 | BEDSIDE
Ambulatory blood pressure monitoring affects sleep quality and blood pressure

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Purpose: During nocturnal non-invasive ambulatory blood pressure monitoring (ABPM), inevitably an undesirable external stimulus due to pump noise and pressure produced by cuff inflation may affect the quality of sleep, influence the physiological nocturnal blood pressure fall and consequently affect dipping status. We assessed the hypothesis that blood pressure monitoring provokes awakenings may affect sleep quality, thus blood pressure and/or heart rate.

Methods: The study population consisted of 108 consecutive subjects with stage I-II essential hypertension (aged 54.9±8 years, 59 male, office BP=148/97 mm Hg). Participants were divided into two groups according to whether they underwent ambulatory blood pressure monitoring (group A, n=60), or not (group B, n=48). Repeated measurements of blood pressure were registered with non-invasive automatic blood pressure monitors (Spacealert 90207, Welch Allyn 6100S devices) every 20 min. Self-reported data regarding the quality of sleep, numbers and duration of arousal were obtained via standardized questionnaire.

Results: Group A compared to group B demonstrated a small but significant increase in the number of nocturnal awakenings (2.8 vs 1.2, p=0.045), although their duration did not significantly differ (p=NS). However, the two groups exhibited similar mean values of nocturnal blood pressure and heart rate (121/73 vs 119/71 mm Hg, 67 vs 65 beats/min, p=NS in both cases). The reported sleep quality did not differ between the two groups but both sleep quality and higher numbers of awakenings (>3) were associated with non-dipping status (p<0.05, in both cases).

Conclusions: Our findings indicate that even though ambulatory blood pressure monitoring affects indices monitoring, sleep disturbances, heart rate and evaluate night-time blood pressure profile and heart rate, without affecting sleep efficiency and quality. Sleep evaluation may be particularly useful in essential hypertension, as poor quality of nocturnal sleep was associated with non-dipping status.

P171 | BEDSIDE
The impact of asleip systolic blood pressure on cerebral white matter lesions in elderly hypertensive patients

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Purpose: Cerebral white matter lesions (WML) are highly prevalent in the elderly population and increase the risk of dementia and stroke. Noninvasive ambulatory blood pressure (ABP) monitoring suggests that high blood pressure (BP) is an important risk factor for WML; however, there is limited information regarding the relationship between ambulatory blood pressure (ABP) levels and WML volumes among elderly hypertensive patients with controlled office BP.

Methods: This cross-sectional study comprised 84 hypertensive patients aged between 65 and 75 years without symptomatic heart failure, ischemic heart disease, atrial fibrillation, stroke, or cognitive dysfunction. We obtained 24h ABP recordings and brain magnetic resonance imaging to quantify the volume of WML.

Results: Linear regression analysis revealed that office BP, HbA1c, LDL, HDL and TG were not associated with WML volume increases. Raised asleip systolic BP (p=0.039) and mean BP (p=0.042) were associated with greater WML volumes during ABP monitoring. There was a trend for smaller nocturnal declines in systolic blood pressure to be associated with increased WML. Higher asleip systolic BP was strongly associated with periventricular hyperintensities (p=0.045). To clarify the effect of asleip systolic BP on WML volume, we then classified patients into two systolic BP groups as follows: <125 mmHg (n=47) and ≥125 mmHg (n=37). Baseline characteristics were similar in both groups. However, WML volume was greater in the group with asleip systolic BP >125 mmHg than that in the ≤125 mmHg group (9.0±6.4 ml versus 4.1±4.3 ml, p=0.015).

Conclusions: Higher asleip systolic blood pressure levels may be observed to contribute greater WML volumes in elderly hypertensive patients. Control of asleip systolic blood pressure levels may be important to protect WML progression in elderly hypertensive patients.

P172 | BEDSIDE
Elevated morning blood pressure surge and uric acid: the deadly combination

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Elevated serum uric acid (SUA) both predicts and is associated with high blood pressure. Studies have shown that the early morning blood pressure surge (MBPS) is a risk factor for cardiovascular events (CVE) but the relationship with SUA is not well understood.

Methods: 821 hypertensive subjects underwent a 24-hour ambulatory blood pressure monitoring (ABPM) and were followed 40 months for major CVE.

Results: During this period, 103 (11.2%) events occurred.SUA was correlated with MBPS (r=0.29, p<0.05), with a significant trend between increasing quartiles of SUA acid level and increasing values of MBPS (p<0.0001). The subjects were classified in one of the four (SUAI/MBPS groups: High/High (5.54%, 51 subjects), Low/Low (8.58%, 79 subjects), High/High (31.5%, 286 subjects), or Low/Low (54.8%, 505 subjects). There were very few major CVEs events in the Low/Low category and in the other MBPS category although the small but significant highest in the High/High category, 15 (23.5%), p=0.0028. Patients in the highest quartile stratified by elevated MBPS and SUA level had a 3.55 odds of major CVEs compared to the lowest quartile.
P174 | BEDSIDE
Impact of gender on the association of epicardial fat thickness and circadian blood pressure variability in patients with essential hypertension
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Background: Epicardial fat thickness (EFT), an indicator of visceral obesity is an emerging cardiometabolic risk factor, and patients with obesity have an increased prevalence of the non-dipper blood pressure (BP) pattern. This study aimed to investigate the effects of gender on the association between EFT and circadian BP changes in patients with recently diagnosed essential hypertension (EH).

Methods: A total of 441 patients with EH (Male/female: 236/205 and mean age: 50.7±10.7 years) underwent office BP monitoring, 24-h ambulatory BP monitoring, laboratory measurements for cardiovascular risk factors and echocardiography. True EH was defined with ambulatory diagnosis, and obesity was defined when the body mass index was more than 25 kg/m2. EFT was averaged from the parasternal long axis and parasternal short axis echocardiographic images.

Results: Obese EH patients showed increased circadian BP profile with BP variability among the males (5.9±2.2 mmHg) and non-obese EH group (6.7±2.8 mmHg) among women, whereas EFT was not changed among the males (5.9±1.9 vs. 6.0±2.7 vs. 5.9±2.4 mm, p=0.937). Multivariate logistic regression analysis demonstrated that the 24 mean BP variability was associated with EFT (standardized β coefficient = 0.16, p=0.016) and BMI (standardized β coefficient=0.19, p=0.006) in female patients, but not in male.

Conclusions: The relationship of circadian BP variability, obesity and EFT was affected by gender in different manners. EFT may be a valuable parameter in the evaluation of BP severity and obesity in women than in men.

Table 1. Cox regression of major adverse cardiac event (MACE) on uric acid as a continuous variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.061 (1.041–1.081)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic (mm Hg)</td>
<td>1.342 (1.090–2.024)</td>
<td>0.1602</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.854 (1.874–4.346)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.741 (0.484–1.334)</td>
<td>0.1674</td>
</tr>
<tr>
<td>Smoker (yes)</td>
<td>1.479 (0.895–2.317)</td>
<td>0.0346</td>
</tr>
<tr>
<td>Previous aortic aneurysm</td>
<td>2.765 (1.217–6.281)</td>
<td>0.0151</td>
</tr>
<tr>
<td>Previous coronary artery disease</td>
<td>2.004 (1.099–3.656)</td>
<td>0.0234</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 25 kg/m2)</td>
<td>2.428 (1.039–5.690)</td>
<td>0.0436</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>0.975 (0.956–0.995)</td>
<td>0.0135</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>1.008 (1.002–1.014)</td>
<td>0.0065</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>0.999 (0.996–1.002)</td>
<td>0.4455</td>
</tr>
<tr>
<td>Systolic B/P (mm Hg)</td>
<td>1.020 (1.000–1.039)</td>
<td>0.0474</td>
</tr>
<tr>
<td>Uric acid</td>
<td>1.425 (1.184–1.715)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Conclusion: SUA is associated with the early MBPS and with development of new CVE.
corrected-sinus node recovery time (CSNRT) was prolonged in WT-STZ mice and IL-10KO mice treated with STZ injection (IL-10KO-STZ mice) compared to corresponding control mice (p <0.01 and p<0.001, respectively). Furthermore, programmed atrial extrastimuli induced AF more frequently in WT-STZ and IL-10KO-STZ mice than in corresponding control mice (43% vs. 0% and 86% vs. 14%, respectively, p <0.05 and p <0.01, respectively). 3) IL-10 administration significantly attenuated both prolongation of CSNRT and AF inducibility in WT-STZ and IL-10KO-STZ mice. 4) The atrial fibrosis in WT-STZ and IL-10KO-STZ mice was greater than in corresponding control mice (p <0.05 and p <0.01, respectively). 5) Immunohistochemical staining demonstrated that hyperpolarization-activated cyclic nucleotide-gated potassium channel 4 expression in sinoatrial node was depressed in WT-STZ and IL-10KO-STZ mice compared to corresponding control mice. 6) In cultured atrial fibroblasts and myocytes, high glucose-conditioned medium increased TGF-β1 protein expression and apoptotic cells (P <0.05). However, administration of IL-10 attenuated the TGF-β1 overexpression and the enhanced apoptosis (P <0.05).

Conclusions: Our results suggest that the decrease or deletion of IL-10 plays an important role in the development of hyperglycemia-induced SND and enhances vulnerability to AF in STZ-induced diabetic mice. The results also suggest IL-10 administration could be a novel therapeutic strategy to prevent those electrophysiological pathology caused by hyperglycemia.

**P177 | BENCH**

**Blocking CD44 attenuates atrial fibrillation and fibrosis via the STAT3 pathway**

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**Purpose:** Atrial fibrillation (AF) has been associated with atrial fibrosis. Inhibition of atrial fibrosis has been recognized as a plausible approach for AF prevention and therapy. This study is designed to evaluate the potential role of blocking CD44, a membrane protein known to control fibrosis, in suppressing AF and atrial fibrosis either in vitro or in transforming growth factor-β (TGF-β), a key mediator of atrial fibrosis, transgenic mice.

**Methods:** TGF-β transgenic mice were treated with anti-CD44 monoclonal antibody (mAb) or control IgG (300mg/week) for 8 weeks. Mice were then paced to analyze AF inducibility. Atria were harvested to assess fibrosis and the expression of CD44, STAT3, and matrix protein (collagen). Cultured rat atrial and ventricular fibroblasts were used to evaluate the in vitro relevance of in vivo findings.

**Results:** Anti-CD44 mAb-treated TGF-β transgenic mice had fewer collagen depositions, STAT3 phosphorylation, and nuclear translocation in their atria than IgG-treated control mice. Programmed stimulation triggered more sustained AF in control IgG-treated group (n=5/6) than in anti-CD44 mAb-treated mice (n=1/6) (P<0.01). In vitro, atrial fibroblasts exhibited a stronger response to TGF-β in CD44 expression and STAT3 phosphorylation than ventricular fibroblasts. Treatment of atrial fibroblasts with anti-CD44 mAb and mutated CD44 plasmids blocked TGF-β-induced collagen expression, STAT3 phosphorylation, and nuclear translocation. Furthermore, transfection of dominant negative STAT3 plasmid in atrial fibroblasts attenuated TGF-β-stimulated collagen expression.

**Conclusions:** CD44/STAT3-dependent pathway plays a crucial role in the pathogenesis of atrial fibrosis and AF. Blocking CD44-dependent signaling may be a feasible way for AF prevention or management.

**P178 | BENCH**

**Secreted phospholipase A2-IIA increases ROS accumulation and lysyl oxidase expression via EGFR transactivation in cardiac fibroblasts: a novel target in myocarditis**

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**Purpose:** Myocarditis is an inflammatory disease of the myocardium, and in some patients it progresses to dilated cardiomyopathy (DCM). Myocardial fibrosis and increased oxidative stress are pathogenic factors associated with these processes. Lysyl oxidase (LOX) is an enzyme that promotes cross-linking of collagen fibers, and increased expression of LOX is linked with fibrosis and cardiac dysfunction. Thus, LOX upregulation has been found in human DCM hearts. The proinflammatory protein secreted phospholipase A2-IIA (sPLA2-IIA) has been shown to play an important role in the pathophysiology of inflammatory diseases, including cardiovascular diseases. Even though sPLA2-IIA has been found up-regulated in some cardiac disorders, its role in myocardial dysfunction still remains unclear. Thus, this study aims to clarify the role of sPLA2-IIA in the pathogenesis of myocarditis, as well as to identify the signal transduction steps involved in its expression.

**Methods and results:** Experimental autoimmune myocarditis (EAM) was induced in BALB/c mice with a myocardiogenic peptide and sPLA2-IIA levels, oxidative stress and fibrosis were evaluated at days 21 and 65 post induction. Histological assessment of hearts showed presence of fibrosis (Masson’s trichrome stain) and elevated supereoxide production (DHE stain) in EAM mice whereas these effects were not detectable in cardiac tissue from healthy mice. sPLA2-IIA levels in serum and cardiac tissue, measured with a commercial ELISA, were also higher in EAM mice than in healthy controls. In vitro studies in adult rat cardiac fibroblasts (CFs) demonstrated that sPLA2-IIA promoted ROS accumulation and proliferation of cardiac cells in a dose dependent manner. Moreover, sPLA2-IIA treatment also up-regulated LOX protein expression in CFs. Molecular studies demonstrated that sPLA2-IIA induced EGFR phosphorylation and shedding of the membrane-anchored heparin-binding EGF-like growth factor (pro-HB-EGF) ectodomain, as well as a rapid phosphorylation of the classical survival proteins ERK, AKT, and P70S6K. We further demonstrated that the biological activities and signaling induced by sPLA2-IIA were abrogated in the presence of an EGFR inhibitor (47F), a matrix metalloproteinase inhibitor (GSM0001), an ADAM inhibitor (TAPI-1) and a HB-EGF neutralizing antibody.

**Conclusions:** Altogether, these results (i) highlight sPLA2-IIA as a mediator in the development cardiac dysfunction through its ability to induce CFs proliferation, ROS accumulation and LOX protein expression, and (ii) point to EGFR transactivation and HB-EGF release as a key mechanism that may underlie sPLA2-IIA biological actions.
Conclusions: Development of an important adjunct to biological heart valve replacement.

Influencing acute inflammation may ameliorate the adverse remodeling after acute myocardial infarction (AMI). Because the AMI patients with higher serum TN-C levels at the acute phase have worse long-term prognosis, TN-C is suspected to play important roles during the development of ventricular remodeling. However, the biological function of TN-C in myocardial infarction (MI) and subsequent ventricular remodeling during the chronic phase was not fully understood. Therefore, we investigated the role of TN-C during an acute inflammatory response after MI and subsequent ventricular remodeling during the chronic phase.

Methods: The 8 to 10 weeks old male wild type (WT) and TN-C knockout (KO) mice were divided into 4 groups of WT+Sham, KO+Sham, WT-MI and KO-MI. Echocardiographic evaluation were performed 4, 8 and 12 weeks after the operation, and then, mice were sacrificed for histological analysis. And, heart samples were taken on day 3, 5 and 7 after the operation for biochemical analysis to examine the acute inflammatory response after MI.

Results: During the chronic phase, 12 weeks after MI, the survival rate of both WT+MI (48.3%, 14 out of 29 mice) and KO+MI (55.6%, 15 out of 27 mice) groups had no significant difference. But Echocardiographic measurements showed the suppression of cardiac dilatation and the preservation of left ventricular (LV) systolic function in TN-C KO+MI group compared with WT+MI group (LV diastolic diameter: 5.45±0.57 mm, P=0.01, LV ejection fraction: 19.02±6.31%, 10.63±4.43%; p<0.001). The histological analysis showed that the interstitial fibrosis at border area, between intact and infarct area, was significantly decreased in the KO+MI group compared with WT+MI group (P=0.001). During the acute phase, Fluorescence activated cell sorting (FACS) analysis revealed that the diminished recruitment of CD45+, F4/80+, CD206+; anti-inflammatory M2 macrophages and the enhanced infiltration of CD45+, F4/80+, CD206+; anti-inflammatory M2 macrophages in the infarct myocardium of KO+MI group compared with WT+MI group on day 7 after MI and RT-PCR analysis showed that the expression of IL-10, an anti-inflammatory cytokine, was significantly higher in KO+MI group than WT+MI group.

Conclusion: TN-C aggravates the left ventricular remodeling after MI partly through the promotion of inflammatory response via the regulation of macrophage subsets during the acute phase.

P181 | BENCH

Tenascin-C promotes inflammatory response and aggravates left ventricular remodeling after myocardial infarction in mice

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Background: Tenascin-C (TN-C), an extracellular matrix glycoprotein, is transcriptionally induced by pro-inflammatory cytokines and pro-inflammatory mediators after acute myocardial infarction (AMI). Because the AMI patients with higher serum TN-C levels at the acute phase have worse long-term prognosis, TN-C is suspected to play important roles during the development of ventricular remodeling. However, the biological function of TN-C in myocardial infarction (MI) and subsequent ventricular remodeling during the chronic phase was not fully understood. Therefore, we investigated the role of TN-C during an acute inflammatory response after MI and subsequent ventricular remodeling during the chronic phase.

Methods: The 8 to 10 weeks old male wild type (WT) and TN-C knockout (KO) mice were divided into 4 groups of WT+Sham, KO+Sham, WT-MI and KO-MI. Echocardiographic evaluation were performed 4, 8 and 12 weeks after the operation, and then, mice were sacrificed for histological analysis. And, heart samples were taken on day 3, 5 and 7 after the operation for biochemical analysis to examine the acute inflammatory response after MI.

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Conclusion: TN-C aggravates the left ventricular remodeling after MI partly through the promotion of inflammatory response via the regulation of macrophage subsets during the acute phase.

P181 | BENCH

Influencing acute inflammatory response leads to decreased calcification of subcutaneously implanted decellularized porcine aorta in mice

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Purpose: Chronic inflammatory processes lead to progressive tissue deterioration of biological heart valve prostheses thereby limiting graft survival. Shock waves were shown to modulate inflammation via Toll-like receptor 3. We hypothesized that shock wave therapy directly after graft implantation leads to enhanced graft survival via the modulation of acute inflammatory response.

Methods: Pieces of ascending aorta were harvested from pigs and decellularized using sodium-deoxycholate and sodium-dodecyl-sulfate. 0.5cm×0.5cm pieces were implanted subcutaneously into 10-12 week-old C57BL/6 mice (n=6 per group). Treatment group (SWT) received shock wave treatment (250 impulses at 0.1mJ/mm2, 5Hz) for modulation of inflammatory response directly after implantation, control animals received sham treatment (CTR). Grabs were harvested 72h and 4 weeks after implantation and analyzed for inflammatory cytokines, macrophage infiltration, tartrate-resistant acid phosphatase (TRAP) positive cells and calcification. In addition, transmission electron microscopy was performed.

Results: RT-PCR revealed increased mRNA levels of pro-inflammatory TGFβ (CTR 0.0110±0.00202 vs. SWT 0.8615±0.2596, p=0.0078) and TNF-a (CTR 0.5150±0.02778 vs. SWT 1.370±0.4197; p=0.05) in the treatment group, whereas anti-inflammatory IL-10 was decreased (CTR 0.002689±3.2488e-005 vs. SWT, p<0.001). Enhanced repopulation with recipient cells could be observed. After SWT (CTR 15.65±1.857 vs. SWT 28.28±4.933, p=0.02), F4/80+ immunofluorescence staining revealed higher numbers of macrophage infiltration in treated animals (CTR 42.53±4.162 vs. SWT 67.72±2.768; p<0.001). TRAP staining showed enhanced recruitment of osteoclastic cells after treatment (CTR 67.60±14.14 vs. SWT 17.40±3.06; p<0.001). Histological assessment showed increased calcification after treatment (CTR 109.8±142.5 vs. SWT 236.4±65.4; p<0.001).

Conclusions: Shock wave therapy reduces calcification of bioprosthetic grafts via the modulation of inflammatory response. Influencing acute inflammation may develop an important adjunct to biological heart valve replacement.
P184 | BEDSIDE
Left ventricular long-axis performance during exercise is an important prognosticator in patients with heart failure and normal ejection fraction
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Purpose: We aimed at evaluating the prognostic value of echocardiographic parameters during exercise in patients with heart failure and normal ejection fraction (HFNEF).

Methods: A consecutive of 80 HFNEF patients (aged 66±18 years; 64% male) received echocardiography (Vivid7, GE Healthcare) examination with symptom-limited exercise testing on a semi-recumbent and tilting bicycle Ergometer (Lode BV, Netherlands). The exercise images for two-dimensional (2D) speckle tracking were acquired with heart rate of 90-100 bpm, while tissue Doppler (TD) images were stored with attainment of > 85% of age-predicted maximal heart rate. All patients were followed for 3 years after stress echocardiography for heart failure hospitalization or all-cause mortality.

Results: During the follow-up, 43 (54%) patients reached the combined end points: 5 (6%) patients died, and another 38 (48%) patients experienced HF hospitalizations. Univariate predictors were: lower maximal heart rate, increased left ventricular stroke volume index (LVSI), elevated E/e ratio, reduced TD Sm and Em, and impaired 2D global longitudinal strain (GLS) during exercise. Only impaired 2D GLS was a predictor of death [HR 0.78, 95% confidence interval [CI] 0.65 to 0.94] remained independent after multivariate analysis (p=0.008).

Conclusion: More than half of HFNEF patients died or hospitalized for HF at 3-year follow-up and this was significantly related to impaired LV long axis function during exercise.

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Preservation of contractile reserve of the left ventricular free wall as one of the main predictors for response to cardiac resynchronization therapy
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Purpose: To evaluate the role of contractile reserve of the left ventricular free wall for the selection of candidates for cardiac resynchronization therapy (CRT).

Methods: A consecutive of 46 patients with NYHA functional class III heart failure (HF) were included in the study; mean age was 51±12 years; 75% were men. Dilated cardiomyopathy (DCM) group included 24 patients; ischemic cardiomyopathy (ICM) groups included 22 patients. All patients had indications for CRT. All patients received cardiac ventriculography. Efficacy of CRT was evaluated 7 days and 12 months after beginning of treatment. Echocardiographic study was performed by using EnVisor cv HDI (Philips). All measurements were taken according to ASE recommendations. Local contractile reserve was studied by assessing dynamics of systolic myocardial velocity (Sm) by the method of spectral tissue Doppler (TDI) at rest and at the peak of anti-orthostatic stress test (AOST). Decrease in end systolic volume by ≥15% six months after CRT compared with corresponding value before treatment was considered a criterion of reverse remodeling. Six-minute walk test was used to determine exercise tolerance before and after CRT.

Results: Initially, DCM and ICM groups did not significantly differ. Data showed that 63% of patients clinically responded to CRT 6 months after beginning of treatment. The highest rate of non-responders was found in ICM group. More than 10% increase in Sm of LV free wall according to TDI data during AOST compared with baseline values was indicative of the preservation of contractile reserve. According to the results of the postural test, 30 individuals (65%) with preserved contractile reserve were included in group A; 35% of patients lacked contractile reserve and comprised group B. In group A, AOST data showed an increase in end diastolic pressure suggesting an increase of LV wall stiffness in these patients; minimal regurgitation increased from 1.8±0.6 to 2.4±1.68 (p=0.002). The ROC analysis showed that, contractile reserve preservation at the peak of postural test (AUC 0.88; CI 0.77–0.98; p=0.001), verified with AOST, and dysynchrony (AUC 0.86; CI 0.71–0.95; p=0.001) strongly predicted the response to CRT. Preservation of contractile reserve was an independent predictor of response to CRT with sensitivity of 95% and specificity of 83%.

Conclusions: Combined approach with the use of such predictors of response to CRT as intra- and interventricular dysynchrony and the presence of contractile reserve may contribute to the correct identification of CRT candidates and decrease of non-respondor rate.

P186 | BEDSIDE
Global longitudinal strain before cardiac resynchronization therapy predicts mortality in heart failure patients
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Purpose: Cardiac resynchronization therapy (CRT) improves mortality in heart failure (HF) patients with wide QRS. Strain by speckle tracking echocardiography (STE) quantifies myocardial function and predicts prognosis. We aimed to prospectively explore the ability of different echocardiographic measures before CRT implantation to predict mortality in HF patients with CRT.

Methods: Echocardiography (2D) was performed before and 6 months after CRT implantation in HF patients fulfilling CRT indications. Left ventricular (LV) function was assessed as ejection fraction (EF), global longitudinal (GLS) and global circumferential (GCS) strain from 16 LV segments by STE. Response to CRT was defined as decline in end systolic volume ≥15% at 6 months. Our composite endpoint was defined as death, heart transplantation or left ventricular assist device (LVAD) during 2 years from CRT implantation.

Results: We included 113 HF patients (84±19 years, 24% women, NYHA class ≥2.8±0.4, 43% ischemic cardiomyopathy). Eleven (10%) endpoints occurred (7 deaths, 2 transplantations, 2 LVADs). Worse GLS before CRT was a marker of endpoint (≥3.6 vs. 3.3%, p=0.009), while EF (22.7% vs. 28.9%, p=0.05) and GCS (-9.7±2.9% vs. -11.2±3.0%, p=0.12) were not. GLS before CRT predicted endpoint independently of CRT response (HR 1.21 (1.01-1.45), p=0.04). GLS worse than -8.0% optimally predicted unfavourable outcome (log rank p=0.004) (Fig. 1).

Figure 1. GLS and survival in CRT patients

Conclusions: Myocardial function by GLS before CRT predicted death, heart transplantation or LVAD 2 years after CRT in HF patients, independently of CRT response. EF and circumferential function were not markers of fatal outcome. Longitudinal myocardial function before CRT may have the greatest impact on outcome in CRT patients.

P187 | BEDSIDE
Contributions of dysynchrony and regional function to impaired myocardial mechanics after right ventricular pacing
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Background: Right ventricular (RV) pacing is associated with LV dysfunction, often attributed to inefficient LV dyssynchronous contraction. As the LV apex is important in LV untwist, we hypothesized that the detrimental effect of RV pacing may be mediated by apical LV impairment as well as inefficient dyssynchronous contraction. We sought to investigate the effect of pacing on LV synchrony, efficiency, and regional function, and their association with global LV function.

Methods: We enrolled 148 pts (78 RV apical (RVA) and 70 non-RVA pacing) with preserved EF and a pacemaker implantation because of atrioventricular block. Echocardiography was performed at baseline (just after the implantation) and at 2 years. Global longitudinal strain (GLS) was measured using speckle tracking. We also assessed LV dyssynchrony and discordination and peak strain at septal apical segment.

Results: Although GLS reduced in both RVA and non-RVA groups after 2 years, deterioration in GLS was larger in pts with RVA pacing than that in non-RVA (10.7±23.6 vs 3.4±23.2%, p=0.05). Septal apical strains were significantly lower in RVA than those in non-RVA at baseline and 2 years. Similarly, the dyssynchronous parameters were significantly reduced in RVA compared with those in non-RVA. In a multivariate linear regression analysis, although baseline dyssynchrony and discordination parameters were not correlated with the change GLS.
in 2 years, septal apical strain, dysynchrony and discordination parameters at 2 years were significantly associated with the change (Table).

**Conclusion:** RVA pacing appears to worsen global myocardial longitudinal deformation more than non-RVA pacing. Not only inefficient dysynchronous contraction but also the decrease in septal apical strain appear associated with global LV impairment.

**P188 | BEDSIDE**

Electromechanical dyssynchrony and the long-term survival of outpatients with systolic heart failure. 3 years follow-up

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**Aim:** To evaluate the role of the left ventricle electromechanical dyssynchrony in predicting the long-term survival in outpatients with systolic heart failure.

**Methods:** 142 consecutive outpatients with SHF (LV ejection fraction — 29.8 ± 8.9%) followed-up in a single heart failure. A complete echocardiographic study using 2D, Doppler, TDI and myocardial strain with 2D strain performed. LV Dysynchrony: standard deviation of the systolic time-to-peak in 12 LV segments (LV-SD12) and the difference between the earliest and the latest time-to-peak. The LV-SD12 was categorized according to the quartiles (58.7, 79.8, 122.45). The ROC curve with area under the curve (AUC), Survival curve (KM-Log-Rank test), Univariate and multivariate Cox regression.

**Results:** (1) The mortality rate was 35.2%. Death was associated with greater LV-SD12 (AUC=0.653; 95%CI 0.558-0.748; p=0.003), with the calculated optimal cut-off of 79.88. (2) Greater the LV-SD12 quartile greater the mortality rate (22.9-19.4-52.8-45.9%; p=0.003), and lower the survival time (Log-Rank p=0.003). Cox regression showed that in relation to the 1st quartile, the 3rd (HR=3.04; 95%CI 1.32-6.96; p=0.007) and the 4th (HR=2.39; 95%CI 1.02-5.6; p=0.003). Cox regression showed that in relation to the 1st quartile, the 3rd (HR=3.04; 95%CI 1.32-6.96; p=0.007) and the 4th (HR=2.39; 95%CI 1.02-5.6; p=0.003) quartiles had greater risk of death.

**Conclusion:** LV dysynchrony measured by the standard deviation of the systolic time-to-peak in 12 LV segments is associated with the long-term survival of outpatients with SHF.

**INNOVATION AND THE HEART 1**

**206 | SPOTLIGHT**

Results of the MELODY REGISTRY - an international multicenter study of transcatheter pulmonary valve implantation

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**Background:** To assess the acute and One-Year clinical outcomes of transcatheter pulmonary valve implantation (TPVI) in a multicenter registry (MELODY Registry).

**Methods:** Between 12/2006 and 09/2013, 1,003 patients (mean age: 21.5±11.4 years) underwent TPVI in 40 cardiac centers. Indications for treatment were predominant stenosis (54%), predominant regurgitation (21%), or combined stenosis and regurgitation (25%). We retrospectively analyzed procedural details, clinical and echocardiographic outcome parameters. The primary outcome was freedom from death / reoperation / reintervention at One-Year (all-cause and TPVI-related); for this analysis, 694 patients were included who reached One-Year follow-up.

**Secondary outcomes included procedural complication rates, rates of endocarditis and stent fractures at One-Year, as well as echocardiographic parameters of TPV device performance (peak right ventricular outflow tract (RVOT) velocity and percentage of patients with significant pulmonary regurgitation (PR) of grade greater than 2).

**Results:** The invasively measured right ventricular systolic pressure fell from 62±18 mmHg to 43±12 mmHg (p<0.0001) and so did the percentage of patients with significant PR of grade greater than 2 (pre: 49% to immediate post-intervention: 1%, p<0.0001). Procedural complications occurred in 2.7% (major) and 11.9% (minor) of TPVI procedures, respectively. The One-Year freedom from the combined endpoint was 92.5% for all-cause events and 94.2% for TPVI-related events. At One-Year, the rate of endocarditis was 2.7% and the rate of stent fractures was 1%. There was sustained hemodynamic performance of the TPVI device at One-Year when compared to immediate post-intervention (peak RVOT velocity: 2.5±0.7 versus 2.6±0.6 m/s; PR of grade greater than 2: 1% versus 2%).

**Conclusion:** The multicenter MELODY Registry represents the largest patient series after TPVI to date with a follow-up of One-Year and offers the great potential for longer clinical observations of this patient population. The analysis of the current data confirms the safety and effectiveness of TPVI in clinical practice utilizing the Melody valve.

**208 | SPOTLIGHT**

Transapical off-pump neochord implantation procedure for mitral valve insufficiency

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**Purpose:** The off-pump transapical implantation of artificial chordae tendineae is a recent mitral valve (MV) repair technique inspired by the well known concept of "respect rather than resect". The NeoChord technique combines this trend together with a minimally invasive approach opening a new surgical opportunity in the MV repair repertoire. The aim of the present study is to present our initial surgical experience using this procedure.

**Methods:** We selected 6 female and 7 male patients with a median age of 76 years, who presented severe symptomatic mitral regurgitation. They had a high risk profile for traditional surgery because of multiple comorbidities such as previous coronary percutaneous and surgical procedures, chronic obstructive pulmonary disease, post-actinic pericarditis, chronic renal failure, history of bleeding, liver cirrhosis, stroke and severe peripheral vascular disease. Two patients presented an anterior leaflet prolapse, meanwhile the others had posterior leaflet prolapse. Four patients showed moderate left ventricular dilatation and dysfunction with severe pulmonary hypertension, three patients had extended annular calcification. These patients were referred to transapical off-pump Neochord implantation using Gore-Tex sutures under real-time 2D/3D transesophageal echocardiography.

**Results:** An average of 4 neochords were implanted for each patient. The early postoperative period was free from both surgical and clinical complications except for two patients who developed respiratory complications medically treated. Discharging echocardiography showed, no residual MR in eight patients, mild MR in three patients and moderate MR in two patients. The patients with moderate MR presented a concomitant small grade of prolapse and moderate annular dilatation. Those results were foreseen in these specific cases, given the anatomical and functional substrate of the MV. Nevertheless, those patients presented a poor preoperative clinical condition that was extremely challenging for conventional surgery. At discharge, patients presented NYHA class I.

**Conclusions:** The NeoChord procedure proved to be safe and effective in all our cases. The transapical off-pump Neochord implantation procedure is belived to be the real minimally invasive procedure to repair the MV insufficiency using a physiological strategy mimicking conventional surgery. These satisfactory results raise the prospect of extending this technique in younger patients with lower surgical risk before ventricular remodeling occurs. Further studies are needed to demonstrate long term durability.
209 | SPOTLIGHT
Changes in aortic root motion and distension after personalized external aortic root support surgery in Marfan syndrome
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Background: Personalized external aortic root support (PEARS) is an innovative surgery for stabilizing aortic root size in Marfan patients (1). A model of patients’ aortic root and ascending aorta is created from Cardiac MRI (CMR) to produce a polymer mesh PEARS for surgical implantation (figure). Systolic downward motion of the aortic root increases aortic wall stress, increasing the risk for aortic dissection (2). The aim of this study is to assess the impact of PEARS on aortic root motion (ARM), aortic root distension (ARD) and left ventricular mass index (LVMi).
Methods: 27 Marfan patients (age 33.0±12.7) had PEARS during 2004-2012; 24 patients had follow-up CMR studies. ARM, ARD and LVMi were measured from cine CMR images before and after surgery. ARM is defined as the largest systolic downward displacement of the aortic annulus. ARD was derived from change in aortic root diameter in diastole (AoD) and systole (AoS); [100 x (AoS - AoD)/AoD]. LVMi was calculated by dedicated CMR software. All measurements were performed randomly and blinded. The pre- and post-operative measurements were compared by paired t test.
Results: Median follow-up was 50.5 months (IQR 25.5-72 months). The mean systolic ARM was significantly decreased after PEARS (12.6±3.6mm pre-operation vs 7.9±2.2mm post-operation, p<0.00001). There was a tendency for ARD to decrease after surgery but this was not significant (median 4.5% IQR 6 vs 3% IQR 4, p=0.21). There was no significant change in LVMi (64.9±10 g/m² vs 67.1±9.9 g/m², p=0.28).
Conclusions: In addition to preventing progression of aortic root dilatation, PEARS provides further benefit by reducing systolic ARM which may reduce longitudinal aortic wall stress and the risk of dissection.

210 | SPOTLIGHT
Prognosis of atypical late gadolinium enhancement by cardiovascular MR in older adults in the ICELAND-MI study
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Purpose: To study atypical late gadolinium enhancement by cardiovascular magnetic resonance imaging in a community-based cohort of older adults. The objective of the study was to assess the utility of routine OCT guided stent implantation in patients with STEMI undergoing primary PCI.
Methods: Two hundred and one patient were enrolled in this study. Patients were randomly assigned either to primary PCI according to the standard practice (group A;N=96) or to primary PCI with the OCT guidance (group B;N=105). The use of GP IIb/IIIa inhibitors and manual thrombus-aspiration were left up to the discretion of the operator. Either biolimus A9 or everolimus drug-eluting stents were used in this study. The OCT images were obtained with C7- XRTM intravascular imaging system using a C7 DragonflyTM intravascular imaging catheter. OCT guided stent implantation during primary PCI was associated with moderate/low risk NSTE-ACS (GRACE <140). SUV was measured in PET imaging system using a C7 DragonflyTM intravascular imaging catheter. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images.
Results: PVAT SUV. In all patients Homeostasis Model of Assessment - Insulin Resistance (HOMA-IR) was calculated using the formula: fasting Glucose (mmol/L) x fasting Insulin (μU/L)/22.5.
Results: PVAT SUV in NSTE-ACS patients was significantly greater than in other fat locations (LM SUV: 1.62; RCA SUV: 1.48; LCX SUV: 1.87; LAD SUV: 2.29 vs SC SUV: 0.58; VS SUV: 0.79; EPI SUV: 0.99, p<0.001; ANOVA). PVAT SUV positively correlated with necrotic core plaque rate (r=0.62, p<0.05), and negatively correlated with fibrous plaque rate (r=−0.52, p<0.05), which was more prevalent in pts with HOMA-IR>2.5 (r=0.69, p<0.05; r=0.57, p<0.05, respectively). There was also positive correlation between PVAT SUV and % plaque volume (r=0.44, p<0.05).
Conclusions: Inflammatory capacity of pericoronary adipose tissue is greater than in subcutaneous, visceral thoracic, or epicardial tissue in NSTE-ACS patients. PVAT SUV correlates with necrotic core component of coronary plaque and plaque volume in patients with NSTE-ACS, especially with elevated insulin resistance index.

212 | SPOTLIGHT
OCT guided stent implantation during primary PCI. A randomized, multicenter study with 9-month angiographic follow-up
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Background: The objective of the study was to assess the utility of routine OCT guidance during stent implantation in patients with STEMI undergoing primary PCI. The aim of the study was to assess the utility of routine OCT guidance during stent implantation in patients with STEMI undergoing primary PCI.
Methods: Two hundred and one patient were enrolled in this study. Patients were randomly assigned either to primary PCI according to the standard practice (group A;N=96) or to primary PCI with the OCT guidance (group B;N=105). The use of GP IIb/IIIa inhibitors and manual thrombus-aspiration were left up to the discretion of the operator. Either biolimus A9 or everolimus drug-eluting stents were used in this study. The OCT images were obtained with C7- XRTM intravascular imaging system using a C7 DragonflyTM intravascular imaging catheter. OCT guided stent implantation during primary PCI was associated with moderate/low risk NSTE-ACS (GRACE <140). SUV was measured in PET imaging system using a C7 DragonflyTM intravascular imaging catheter. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images. SUV was measured in PET images.
icant malposition and 4) No dissection at the edges of the stented segment. Dual antiplatelet therapy was recommended for 12 months in both groups. MACE’s at 30 day and 9-month were assessed in both groups. Coronary angiography was scheduled in all patients at 9-month follow-up.

Results: Baseline demographic and procedural characteristics were well balanced in both groups. At the end of procedure, both the minimal lumen diameter and final dilatation pressure were significantly higher in the OCT group (p<0.03 and 0.02 respectively). On the other hand, the fluoroscopy time was significantly shorter in the standard PCI group (p<0.0001). Based on the OCT data, more stent overlap in the OCT group and implanted stents were significantly longer in this cohort of patients (p=0.03 and 0.02 respectively). The ejection fraction was comparable at discharge in both groups (p=NS). At 30 day, there was one death (extracardial) in the standard primary PCI group. There were 2 acute stent thrombosis requiring PCI and 1 additional target vessel revascularization in the OCT guided primary PCI group B versus 1 stent thrombosis in the standard primary PCI group (p=NS). Furthermore, the rate of MACE’s at 9-month did not differ significantly between both groups (p=NS).

Conclusions: Our study failed to demonstrate the superiority of the OCT guidance during DES implantation in patients undergoing primary PCI for STEMI regarding either the incidence of MACE’s or angiographic restenosis at 9 month FU.

213 | SPOTLIGHT
Role of multi-detector computed tomography coronary angiography in percutaneous coronary intervention of chronic total occlusions: TACTO prospective randomized trial
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Purpose: There is no randomized trial assessing clinical benefit in improving procedural success of a Computed tomography coronary angiography (CTCA) in-vestigation prior to CTO recanalization. We performed a prospective randomized trial so as to assess clinical impact of CTCA in improving immediate procedural results.

Methods and results: Between February 2012 and January 2014, 98 eligible patients who were scheduled for percutaneous recanalization of a true CTO and underwent CTCA were included in the study (TACTO). All patients were randomized to be or not to be aware of the result of the CT-scan prior to CTO recanalization. Therefore, CTCA versus conventional coronary angiography (CCA) group were compared regarding immediate procedural success. By protocol we pre-defined the same 10 CTO key characteristics by CCA and CTCA based on previously published independent predictors of failure. Two experienced interventional cardiologist and two imaging specialists, who were unaware of the CTCA and CCA respectively, analysed CTO characteristics. In the CTCA group, all the CT scans were discussed between the operator of CTO procedure and the imaging specialist prior to the interventional procedure. A 64-CT detector was used for all studies. Post processing was performed with specific software. The mean age was 62.10 years (7.8. years). Diabetes, According to the Japanese-CTO score 51% of lesions were classified as difficult or very difficult. In most cases (88%) the strategy was antegrade. The total DES length implanted per lesion was of 51.6±20.3mm. There were no significant differences in demographic, angiographic-lesion and procedural characteristics, as well as there were no differences in the Japanese CTO complexity score between the two groups. In the first attempt, procedural success was achieved in 85.7% of the patients in the CCA group and 81.6% of those in the CTCA group (p=0.10). According to the J-CTO score 2 subgroups of complexity were done: a) easy-intermediate and b) difficult-very difficult. In sub-group a), procedural success was achieved in 96.4% of the patients in the CCA group and 100% of those in the CTCA group (p=0.85). In sub-group b), procedural success was achieved in 71.4% of the patients in the CCA group and 73.1% of those in the CTCA group (p=0.78).

Conclusions: According to the results of this prospective randomized trial, in our current era, with new CTO material and techniques, it seems that in dedicated CTO centers, the information provided by CTCA could be useful, but did not provide a significant impact in procedural success.

214 | SPOTLIGHT
Improved quality of life in 13,860 patients treated by surgical aortic valve replacement with transcatheter aortic valve implantation
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1German Heart Center, Hospital rechts der Isar at the Technical University of Munich, Munich, Germany; 2German Society for Thoracic and Cardiovascular Surgery, Berlin, Germany; 3University Hospital of Essen (Ruhrgorge), Department of Cardiac Surgery, Essen, Germany; 4University Hospital Bonn, Department of Cardiac Surgery, Bonn, Germany; 5Klinikum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany; 6University Medical Center of Schleswig-Holstein, Department of Cardiovascular Surgery, Kiel, Germany; 7Asklepios Clinic St. Georg, Department of Cardiology, Hamburg, Germany;

Conclusions:

was very low in both groups (3% versus 3%; p=NS).

bosis (both in one patients) and 1 additional target vessel revascularization in (extracardial) in the standard primary PCI group. There were 2 acute stent throm-

comparable at discharge in both groups (p=NS). At 30 day, there was one death

stents were used in the OCT group and implanted stents were significantly longer

FU.

garding either the incidence of MACEs’ or angiographic restenosis at 9-month

ance during DES implantation in patients undergoing primary PCI for STEMI re-

valve replacement or transcatheter aortic valve implantation

213 | SPOTLIGHT
Diabetes is associated with increased risk of developing Atrial fibrillation Independent of age with a mean time from onset of DM to AF diagnosis of 4.6 years - nationwide cohort Study

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Objective: The purpose of this study was to identify Diabetes Mellitus (DM) as a risk factor of developing atrial fibrillation (AF) in five specific age groups, and to identify the time from onset of DM to AF diagnosis.

Methods: We conducted a nationwide cohort study including the entire popu-

lation from 1996 to 2011 by cross-linking several of the Danish registries. The cohort was divided into two groups: Patients with DM and the background pop-

ulation, patients with prior DM, and AF were excluded. The cohort was further divided into five age groups: 18-49; 50-59; 60-69; 70-79; 80-100. Incidence rates (IR) of AF per 1000 person years were calculated, and the mean time period from onset DM to AF diagnosis was identified.

Results: 6,228,157 were eligible to enter the study cohort. During follow-up 210,462 (3.4%) developed atrial fibrillation; 14,281 (5.6%) in the diabetes-group and 195,706 (3.3%) in the background population. The DM patients had respec-
tively 3.8, 2.7, 2.1, 1.4 and 1.2 fold higher IR per 1000 person years, of AF in the five age groups. The mean time from onset DM to AF diagnosis was respectively 6.3, 5.8, 5.1, 4.3 and 3.0 years in the five age groups.

Conclusion: In a nationwide cohort, diabetes patients were at increased risk of developing AF in all age groups, but this was especially prevalent among younger diabetes patients. Focus on risk of AF in diabetes patients is warranted.
216 | SPOTLIGHT
Endocardial botulinum toxin injection in ganglionated plexi for prevention recurrences of atrial fibrillation
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Background: Prior animal studies suggest that botulinum toxin injection into the epicardial fat pads can suppress atrial fibrillation (AF) inducibility. The aim of this study was to assess the efficacy and safety of botulinum toxin injection into atrial ganglionated plexi (GP) by endocardial injection for preventing AF.
Methods and results: In 20 dogs, transvenous catheters were passed into the left atrium. Sites selected for injection were tagged on the CARTO system when vagal reflexes were evoked by high-frequency stimulation (HFS). Endocardial in- jection was accomplished using the MyoStar catheter. A mean number of 5.8±0.3 intramyocardial injections (Xeomin, Germany; 10 U/0.2 mL at each) of botulinum toxin were administered into each site exhibiting a positive vagal response. In addition, two empiric injections were made into the fat pads containing the anterior right and inferior right GP (50 U/mL at each). The vagal reflexes by HFS and AF inducibility were evaluated before injections and then every 2 weeks until the return of all changes to baseline by precise catheter reposition and stimulation over the GP sites marked on the CARTO map.
At 2 weeks after procedure, all dogs demonstrated complete elimination of the vagal response. First signs of recovery of vagal response occurred at 9.0±0.6 weeks (p<0.001), and full recovery to baseline values at 14.0±1.1 weeks. The threshold of stimulation that induced AF increased from 4.9±0.5 V at baseline to 12.1±1.1 V at 2 weeks (P<0.001). The effects of AF suppression was complete eliminated at 16±0.9 week. No procedure-related complications occurred.
Conclusions: Endocardial botulinum toxin injection into intramyocardial GPs and epicardial fat pads was feasible and safe, and provided complete abolition of cardiac vagal responses and significant AF suppression. This approach holds promise as a novel therapeutic option for AF.

226 | BEDSIDE
Area strain from 3D speckle-tracking echocardiography as a new predictor of symptoms development in severe mitral regurgitation with preserved ejection fraction
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Background: Severe mitral regurgitation (SMR) with preserved ejection fraction (EF) is known to have a poor prognosis without surgery when symptoms of heart failure (HF) are present. However in asymptomatic patients the indication of surgery remains controversial. We sought to test some 3D speckle tracking-derived parameters including area strain (AS) which is a new index that integrates longitudinal and circumferential strain data, as possible predictors of HF.
Methods: 41 consecutive asymptomatic patients with SMR and EF>60% underwent 3D-speckle tracking echocardiography, and a follow-up visit was programmed every 6 months. New onset of dyspnea or admissions for HF were considered as events.
Results: From the 41 patients (54% male, aged 66.7±13.2), we found 8 events (19.5%) in a follow-up time of 9.9±5.4 months (maximum 18 months). When comparing the remaining patients with this new onset HF group we found significant differences in several parameters such as global 3D longitudinal strain (-17.85 vs. -15.39; p=0.042), global 3D circumferential strain (-35.66 vs. -31.12; p=0.028) and global area strain (-48.52 vs. -42.92; p=0.014). Other indexes such as EF, 3D strain, 3D radial strain didn’t show significant differences. Furthermore, a global AS>47.5 was found in 7 of 8 patients with events (85.5%). When using this cutoff point, the Kaplan Meier survival curves showed a significant difference (Breslow test p=0.037) between normal and abnormal AS, as shown on figure.
Conclusions: In asymptomatic patients with SMR and preserved ejection fraction, area strain from 3D speckle-tracking echocardiography is a promising tool for predicting the development of symptoms. This finding may be useful for guiding the selection of patients for early mitral valve replacement surgery.
Conclusion: Evaluation of LAA morphology by 3D-TEE is feasible and not inferior to CT and MRI. In our study population, patients with Chicken Wing LAA morphology were significantly less likely to have SEC or thrombus than patients with Non-Chicken Wing morphology. 3D-TEE can serve as a widely available, cost-efficient and radiation-free image modality in the evaluation of LAA morphology, permitting further risk stratification in formation of thrombi and cardioembolic events.

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Interventional left atrial appendage occlusion: Added value of 3D transesophageal echocardiography for orifice sizing


Introduction: The objective of this study was the assessment of left atrial appendage (LAA) dimensions comparing 2D- to 3D-TEE measurements in patients undergoing percutaneous LAA occlusion by the Watchman® device.

Methods: Patients underwent transesophageal echocardiography (TEE) before, during and 45 days after intervention. The maximal LAA orifice diameters in 2D-TEE (LODmax 2D) were obtained from multiple views (0°, 45°, 90° and 135° views). Additionally, the maximal diameter (LODmax 3D) and the eccentricity index of the LAA orifice were determined in 3D-TEE datasets. Test-retest reliability (screening vs. implantation), inter- and intra-observer variability for echocardiographic parameters where assessed by two independent examiners.

Results: Overall, 74 patients underwent percutaneous LAA occlusion. The results of the echocardiographic measurements are summarized in Table 1. The correlation between 2D and 3D measurements of maximal LAA orifice diameter was low (r=0.49, p<0.01, 95% range of agreement -2.75 to 2.68).

2D-TEE significantly underestimated LAA orifice diameter, compared with 3D-TEE (screening TEE p<0.001 for 2D vs. 3D, during implantation p<0.001 for 2D vs. 3D). The interobserver coefficient of variation for LODmax 2D was 9.69% and for LODmax 3D 6.07%. Compared to 3D-TEE, the re-test reliability of the novel automated model shows an excellent interobserver reproducibility compared with traditional manual methods. The feasibility of determining TAVR results with geometric models based on image, prior to procedure, is one of the possibilities of this new software.

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Comparison between automatic measurements of the aortic root with a new automated quantitative 3-D model vs. the traditional manual method in candidates for transcatheter aortic valve replacement

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Background: Precise knowledge of the aortic root anatomy is basic prior to transcatheter aortic valve replacement (TAVR). To this end, new specialized software has been developed with the ability to automate quantitative modeling of the aortic valve and root. The purpose of this study was to compare interobserver variability using this new automated method vs. the traditional manual measurements.

Conclusion: TEE 3D PISA RVol correlates better with CMR RVol than TEE 3D PISA RVol and is more accurate for the detection of severe MR. The better spatial resolution of TEE probably explains this phenomenon.

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Impact of imaging modality, TTE vs. TEE, on the measurement of mitral regurgitant volume by three-dimensional integrated PISA

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Introduction: Three-dimensional integrated PISA (3D PISA) is a new technique to measure the regurgitant volume (RVol) of mitral regurgitation (MR) without geometrical assumption and taking into account the dynamic changes of PISA orifice distal area. Little is known about the impact of the imaging modality (transesophageal echocardiography vs. transthoracic echocardiography) on the measured RVol.

Methods: In patients with MR, cardiac MRI (CMR), TTE and TEE were performed the same day. Color Doppler volumes focused on MR-PISA were recorded using ECG-triggered multiple beats 3D echocardiography (3-DE). For each patient, all PISA visible during systole were 3D reconstructed using a customized software (fig. 1). RVol of each PISA was calculated as: Nyquist limit x PISA x time between frames. Total RVol is the sum of these volumes. By CMR, RVol was derived as ventricular stroke volume (SV) minus the SV in the aorta.

Results: Sixty patients were included, 72% had organic MR. 3D PISA were anlyzable in 96% of patients by TEE and in 78% by TEE. Temporal resolution of 3-DE was similar for both modalities (TEE 32±7 vs. TTE 31±7, p=0.57); the number of PISA analyzed per systole was higher for TEE (12.4 vs. 10.4±0.02). TEE correlated better with CMR than TEE (fig. 2). Both modalities underestimated RVol compared to CMR and TEE-RVol was higher than TTE-RVol (39±3 vs. 34±3 vs. 27±3, p=0.06). By ROC analysis, the 3D PISA RVol cutoff for detecting severe MR with the maximal surface under the ROC curve was 42ml for TEE (AUC 0.99, sensitivity 100%, specificity 96%) and 35ml for TTE (AUC 0.96, sensitivity 100%, specificity 90%).

Conclusion: The findings of this study are as following: 1. 2D-TEE compared to 3D-TEE significantly underestimates maximal LAA orifice diameter. 2. 3D-TEE measurements are associated with lower observer variability and higher reliability than 2D-TEE. 3. Comparing the eccentricity indices, device implantation leads to a change of LAA orifice shape and dimensions.

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Spontaneous switching from cardiomyocyte to adipocyte cell fate in arrhythmogenic right ventricular cardiomyopathy

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Background: An unexpected level of cellular plasticity was recently revealed by reprogramming to pluripotency or lineage switching of mature somatic cells by ectopic expression of transcription factors. The aim of this study was to utilize patient-specific induced pluripotent stem cell (iPSC) technology to investigate

NOVEL PERSPECTIVES OF STEM CELLS AND CELL THERAPY

Aortic root by automated 3D-TEE
disease mechanisms underlying arrhythmogenic right ventricular cardiomyopathy (ARVC), a genetic disorder caused by mutations in desmosomal proteins. The phenotypic hallmark of ARVC is fibroadipocytic replacement of cardiomyocytes. We speculated that cell lineage switching might be an integral part of the pathophysiology of ARVC.

Methods and results: We established induced pluripotent stem cells (iPSCs) from ARVC patients harboring mutations in the PKP2 gene by Sendai virus-mediated reprogramming of patient dermal keratinocytes. Patient-specific iPSCs expressed pluripotency markers and were able to differentiate into cells of all three germ layers. Differentiation to cardiomyocytes was achieved by embryoid body formation followed by manual dissection and further culture of beating foci.

When cultured for prolonged time periods in patient EB-conditioned medium, cardiomyocytes generated from patient-specific iPSCs spontaneously accumulated fat droplets in their cytosol and displayed a progressive disruption of their sarcomere organization. These morphological alterations were not observed in control cardiomyocytes generated from iPSCs not harboring the disease-causing mutation. The change in cell morphology was accompanied by altered expression patterns of transcripts involved in muscle contraction, lipid metabolism and extracellular matrix remodeling, as well as transcription factors and components of signaling pathways involved in cardiogenesis and adipogenesis. An up-regulation of adipogenic genes in conjunction with a down-regulation of myocytic genes were common features in ARVC iPSCs. By analyzing the consequences of the change in the epigenetic profiles further supported this mechanism.

Conclusion: We provide evidence for a direct lineage switching from the cardiomyocyte to the adipogenic lineage as the pathomechanism of ARVC. The ability of cardiomyocytes to spontaneously adopt a beige adipocyte phenotype in specific disease-associated conditions suggests a possible, yet undefined, developmental relationship between these two mesodermal cell lineages. A further characterization of the signaling pathways involved in this cell fate conversion might provide the basis for future specific therapeutic interventions.

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Modelling dilative cardiomyopathy by induced pluripotent stem cell-derived cardiomyocytes from patients harboring a RBM20 mutation

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Purpose: Heart disease can be modeled by using human patient-specific induced pluripotent stem cell-derived cardiomyocytes (ps-iPSC-CM). A common cause of cardiovascular mortality is dilated cardiomyopathy (DCM), which leads finally to heart failure. About 25-35% of patients have familiar forms of the disease, with mutations in many genes including the RNA-binding motif 20 (RBM20). The aim of this study was to generate iPSCs from DCM patients with different RBM20 mutations, and to analyze the resulting RBM20-iPSC-derived cardiomyocytes with regard to the cardiac DCM phenotype.

Methods and results: Fibroblasts from two DCM patients with different RBM20 mutations were reprogrammed to ps-iPSCs via infection with a single lentiviral vector encoding OCT4, SOX2, KLF4, and cMYC. The ps-iPSCs are pluripotent by expressing pluripotency markers on mRNA and protein level and by showing a mesodermal gene expression pattern comparable to control iPSCs. Under basal conditions, ps-iPSC-CM exhibited spontaneous activity for 14 days. In addition, we found a completely different isoform expression pattern of α-actinin in RBM20-iPSC-CM and control iPSC-CM. A significant reduction in the number of the engrafted cells compared to control iPSCs. Moreover, the generated RBM20-iPSCs are able to differentiate in vitro and in vivo into derivatives of all three germ layers. We analyzed the cardiac differentiation capacity and found that there was no significant difference in differentiation into beating cardiomyocytes of the RBM20-iPSCs when compared with control iPSCs. Under basal conditions, ps-iPSC-CM exhibited spontaneous activity potentials characteristic for pacemaker-, atrial-, ventricular- and Purkinje-like cells in a similar manner as control iPSC-CM. We analyzed the organization of the sarcomere structure by investigating the sarcomere-associated periodic signal amplitude for α-actinin in RBM20-iPSC-CM and control iPSC-CM. A significant higher percentage of RBM20-iPSC-CM showed abnormal sarcomeric α-actinin distribution compared to control CM, suggesting disorganized myofibril structure. In addition, we found a completely different isoform expression pattern of α-actinin in RBM20-iPSC-CM compared to control CM. Further studies regarding the RBM20-dependent regulation of genes expressing proteins that maintain sarcomeric structure and cardiac function are in progress.

Conclusion: In this study we demonstrate a RBM20-dependent regulation of organized myofibril structure and thin lining in an in vitro ps-DCM-iPSC-CM model. RBM20-derived CM recapitulate the abnormalities that were found in individuals with DCM caused by the same mutation. The differentiated cardiomyocytes may be used for the development of novel treatments for this inherited disorder.

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Donor age impairs cardioprotective paracrine effect of mesenchymal stem cells through down regulation of soluble factors

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Introduction and aims: We recently demonstrated that cytoprotective but not proangiogenic paracrine properties of human mesenchymal stem cells (MSC) are impaired in cells isolated from elderly donors (o-MSC; age > 65). MSC of fetal origin from human placenta (F-MSC) exert remarkable cardioprotective paracrine effects. Here, our goal was to study the functional and structural effects of intramyocardial injection of conditioned medium (CM) from F-MSC (F-CM) and o-MSC (o-CM). We developed a novel model of myocardial infarction (MI) in rats. Moreover we aimed to unravel new putative active mediators of cardioprotection produced by MSC.

Methods: Myocardial infarction (MI) was induced in rats by temporary ligation of the coronary artery. Three groups (n=26 animals in each group) were considered: saline, F-CM or o-CM treatments. Injections were performed at the infarct border zone. Cardiac function and vascular density were assessed at 48 hrs and 30 days after surgery, infarct size (IS) at 48 hrs. CM was assayed with Cytokine Antigen Detection Array. Genome-wide expression profiling was performed with illumina HiSeq.

Results: F-CM determined an improvement in cardiac function compared with saline and F-CM-MI was associated with a reduction in the IS. Consistently, F-CM resulted in a significant reduction in the numbers of the engrafted cells compared to saline and o-CM conditions, while o-CM had no effect. F-CM and o-CM equally increased the number of vessels at both 48 hrs (p<0.05) and 30 days (p<0.001) compared to saline and o-CM, and demonstrated that both F-MSC and o-MSC secrete high amounts of proangiogenic factors. In addition, bioinformatic comparison of MSC gene expression profiles revealed 330 genes up-regulated in F-MSC, including 36 encoding for secreted factors. Among them we identify 5 genes encoding for known secreted mediators of cardiac repair.

Conclusions: Single intramyocardial injection of F-CM leads to a sustained improvement in cardiac function by limiting infarct size. In contrast, o-CM fails to restore cardiac function after MI injection. However, proangiogenic paracrine properties of MSC are not affected by donor age. Interestingly, combined transcriptomic and cytokine profiling lead to the identification of several putative active mediators of cardioprotection.

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Apurinic/apyrimidinic endonuclease/redox factor-1 gene promotes anti-oxidative state to sca-1 positive cardiac progenitor cells and promotes cardiac repair in ischemic environment

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Purpose: Poor survival of engrafted cells in the host heart hinders cardiac regeneration after myocardial infarction (MI). However, pro-angiogenic paracrine properties of Apurinic/apyrimidinic endonuclease/redox factor-1 (APE1/ref1) has a potent anti-oxidative activity mediated through multiple functions. Here, we investigated the roles of APE1/ref1 in Stem cell antigen-1 (Sca1)-positive cardiac progenitor cells (Sca1-CPC) engrafted into ischemic/reperfused hearts.

Methods: Sca1-CPCs were obtained from the hearts of 8-10 week-old C57BL/6 mice using Magnetic-activated cell sorting and anti-Sca1 antibody. Reroviruses harboring the DsRed gene co-expressed with or without human APE1/ref1 gene were used to transfect the APE1/ref1-DsRed gene (Ape1-CPC) or DsRed alone (DsRed-CPC) into Sca1-CPC. In DsRed- and Ape1-CPCs exposed to H2O2, the production of reactive oxygen species (ROS) was evaluated using dichlorofluorescin, and the TUNEL assay was used to detect apoptosis in vitro. We conducted a randomized study wherein 26 mice received an intramyocardial injection of placebo, Ape1-CPC or DsRed-CPC. Apurinic/apyrimidinic endonuclease/redox factor-1 (APE1/ref1) has a potent anti-oxidative activity mediated through multiple functions. Here, we investigated the roles of APE1/ref1 in Stem cell antigen-1 (Sca1)-positive cardiac progenitor cells (Sca1-CPC) engrafted into ischemic/reperfused hearts.

Results: Ape1-CPCs were obtained from the hearts of 8-10 week-old C57BL/6 mice using Magnetic-activated cell sorting and anti-Sca1 antibody. Reroviruses harboring the DsRed gene co-expressed with or without human APE1/ref1 gene were used to transfect the APE1/ref1-DsRed gene (Ape1-CPC) or DsRed alone (DsRed-CPC) into Sca1-CPC. In DsRed- and Ape1-CPCs exposed to H2O2, the production of reactive oxygen species (ROS) was evaluated using dichlorofluorescin, and the TUNEL assay was used to detect apoptosis in vitro. We conducted a randomized study wherein 26 mice received an intramyocardial injection of placebo, Ape1-CPC or DsRed-CPC. Apurinic/apyrimidinic endonuclease/redox factor-1 (APE1/ref1) has a potent anti-oxidative activity mediated through multiple functions. Here, we investigated the roles of APE1/ref1 in Stem cell antigen-1 (Sca1)-positive cardiac progenitor cells (Sca1-CPC) engrafted into ischemic/reperfused hearts.
Conclusions: APE1/ref1 gene expression enhanced the survival of the engrafted Sca1-1CPCs against oxidative stress in the ischemic myocardium. The great number of engrafted Sca1-1CPCs restored the loss of LV function, which reduced the myocardial infarction and inflammation via macrophage transition. These results propose that APE1/ref1 gene expression may be as a novel strategy to innovate the cardiac cell-therapy.

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Embryonic Nkx2.5 enhancer positive cardiac progenitor cells re-emerge after ischemic injury in the adult mouse heart: Identification and characterization of a potential regenerative cell source

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Purpose: Recently, a limited regenerative capacity induced by myocardial ischemia was postulated for the mammalian adult heart. Though, the underlying cellular mechanisms remain poorly understood. We sought the same number of GFP+ cells as a sensor cell population in a transgenic mouse model, which interestingly re-emerges after myocardial ischemia in the adult heart.

Methods: Nkx2.5 cardiac enhancer (CE) GFP mice exhibit a cardiac restricted GFP expression during embryonic development (EB-E11) that vanishes completely 3 weeks after birth. Myocardial infarction (MI) was induced by left artery descendens (LAD) ligation in adult mice (<7 wks of age). The frequency of GFP+ cells in explanted hearts after ischemic injury was analyzed by FACS and subsequent lineage tracing for the negative cardiac cell populations were isolated. Gene expression analysis for candidate genes was performed by qRT-PCR. Results were confirmed by immunostaining and subsequent FACS analysis. Furthermore, heterotopic transplantation of Nkx2.5 CE GFP and C57Bl/6 mouse hearts (6th old ischemia) into an Nkx2.5 CE GFP background was performed.

Results: About 1% GFP+ cells re-emerged 5 to 9 days post MI in hearts of Nkx2.5 CE GFP mice. Even in mice up to one year GFP+ cells could be detected (<0.5%). Gene expression analysis revealed high mRNA levels of several cardiac and cardiac developmental marker (e.g. Tbx1, Bmp4, Wnt1, Tbx5, Tbx18) in the GFP+ compared to the GFP negative cells. GFP+ cells lack Tnnt2 expression which excludes a cardiomyocyte origin by de-differentiation. Interestingly, the stem cell marker Sca1 is expressed on about 90% of the GFP+ cells which was further confirmed by the hematopoietic marker CD45 were detected. To further include an extra-cardiac origin of the GFP+ cells C57Bl/6 hearts that underwent 6th of ischemia were cervically transplanted into transgenic recipients and did not exhibit GFP+ cells after one week. However, we could show that ectopic transplantation of ischemic Nkx2.5 CE GFP hearts indeed led to the appearance of about 1% GFP+ cells as seen even after MI. In culture the isolated GFP+ cells reveal a round, stem-cell like shape.

Conclusion: By identifying and characterizing an embryonic Nkx2.5 CE+ cell population, re-emerging after myocardial ischemic injury in the adult mouse, we detected a cellular source with progenitor properties that may be involved in endogenous cardiac repair mechanisms.

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Endogenous cardiac lineage progenitor cells regenerate myocardium in mammalian heart failure

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Recent studies have identified populations of cardiac progenitor cells that contribute to developmental cardiogenesis. Marked by the expression of a key cardiac transcription factor, Nkx2.5, these cells are competent to differentiate into cardiomyocytes, smooth muscle cells, and to a limited extent, endothelial cells. We hypothesized that these cardiac progenitor cells might mediate cardiac regeneration in the mammalian heart failure. To test this hypothesis, we generated a Nkx2.5 conditional knockout mouse model, which interestingly re-emerges after myocardial ischemia in the adult heart.

To create an animal model of non-ischemic heart failure, we designed a genetic cardiomyocyte-depletion model by interbreeding inducible myo-Cre transgenic mice with ROSA-DTA mice. After the animal received tamoxifen i.p. injection, a percentage of cardiomyocytes were depleted by Diphtheria toxin fragment A (DTA). The frequency of GFP+ cells in explanted hearts after ischemic injury was analyzed by FACS and subsequent lineage tracing for the negative cardiac cell populations were isolated. Gene expression analysis for candidate genes was performed by qRT-PCR. Results were confirmed by immunostaining and subsequent FACS analysis. Furthermore, heterotopic transplantation of Nkx2.5 CE GFP and C57Bl/6 mouse hearts (6th old ischemia) into an Nkx2.5 CE GFP background was performed.

Results: About 1% GFP+ cells re-emerged 5 to 9 days post MI in hearts of Nkx2.5 CE GFP mice. Even in mice up to one year GFP+ cells could be detected (<0.5%). Gene expression analysis revealed high mRNA levels of several cardiac and cardiac developmental marker (e.g. Tbx1, Bmp4, Wnt1, Tbx5, Tbx18) in the GFP+ compared to the GFP negative cells. GFP+ cells lack Tnnt2 expression which excludes a cardiomyocyte origin by de-differentiation. Interestingly, the stem cell marker Sca1 is expressed on about 90% of the GFP+ cells which was further confirmed by the hematopoietic marker CD45 were detected. To further include an extra-cardiac origin of the GFP+ cells C57Bl/6 hearts that underwent 6th of ischemia were cervically transplanted into transgenic recipients and did not exhibit GFP+ cells after one week. However, we could show that ectopic transplantation of ischemic Nkx2.5 CE GFP hearts indeed led to the appearance of about 1% GFP+ cells as seen even after MI. In culture the isolated GFP+ cells reveal a round, stem-cell like shape.

Conclusion: By identifying and characterizing an embryonic Nkx2.5 CE+ cell population, re-emerging after myocardial ischemic injury in the adult mouse, we detected a cellular source with progenitor properties that may be involved in endogenous cardiac repair mechanisms.

THE BATTLE OF MODIFYING CARDIOVASCULAR RISK FACTORS: KEEP GOING STRONG

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Fifteen years of statin pharmacogenetics: a system review

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Purpose: Statins lower LDL cholesterol (LDLc) and thereby reduce the risk of cardiovascular events. The search for genetic variation in LDLc response has been the focus of many studies. We conducted a systematic review covering all published research worldwide in genetic variation influencing statin response. We evaluated the evidence of these pharmacogenetic associations.

Methods: PubMed was systematically searched to retrieve publications reporting on the pharmacogenetics of statins. Two separate outcomes were considered of interest: modification of LDLc response and modification of risk for cardiovascular events; publications investigating other outcomes were excluded. Results: 597 publications were identified in the initial search, of which 139 relevant to applying the search criteria. The remaining publications varied widely on design, statistical procedures, selection of participants, and reporting of results. SNPs in CETP, APOE, HMGCR, SLC0181, ABCDL and LDLR were investigated most often in the candidate gene studies, with 15 or more publications each. In these candidate gene studies, more than 150 loci were claimed to be associated with statin response, but less than 10% of these associations were positively replicated and none of these showed conclusive evidence. For example, a SNP in KIF6 (rs20455) was shown to affect clinical statin benefit, and successful replicated once, but 8 subsequent studies did not find this association. Five genome-wide association (GWAS) studies were performed, all investigating modification of the lipid-lowering effect. SNPs in APOE, LPA and ABCG2 reached genome-wide significance and were replicated. Effect sizes found in GWAS were modest, approximately 2-3% of the usual LDLc-response to statins.

Conclusions: While many papers have been published on statin pharmacogenetics, there are only three associations of SNPs with LDLc-response to statins with strong evidence. None of the investigated SNPs consistently affect clinical outcome. A more standardized way of reporting results will facilitate efforts to replicate findings. Larger samples and meta-analyses of genome-wide association studies might increase the number of associated loci. However, as effect sizes found thus far are generally small, at this moment there is no role for genetic testing in clinical practice to guide statin treatment.

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ISIS APO(a)Rx, an antisense inhibitor to apolipoprotein(a), reduces plasma levels of Lp(a) and oxidized phospholipids/apoB-100 in healthy volunteers

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Plasminogen activator (PA) and proto-oncogene (a) is a protease that plays a key role in the coagulation cascade and fibrin formation. APO(a) is a genetically variant molecule of apolipoprotein(a), a inhibitor of the PA activity. Antisense oligonucleotides (ASOs) are therapeutic agents designed to target mRNA overexpression in a variety of disease states. ISIS APO(a)Rx specifically reduces the hepatic biosynthesis of APO(a) via inhibition of the APO(a) gene in the human Phase 2b trials, it is assessed the safety, tolerability, and pharmacodynamics of ISIS-APO(a)Rx in healthy volunteers. In this blinded, single (SAD) and multiple ascending-dose (MAD) study, healthy subjects, 18 to 65 years, were randomly assigned to receive ISIS-APO(a)Rx or placebo (normal saline) subcutaneous (SC) injections. In the SAD portion of the study, subjects received a single injection (50, 100, 200, or 400 mg; n=10/cohort, randomized 8 active:2 placebo). Lp(a) and other lipoprotein levels were monitored during the dosing phase and for an additional 12 weeks thereafter, Plasma levels of oxidized phospholipids bound to apoB-100 lipoproteins (OxPL/apoB) and apo(a) isoforms were also determined. In the MAD portion of the study, subjects received six subcutaneous injections over four weeks; a loading regimen of three doses of the first week followed by once weekly dosing over three weeks, (100, 200, or 300 mg; n=10/cohort, randomized 8 active:2 placebo). Lp(a) and other lipoprotein levels were monitored during the dosing phase and for an additional 12 weeks thereafter. Plasma levels of oxidized phospholipids bound to apoB-100 lipoproteins (OxPL/apoB) and apo(a) isoforms were also determined. There was no significant safety profile associated with ISIS-APO(a)Rx treatment. Adverse events were mostly mild, consisting mainly of injection site reactions and occasional flu-like symptoms which predominantly occurred at the highest dose. ISIS-APO(a)Rx pharmacodynamic results showed robust and durable,
dose-dependent reductions in Lp(a) levels and was equally efficacious regardless of individual starting plasma concentrations. Mean percentage change from baseline Lp(a) values in the 100, 200 and 300 mg multiple-dose groups were 38%, 62%, and 83%, respectively, two weeks after the last dose (p < 0.001). Importantly, suppression of Lp(a) produced a concordant reduction in levels of plasma OxPL-apoB. This finding in human study demonstrates potent, durable, dose-dependent, and selective reductions of plasma Lp(a) and OxPL-apoB. Maximal reductions of Lp(a) and OxPL-apoB of up to 95% and 91% respectively were observed at the highest administered dose. A Phase 2 trial in patients with high levels of Lp(a) is planned to commence in June 2014.

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Dual renin-angiotensin blockade does not improve cardiac-renal outcomes - a meta-analysis of randomized controlled trials
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Background: Dual renin-angiotensin (RAS) blockade has been shown to reduce surrogate endpoints like proteinuria but its long term effect on hard cardiac-renal endpoints is not clear. We performed a meta-analysis to evaluate the effect of dual blockade compared to single agent on long term cardiac-renal outcomes.
Methods: A systematic search of electronic databases was performed to identify randomized controlled trials (RCT) evaluating the effect of dual RAS compared to single RAS blockade on clinical end points. Studies with less than 1 year follow up and non-heart failure patients were excluded. A random effect meta-analysis was performed to summarize the relevant clinical end points.
Results: Three RCTs with a total of 35,629 patients (13,500 dual; 22,129 single) met the inclusion criteria. Included patients either had diabetic nephropathy or atherosclerotic cardiovascular disease. Dual blockade was associated with higher risk of all cause mortality and acute kidney injury. There was no reduction in progression to end stage renal disease, myocardial infarction, stroke or heart failure with use of dual blockade compared to single agent.

Conclusions: There is no benefit and potential harm of use of dual RAS blockade in high risk patients compared to single agent RAS blockade.

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Long-term effect of antihypertensive drugs on the risk of New-onset Atrial Fibrillation: a longitudinal cohort study
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Antihypertensive drugs have been linked to new-onset atrial fibrillation (NAF); however, data on the effect of these drugs on the development of NAF in hypertensive patients has not been well determined. The aim was to investigate the association between antihypertensive drugs and NAF in a population. We examined the association between all antihypertensive drug therapy and the risk of NAF in a population-based study. The sample consisted of 47,682 hypertensive patients. Our data were taken from claim forms provided to the central region branch of the Bureau of National Health Insurance from January 2005 to December 2010. Prescriptions for antihypertensive drugs before the index date were retrieved from a prescription database. We estimated the hazard ratio (HR) of NAF associated with antihypertensive drug use; non-NAF subjects served as the reference group. The risk of NAF after adjusted age and sex was higher among users of diuretics (HR, 1.39; 95% confidence interval [CI], 1.06-1.82) than among non-users. Patients who take angiotensin converting enzyme (ACE) inhibitors (HR, 0.79; 95% CI, 0.65-0.97) are at a lower risk of developing NAF than non-users. Angiotensin receptor blockers, alpha-blockers, beta-blockers, and calcium channel blockers were not associated with risk of NAF. The results of this study suggest that hypertensive patients who take ACE inhibitors are at lower risk of NAF. Diuretics were associated with a significant increase in the risk of NAF.

NEW INSIGHTS IN PULMONARY ARTERIAL HYPERTENSION IN CONGENITAL HEART DISEASE

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Impact of disease targeting therapies on quality of life and survival in patients with Eisenmenger syndrome: results of a Markov multi-state model of longitudinal data in 297 patients
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Background: Oral disease targeting therapies (DTT) have been shown to improve symptoms and exercise capacity in Eisenmenger syndrome patients. The long-term impact of DTT on quality of life (QoL) and survival is not well understood. These aspects are of interest given the costs of DTT and to enable health economic evaluations using a lifetime horizon. We aimed to define a suitable Markov multistate model of the condition and populate it with transition probabilities based on a unique dataset including a large number of adult Eisenmenger patients.
Methods and results: A Markov Model based on patients’ NYHA class was build. To populate the model with transition probabilities we used a dataset including all medical contacts with Eisenmenger patients between 2000 and 2011. The data included information on all 1,996 medical encounters of 297 Eisenmenger patients. A continuous-time Markov multi-state model was fitted by maximum likelihood estimation from transition probabilities (mean 1.8 life-years gained) or operating (CAMPHOR score) for pulmonary hypertension were used. Patients without DTT had higher probabilities of death compared to DTT. This is illustrated in the Figure. In addition the simulation shows that approx. 80% of patients treated with DTT improved from NYHA class III to class II, while this was a rare phenomenon in the absence of DTT.

Conclusions: DTT were associated with significant gains in life years (8.7 years) and quality adjusted life years (8.4 QALYs). These are higher than life years gained for those with severe CHD and survival of patients with Eisenmenger syndrome. The probability of targeting disease specific myocardial revascularization (approx. 1 year). While these numbers await validation in prospective studies these results should be useful for counselling patients and for future health economic evaluations.

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Pulmonary arterial hypertension in patients with congenital heart disease: overview over clinical symptoms, medical therapy and prognosis based on data from the German national registry of congenital heart disease

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Background: Approximately 5-10% of patients with congenital heart disease (CHD) develop pulmonary arterial hypertension (PAH). Patients with PAH have been found to be affected by an increased morbidity and mortality. We provide an overview over the spectrum of disease, clinical presentation, therapy and outcome based on the data of the German National CHD Registry.

Methods and results: Patients with PAH-CHD were systematically identified from the German National CHD Registry. We included CHD patients with PAH > 40% WHO category 4 PAH after adult surgery or unoperated patients. Patients with isolated postcapillary pulmonary hypertension, patients in whom pulmonary pressures normalized after timely surgical intervention, patients with idiopathic PAH or patients with persistent pulmonary hypertension of the newborn were excluded. Presence of PAH was defined in accordance with current recommendations. We collected data on clinical symptoms, exercise limitation, medical therapy and outcome in this population. Overall, 184 patients were included (mean age 24.6±14.9 years, 58.7% females). Of these, 108 patients had ES. Eisenmenger patients were on average approximately 10 years older compared with the remaining patients (mean age 29.3±12.8 years vs. 17.8±15.2 years, p<0.001). Overall, 61.9% of patients were in NYHA class III. The mean 6-minute walk test distance was 382±122 m (ES 368±118 m). Overall, 44% of patients (ES 51%) were treated with advanced PAH specific therapies (69.9% Bosentan, 25.3%). Sildenafil, while 14% were on a dual medical therapy. In addition, 51% of patients received heart failure medication. Only 16% of patients were treated with oral anticoagulants (ES 15%), while 22% (ES 25%) of patients received Aspirin. The mean survival rate at 1, 3, 5 and 10 years of follow-up was 94.8%, 87.7% and 64% in the entire cohort, whereas survival was even worse in ES patients (survival rates 93%, 76%, 66% and 49% at 1, 3, 5 and 10 years of follow-up).

Conclusions: Despite the availability of widespread and timely surgical correction for CHD patients in Germany, we could identify a considerable number of PAH-CHD patients with ES. The majority of patients are asymptomatic and have a markedly reduced subjective exercise capacity. Interestingly, a large proportion of patients was found to be managed with heart failure medication and especially Aspirin, which is not supported by current recommendations. In addition, our data illustrate the poor prognosis of PAH-CHD patients despite the use of disease targeting therapies in 44% of patients.

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Poor survival prospects of treatment naïve Eisenmenger patients in the current era - a systematic review and report of own experience

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Background: Despite representing the extreme form of congenital heart disease with pulmonary hypertension, Eisenmenger patients are believed to have favorable survival prospects. We investigated survival based on a systematic review of the literature and re-analysis of data. Specifically we tested the hypothesis that previous publications may have been subject to immortal time bias, confounding such survival analyses.

Methods and results: A systematic review of the literature was performed to identify outcome data in treatment naïve Eisenmenger patients and standardized mortality ratios (SMRs) were calculated. To combine the short term survival data from various studies a meta-analytic summary of survival curve data was performed based on fitting a multivariate, random mixed effects model to in-minus-in-transformed survival proportions at multiple time points. In addition, we used a contemporary cohort of 219 treatment naïve EM patients from the own institution as a comparison group. Overall, 12 studies were identified, including a total of 1,131 patients. Only one study dealt appropriately with immortal time bias in this setting. All other studies did not account for this effect, thus overestimating survival prospects of Eisenmenger patients by up to 20 years. After accounting for this effect we found high SMRs (ranging between 33 and 76) and no evidence of survival or survival prospects of current era Eisenmenger patients worse than those seen in the 1970s, 80s and 90s. Only, a historic Eisenmenger-cohort from the 1950s/60s had worse survival. In addition, 8 studies provided survival data for Eisenmenger patients during short-term follow up. From these, survival rates were combined to obtain average survival rates. Overall, the predicted 10-year survival of treatment naïve Eisenmenger patients was in the range of 60-70%

Conclusions: Using a systematic review of the literature and analysis of own data, the current study highlights the relatively poor survival prospects of untreated Eisenmenger patients. 10-year mortality rates ranging between 30-40%. In addition, the relative mortality rate in comparison to the general population is 30 to 70-times higher than expected. This high mortality is true for, both, contemporary Eisenmenger patients and those reported in the literature up to four decades ago, with no obvious improvements in survival over time. These results support the use of disease targeting therapies but also call for rethinking the dogma of benign survival prospects of Eisenmenger patients and a more aggressive approach trying to avoid the development of the condition.

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Mean platelet volume levels predict pulmonary artery hypertension in patients with atrial septal defect

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Introduction: A few reports have shown increased platelet aggregation and activation in patients with pulmonary artery hypertension (PAH). Mean platelet volume (MPV) is a simple and easy method of assessing platelet function. We aimed to investigate the mean platelet volume levels in patients with atrial septal defect (ASD) and the association between MPV levels and pulmonary artery hypertension.

Method: One hundred and forty consecutive patients (42 male and mean age 35±9) and forty healthy controls (15 male and mean age 35±4) were enrolled in the study between December 2008 and February 2011.

Result: The ASD group demonstrated a significantly higher right ventricular size and pulmonary artery pressure than the control group (42±4 mm vs. 36±3 mm and 43±12 mmHg vs. 32±11 mmHg; p<0.001 and p<0.001, respectively). MPV levels were higher in the ASD group than control group (9.3±1.2 fl vs. 8.6±0.8 fl; p<0.001). There was a significant positive correlation between MPV and systolic pulmonary artery pressure (PAP) (r=0.542 and p<0.001) in the ASD group. MPV was also significantly correlated with right ventricular size but not ASD diameter in the ASD group (r=0.441, p<0.001 and r=0.126, p=0.268, respectively).

Conclusion: In the present study, we found that MPV levels, an indicator of
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Use of IV iron in cyanotic patients with congenital heart disease and/or pulmonary hypertension


Introduction: An increase in haemoglobin (Hb) is common in patients with cyanosis secondary to congenital heart disease (CHD) and/or pulmonary arterial hypertension (PAH). It is aimed at increasing oxygen delivery but requires adequate iron stores. Iron deficiency is common in these patients and the optimal method of supplementation remains controversial, with fears of excessive erythropoiesis and hyperviscosity. We describe our experience using IV ferrous carboxymaltose in this setting.

Methods and results: A total of 45 consecutive adult patients were treated over 2 years in a single centre: 22 (48.9%) male, mean age 41.8±13.1 years. Eisenmenger syndrome was present in 25 (55.6%), other PAH related to CHD in 12 (26.7%), other cyanotic CHD (without PAH) in 6 (13.3%) and other types of PAH with cyanosis in 2 (4.4%). Baseline Hb was 14.9±3.8 g/L and haematocrit (Hct) 40.4±6.12. Baseline ferritin was 51.1±87.1 µg/L and transferrin saturation was 111.5±3.3%. An average 722.2±251.3 mg of IV iron was administered: 500 mg in 25 (55.6%), and 1000 mg dose in 20 (44.4%). A significant improvement in average Hb, Hct, ferritin and transferrin saturation was observed after a median follow-up of 91 [IQR48-156] days (Figure). No cases of excessive erythropoiesis (Hct) > 0.46 (WHO-FC) or hyperviscosity. We describe our experience using IV ferrous carboxymaltose in this setting.

Conclusion: IV iron carboxymaltose at a dose between 500 and 1000mg appears to be safe in iron deficient patients with cyanosis due to congenital heart disease and/or PAH. Further studies are needed to confirm our findings.

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Definition and validation of clinical worsening as a composite endpoint in pediatric pulmonary arterial hypertension

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Purpose: Clinical worsening (CW) is frequently used as composite endpoint in studies in pulmonary arterial hypertension (PAH). In pediatric PAH, no definition of CW has currently been validated. The various components that make up the composite endpoint have to be validated for their predictive value regarding the hard endpoints death and lung-transplantation (LTx). We aimed to evaluate a proposed definition of CW in pediatric PAH, by assessing the event rate and prognostic value of (1) each separate component endpoint and (2) the composite CW endpoint.

Methods: Seventy consecutive, treatment-naive PAH-patients from the Dutch National Network for Paediatric Pulmonary Hypertension in whom PAH-targeted therapy was initiated between January 2000 and December 2013 were included and underwent standardized follow-up. As part of this prospective registry, the follow-up CW components were registered: (1) death, (2) LTx, (3) non-elective, PAH-related hospitalizations (4) IV-prostanoid initiation and (5) functional deterioration. Functional deterioration was defined as worsening of WHO-FC functional class (WHO-FC) or > 15% decrease in 6-minute walk distance (6MWD). The event rate per 100 person years (100PY) was calculated for each component and for the composite of these. Furthermore, the predictive value of the CW components 3, 4 and 5 for death/LTx was assessed, using time-dependent Cox regression analysis.

Results: During a total observation time of 276 person years in 70 patients, 40 died, 10% underwent LTx, 54% were hospitalized because of PAH (once or repeatedly), 22% received IV-prostanoids. WHO-FC and 71% had functional deterioration (once or repeatedly). The event rates of these separate components were 10.1, 2.5, 21.4, 9.4 and 48.1 per 100PY, respectively. The composite CW endpoint occurred in 59/70 patients, with an event rate of 91.5 per 100PY. The occurrence of either PAH-related hospitalization or IV-prostanoid initiation or functional deterioration were associated with death/LTx (p < 0.0001 for each component). The first occurrence of one of the combined components, was also associated with death/LTx (HR 19.1, p < 0.0001). In this pediatric cohort, 1-, 3- and 5-year freedom from death/LTx was 76%, 64% and 56%, respectively. 1-, 3-, and 5-year freedom from CW was 43%, 22% and 17% respectively.

Conclusion: PAH-related hospitalization, IV-prostanoid initiation, deterioration of WHO-FC and decrease in 6MWD have relatively high event rates in pediatric PAH and are associated with death/LTx. Therefore, these events qualify for a composite endpoint “clinical worsening”, that appears valid in children with PAH.

NEW PERSPECTIVES ON ST-ELEVATION MYOCARDIAL INFARCTION

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The randomized Physiologic Assessment of Thrombus Aspiration in Patients with ST-segment Elevation Myocardial Infarction (PATA STEMI) Trial


Background: Routine thrombus aspiration is superior to conventional primary percutaneous coronary intervention (PCI) in terms of improved myocardial perfusion and microcirculatory resistance (IMR). However, myocardial perfusion after thrombus aspiration has not been evaluated by a quantitative index of microcirculatory resistance (IMR).

Methods: We performed a randomized, controlled clinical trial to evaluate improvement in minimal thrombus aspiration and microcirculatory resistance after primary PCI in 128 patients with the first STEMI randomly assigned to thrombus aspiration or conventional PCI group before coronary angiography. The primary endpoint was defined as a mean value of corrected IMR in thrombus aspiration compared to conventional PCI group. Myocardial perfusion grade, resolution of ST-segment elevation, enzymatic infarct size, left ventricle remodeling and rate of adverse cardiac events were secondary endpoints.

Results: Manual thrombus aspiration, as compared with conventional PCI, resulted in significantly lower corrected IMR (27.5±16.8 U vs. 39.9±32.7 U, p < 0.0087). Treatment with thrombus aspiration, as compared with conventional PCI, resulted in similar rates of myocardial perfusion grade 0 or 1 (21.5% vs 28.6%, RR 0.75; 95% CI, 0.41 to 1.38; P=0.36) and complete resolution of ST-segment elevation (61.5% vs. 49.2%; RR 1.25; 95% CI, 0.91 to 1.71, P=0.16), with lower infarct size (AUC CK 26157±40090,0U vs. 32013±52676,1U, p=0.028) and trend toward greater percent mean decrease in WMSI at follow-up (0.082 vs. -0.008, P<0.094). The rate of adverse events (death, myocardial infarction, stroke or hospitalization for heart failure) was similar 4.6% vs. 11.1%, P=0.23. In a multiple regression model with the log-transformed IMR as dependent variable, after adjusting for clinical, angiographic and procedural variables, thrombus aspiration remained a strong independent predictor of lower IMR (27.14 U; 95% CI, 23.79 to 39.05 U, vs. 36.11 U; 95% CI, 30.74 to 42.41 U, P=0.0078). Histopathological examination confirmed successful thrombus aspiration in 89.6% of patients.

Conclusions: Manual thrombus aspiration reduces microcirculatory resistance indicating better myocardial perfusion compared to conventional PCI in patients with STEMI. Manual thrombectomy aspiration tended towards improved clinical outcome.
46 (56.1%) lesions with a median malapposition area at index and follow-up of 0.26 mm² (IQR 0.12-0.59) and 0.10 mm² (IQR 0.05-0.23), respectively. Newly-acquired ISA (NA-ISA) was detected in 39 (34.2%) EES-treated lesions. While NA-ISA was localized mostly at the stent body (82.0%), persistent ISA was most (78.0%) prominent at the stent edges (p=0.001). No differences in clinical-procedural characteristics and in culprit lesion phenotypes (rupture lesion) were observed between patients with and without NA-ISA. Conversely, NA-ISA was associated with longer underlying thin cap fibroatheroma (3.20 mm vs. 1.80 mm, p=0.032) and larger volume of the red thrombus (0.69 mm³ vs. 0.00 mm³, p=0.020), respectively, as compared with non NA-ISA. The rate of post-dilatation after EES implantation was less frequent in lesions who developed NA-ISA (17.0% vs. 49.0%, p=0.021). At 9-month follow-up NA-ISA was associated with less frequent in-hospital and long-term mortality OR (0.63, 95%CI 0.22-1.22; p=0.17). The rate of manual thrombus aspiration after such intervention as Class IIa in ESC Guidelines. However the recent TASTE trial showed lack of clinical benefit using routine TA. Therefore, we aimed to evaluate the impact of manual thrombus aspiration on in-hospital mortality in “real world” settings.

Methods: We performed an observational, retrospective study, using data from the National Registry of Interventional Cardiology on consecutive patients with ST-elevation myocardial infarction treated with P-PCI, registered between January 2006 and December 2012. Demographic and clinical characteristics of the population were evaluated. Our primary outcome was in-hospital mortality. Descriptive statistics were used to characterize the population. Prognostic data were analyzed using logistic regression in order to estimate outcomes’ odds ratio (OR) and 95% confidence intervals (95%CI).

Results: We assessed data for 9458 STEMI patients that undergone P-PCI during the study period, included in the National Registry of Interventional Cardiology. The yearly proportion of TA performed in patients with STEMI increased significantly from 2006 (3.1%) until 2012 (46.1%). Overall about 35.0% of STEMI patients were treated with TA (3311 patients). Patients treated with TA were slightly younger (60 [SD 13] vs. 63 [SD 13] years; p=0.002), had a higher proportion of diabetic patients (18.7% vs. 24.0%, p=0.001). Manual thrombus aspiration group also had a higher proportion of TAMI 0 coronary flow before P-PCI (68.8% vs. 45.4%, p<0.001), however post P-PCI TIMI 3 coronary flow was more prevalent in non-TA group (85.7% vs. 90.0%, p<0.001).

Regarding the primary outcome, TA group was associated to a non-significant decrease of in-hospital mortality (2.2% vs. 2.8%; crude OR 0.76, 95%CI 0.55-1.05; p=0.09). After multivariable adjustments TA was not associated to decreased risk of in-hospital mortality OR (0.63, 95%CI 0.22-1.22; p=0.17).

Conclusions: The use of manual thrombus aspiration in STEMI has been increasing but it is not currently used by routine, TA did not show significant impact in the short-term prognosis of STEMI patients that underwent P-PCI, in accordance with TASTE trial.

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Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio combination can predict prognosis in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention

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Objectives: The aim of this study was to assess the effect of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) combination in predicting in-hospital and long-term mortality in patients undergoing primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI).

Methods: 2518 patients with STEMI undergoing primary angioplasty were enrolled. Cut-off values for NLR and PLR were calculated with receiver-operating characteristics curves. If both PLR and NLR were above the selected threshold values, patients were classified as “high risk”. If either PLR or NLR were above the threshold individually, patients were classified as “intermediate risk”. If both levels were under threshold values, patients were classified as “low risk”. Effect of these risk groups and other possible prognostic factors on mortality was evaluated by a stepwise multivariate Cox-Regression model.

Results: Median follow-up time was 22 months. Cut-off points were 162.31 for PLR and 6.65 for NLR. High risk (n=693) and intermediate risk (n=545) groups had a significantly incidence of in-hospital and long-term mortality (72.4%, 4%, vs. 7%, P<0.001; 14.1%, 9.5%, vs. 4.5%, P<0.001, respectively). Intermediate risk group (HR: 1.492, 95%CI 1.022-2.178, p=0.038) and high risk group HR (1.845, 95%CI 1.313-2.594, p<0.001) was found as an independent predictor of in-hospital and long-term mortality.

Predictors of all cause mortality

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
<th>Multivariable</th>
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<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Age ≥70, years</td>
<td>4.577 (3.482-6.016)</td>
<td>0.001*</td>
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<tr>
<td>Diabetes mellitus (+)</td>
<td>3.374 (2.571-4.429)</td>
<td>0.001*</td>
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<tr>
<td>Killip class &gt;1</td>
<td>9.761 (2.889-33.072)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.644 (1.505-1.786)</td>
<td>0.001*</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.991 (0.986-0.996)</td>
<td>0.001*</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>0.742 (0.605-0.792)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Intermediate risk PLR-NLR</td>
<td>2.107 (1.449-3.064)</td>
<td>0.001*</td>
</tr>
<tr>
<td>High risk PLR-NLR</td>
<td>3.172 (2.249-4.389)</td>
<td>0.001*</td>
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LVES: left ventricular ejection fraction; LDL, low density lipoprotein; PLR, platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio.

Conclusion: Combination of PLR and NLR can be a useful parameter for prediction of in-hospital and long term mortality of STEMI patients undergoing primary PCI.

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Thrombus aspiration in patients with ST-elevation myocardial infarction: results of a national registry of interventional cardiology

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Introduction: Manual thrombus aspiration (TA) during primary percutaneous coronary intervention (P-PCI) has been associated to blood flow improvement and resolution of ST-segment elevation. A previous study [TAPAS] suggested a survival benefit for patients treated with TA and supported the current recommendation for such intervention as Class IIa in ESC Guidelines. However the recent TASTE trial showed lack of clinical benefit using routine TA. Therefore, we aimed to evaluate the impact of manual thrombus aspiration on in-hospital mortality in “real world” settings.

Methods: We performed an observational, retrospective study, using data from the National Registry of Interventional Cardiology on consecutive patients with ST-elevation myocardial infarction treated with P-PCI, registered between January 2006 and December 2012. Demographic and clinical characteristics of the population were evaluated. Our primary outcome was in-hospital mortality. Descriptive statistics were used to characterize the population. Prognostic data were analyzed using logistic regression in order to estimate outcomes’ odds ratio (OR) and 95% confidence intervals (95%CI).

Results: We assessed data for 9458 STEMI patients that undergone P-PCI during the study period, included in the National Registry of Interventional Cardiology. The yearly proportion of TA performed in patients with STEMI increased significantly from 2006 (3.1%) until 2012 (46.1%). Overall about 35.0% of STEMI patients were treated with TA (3311 patients). Patients treated with TA were slightly younger (60 [SD 13] vs. 63 [SD 13] years; p=0.002), had a higher proportion of diabetic patients (18.7% vs. 24.0%, p=0.001). Manual thrombus aspiration group also had a higher proportion of TAMI 0 coronary flow before P-PCI (68.8% vs. 45.4%, p<0.001), however post P-PCI TIMI 3 coronary flow was more prevalent in non-TA group (85.7% vs. 90.0%, p<0.001).

Regarding the primary outcome, TA group was associated to a non-significant decrease of in-hospital mortality (2.2% vs. 2.8%; crude OR 0.76, 95%CI 0.55-1.05; p=0.09). After multivariable adjustments TA was not associated to decreased risk of in-hospital mortality OR (0.63, 95%CI 0.22-1.22; p=0.17).

Conclusions: The use of manual thrombus aspiration in STEMI has been increasing but it is not currently used by routine, TA did not show significant impact in the short-term prognosis of STEMI patients that underwent P-PCI, in accordance with TASTE trial.
314 | BENCH
Neurohormonal response to Heated water-based Exercise training in chronic stable HF: results from the HEx Trial
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Background: Heated water-based exercise training (HEx) reduces office and ambulatory blood pressure in patients with resistant hypertension. However, no data are available concerning the mechanisms that promote these effects on blood pressure after heated water exercise. This study examines the effects of HEx in neurohormonal response in resistant hypertensive patients.

Design and methods: This is a subanalysis of the parallel randomized HEx trial. 32 patients aged 53±6 years with resistant hypertension (antihypertensive drugs 4-6) were allocated in two groups (HEx n=16 and control n=16). We analyzed the changes on office blood pressure, and on circulating concentrations of catecholamines, renin, aldosterone, endothelin-1 and nitric oxide from baseline. The HEx training was performed for 60-minutes sessions in a heated pool (32°C), three times a week for 12 weeks. The HEx protocol consisted of calisthenic exercises and walking inside the pool. The control group was asked to maintain habitual activities.

Results: Office BPs reduced significantly after heated water exercise (systolic from 160±28 to 136±14 and diastolic from 83±15 to 77±11 mmHg), HEx decreased catecholamines (from 720±280 to 306±184 ng/ml, p<0.0001), renin (from 35±14 to 3.4±3.4 ng/ml, p<0.0001), aldosterone (from 101±52 to 78±18 pg/ml, p<0.01), endothelin-1 from (41±15 to 26.9 pg/ml) and increased nitric oxide (from 25±8 to 75±24 pg/ml, p<0.0001). The control group after 12 weeks did not present any changes on office systolic and diastolic BPs and neurohormones. All patients completed the protocol and there were no clinically relevant changes during the intervention.

Conclusion: HEx improves the neurohormonal response in patients with resistant hypertension. This may help to establish the possible mechanisms involved in reduction of BPs with HEx. Thus, we should consider the possibility of HEx associated to treatment of hypertensive patients who do not achieve appropriate blood pressure control, in order to avoid the early onset of fatal cardiovascular events.

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Functional electrical stimulation of lower limb muscles reduces heart failure hospitalizations in chronic heart failure
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Purpose: Functional electrical stimulation (FES) of lower limb muscles is an alternative method of training that improved physical status, exercise capacity and quality of life in patients with heart failure (HF). However, its effects on long-term outcome have not yet been investigated in HF.

Methods: We randomized 120 patients, 68% male, aged 71±7 years, with chronic stable HF (New York Heart Association (NYHA) class II/III (63%/37%), left ventricular ejection fraction (LVEF) 28%-51%,) to a 6-week FES training program or placebo. Patients were followed for up to 19 months for death or hospitalization for HF.

Results: No differences in gender, age, NYHA class, LVEF or HF medication were observed between the 2 groups. During a median follow-up of 383 days, 14 patients died (12%, 11 cardiovascular deaths, 3 non-cardiac deaths), while 40 patients were hospitalized for HF (33%). Compared to placebo, FES was followed by a lower occurrence of death or hospitalization for HF (unadjusted Hazard Ratio (HR) 0.45, 95% confidence interval (CI) 0.25-0.83, p=0.010; log-rank p=0.008, Figure), a difference that remained significant after adjustment for age, gender, baseline NYHA class and LVEF (adjusted HR=0.24, 95%CI=0.12-0.48, p<0.001). Regarding the individual endpoints, the occurrence of death did not differ between the two groups (log rank test p=0.680), while the risk of hospitalization was significantly lower in the FES group (HR=0.43, 95%CI=0.21-0.78, p=0.007, log rank test p=0.005), a difference that remained significant after adjustment for the above variables (HR=0.22, 95%CI=0.10-0.46, p<0.001).

Conclusions: In chronic HF, FES is followed by a favorable long-term outcome, which is driven by a lower risk of hospitalization for HF. The beneficial long-term effects of this alternative method of training warrant further investigation.
Conclusions: before and after the exercise period in the two groups. DM (p < 0.01) had higher triangle index value at post-CR AECGM (p < 0.001) in the whole group, and significant improvement was present in A) Inter-subsets comparison In pts with DM, both baseline (p < 0.01) and post-CR (p < 0.05) DC, rMSSD and triangle index values were lower. They had lower baseline SDNN value (p < 0.01). In pts over 60 years of age baseline DC (≥ 60 vs < 60 years), baseline DC (< 45 vs 45 – 49.5 ms) was considered abnormally low. Methods: 114 patients (pts, mean age 58 years, 24 females, mean LVEF 49%) undergoing 12-week ambulatory cardiac rehabilitation (CR) initiated within month after acute coronary syndrome (ACS) were studied. AECGM and exercise test (ExT) were performed twice – before (baseline) and after CR (post-CR) to determine HRV parameters, DC and exercise capacity and identify indicators of their improvements. We sought for differences between patients regarding diabetes mellitus (DM), age ≥ 60 or < 60 years, baseline DC (< 45 vs 45 – 49.5 ms). We evaluated usefulness of baseline DC as predictor of CR outcome. DC was calculated using custom software. Results: A) Inter-subsets comparison In pts with DM, both baseline (p < 0.01) and post-CR ExT were lower (p < 0.05). Pts with baseline DC > 45 ms were less likely to have DM (p < 0.05) and had higher exercise capacity at post-CR ExT. Pts with abnormal DC had higher triangle index value at post-CR AECGM (p < 0.001). B) Improvement depending on subsets. After CR exercise capacity rised from 8.8 to 9.8 MET (p < 0.0001) in the whole group, and significant improvement was present in all subsets of patients. Exercise tolerance was significantly improved in pts with normal baseline DC (p < 0.0001). However, ROC analysis showed that baseline DC value could not predict improved ExT result. Post-CR values of SDNN, rMSSD and triangle index did not change significantly compared to baseline. However, in pts with abnormal baseline DC there was a significant (p < 0.01) improvement in triangle index value. ROC analysis showed that patients with baseline DC < 5.5msms had the best chance of significant improvement in SDNN (baseline 96 vs post-CR 115 ms), rMSSD (17 vs 20 ms) and triangle index (25 vs 31), AUC 0.633, 95% CI 0.529-0.728. Conclusions: CR after ACS improves exercise capacity only in patients with initially normal DC, regardless of their age or diabetic status. HRV parameters improve only in some patients and baseline DC < 5.5msms may be used as a predictor of SDNN, rMSSD and triangle index improvement in patients undergoing CR.

Effects of functional electrical stimulation of peripheral muscles on body composition, bone mineral density and catabolic/anabolic imbalance in chronic heart failure

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Purpose: Functional electrical stimulation (FES) is a safe and beneficial alternative to physical training in chronic heart failure (CHF) patients unwilling or unable to exercise that improves symptoms, quality of life and exercise capacity. We sought to determine whether FES affects body composition, bone mineral density and catabolic/anabolic imbalance in CHF.

Methods: Thirty stable CHF patients (67% male, aged 68 ± 8 years) were randomized to a 6-week FES training program or placebo. All patients underwent dual-energy X-ray absorptiometry (DEXA) and bone density levels of adiponectin, leptin and ghrelin at baseline and after completion of training protocol.

Results: FES induced a significant increase in lean body mass (mean change = 1.6 ± 0.53 vs -1.07 ± 0.21 kg, F = 54.4, p < 0.001) but not in % body fat (0.36 ± 0.53 vs -0.10 ± 0.18%, F = 0.63 vs p = 0.432). FES was also followed by a significant improvement in total BMD Z-scores (1.16 vs 0.13 ± 0.20 ± 0.06, F = 5.7, p = 0.022) and T-scores (0.10 ± 0.10 vs -0.25 ± 0.06, F = 7.9, p < 0.001). FES further induced a significant decline in adiponectin (-2.8 ± 0.3 in FES vs 2.4 ± 0.5 µg/ml in placebo, F = 6.44, p < 0.002) and leptin (-2.3 ± 0.9 vs 1.21 ± 0.3 ng/ml, F = 11.8, p < 0.001) and a significant increase in total ghrelin (91.6 ± 21.6 vs -83.7 ± 22.9 pg/ml, F = 31, p < 0.001) and total ghrelin/acetylated ghrelin ratio (F = 32.4, p < 0.001). Conclusion: In CHF patients, FES improved muscle mass and BMD and seemed to restore the catabolic/anabolic imbalance by decreasing adiponectin and leptin and increasing ghrelin. Those beneficial effects may partly account for the observed improvement in exercise capacity and quality of life afforded by FES in CHF.

IMPLANTABLE CARDIOVERTER DEФIBRILLATOR IN REAL LIFE

13-year implantation and survival rates of patients with implantable cardioverter-defibrillators, and the prognostic impact of age, sex and comorbidity

S.B. Pedersen1, M. Schmidt2, D.K. Farkas2, S.P. Hjortshoj2, H.E. Bokter1, J.C. Nielsen1, H.T. Sorensen2, 1 Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark; 2 Aarhus University Hospital, Skejby, Department of Clinical Epidemiology, Aarhus, Denmark; 3 Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark

Purpose: To examine long-term implantation and survival rates of patients with implantable cardioverter-defibrillators (ICDs) in routine clinical practice compared with the background population, and the prognostic impact of age, sex and comorbidity.

Methods: We conducted a nationwide population-based cohort study. Using medical databases, we identified all first-time ICD implantations during 2000-2012 (n=8,460), an age-, sex- and comorbidity-matched comparison cohort (n=84,600) and complete mortality. Comorbidity categories were defined by Charlson Comorbidity Index scores of 0 (low), 1 (moderate), 2 (severe) and 3 or more (very severe). We computed standardized implantation rates and assessed mortality rate ratios (MRRs) within 13 years using a comparison cohort from the background population. Within the ICD cohort, we compared mortality rates associated with age, sex and comorbidity.

Results: To the standardized implantation rate (per million people) increased five-fold from 2000 to 2012, both overall (from 42 to 213) and for men (from 34 to 174) and women (from 8 to 39). The rate increase was greatest for patients with age ≥70 years (from 10 to 80), for patients with severe comorbidity (from 4 to 36) and for patients with cardiac resynchronization therapy (from 3 to 39 for age, sex and comorbidity category, ICD patients had a 70% increased MRR within the first and the subsequent four years compared with the background population. However, no increased mortality was observed when adjusting addition-
ally for cardiovascular morbidity (1-year MRR=1.05, 95% CI: 0.92-1.20; 1-5 year MRR=1.01, 95% CI: 0.92-1.10). Old age and increasing comorbidity burden were poor prognostic factors for both short- and long-term mortality. One-year mortality rates were equal for men and women, but higher for men thereafter.

**Conclusions:** The rate of ICD implantation increased five-fold in Denmark between 2000-2012. ICD patients had the same five-year survival probability as the background population when taking cardiovascular and other comorbidity into account. Age and comorbidity were strong prognostic factors for short-term mortality, while sex was not.

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**How well do results from large randomized clinical trials diffuse into clinical practice? impact of MADIT-RIT in a large cohort of implantable cardioverter-defibrillator patients (ALITUDE)**

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**Background:** The time course for diffusion of results from important clinical trials into daily practice can be variable. Remote monitoring of patients with networked implantable cardiac devices generates databases that may reveal shifts in practice in electrophysiology. We tested reaction to the publication of MADIT-RIT (Nov 2012), a trial demonstrating that ICD programming with high rate cut-off (Arm B) or extended duration of detection (Arm C) for VT therapy reduces inappropriate shocks and mortality in ICD recipients, using the ALITUDE database.

**Methods and results:** Device programming was assessed by change of parameters to i) strict trial specified settings or ii) adoption of trial principles ie VT therapy for >200 bpm or >60s duration. A total of 129,400 patients were analyzed. In fresh implants, MADIT-RIT programmed parameters (Arm C) was lower prior to publication (~5%) but increased to 8.9% for implants following publication (p<0.001). In patients monitored after publication, but implanted prior to publication, programming alterations reflecting the trial results occurred in only 0.6% of pts. In comparison, patients implanted following publication had 16 times greater odds of MADIT-RIT programming (p<0.001). When considering adoption of trial principles in fresh implants following publication (n=19,177), VT therapy for >200 bpm (quasi-Arm B) programming occurred in 21.7% (n=4165), and extended delay (60s) (quasi-Arm C) in 3.5% (n=670), totaling 25% (4834) with quasi-Arm B or C.

**Conclusions:** MADIT-RIT elicited an immediate effect in the practicing community. However, the degree of adoption, whether assessed by strict trial specified parameters or by its principles, was relatively low. When it occurred, high rate threshold for VT therapy rather than prolonged duration for detection, in new rather than pre-existing implants, was preferred. Significant inertia exists in translation of trials demonstrating mortality benefit into general clinical practice.

### 330 | BEDSIDE

**Arrhythmic storms and primary prevention ICD patients: incidence, characteristics and outcomes**


The electrical storm (ES) is an unpredictable life threatening arrhythmic event related to the severity of the underlying cardiac pathological substrate. Incidence, clinical characteristics, and outcomes of primary prevention patients with implantable cardioverter defibrillator (ICDs) who have not been described so far.

**Methods:** DAI-PP Registry (NCT01992458) was an observational multicentric French registry of ICD recipients with ischemic heart disease or dilated cardiomyopathy, implanted in the setting of primary prevention between 2002 and 2012. Incidence of ES was determined, and characteristics and outcomes were compared between patients developing ES (ES group), those who developed isolated ventricular arrhythmias (VA group) and those who developed no ventricular arrhythmia (no-VA group), during a mean follow-up of 3.2±2 years.

**Results:** Of the 5,327 consecutive patients enrolled, 157 (2.9%) patients developed at least one ES, giving an annual incidence of 9.03 (7.57-10.48) 1000 person-year. Compared to the 1034 (19.4%) patients who developed VA and the remaining 36 (77.6%) patients who did not develop any ventricular arrhythmia, we observed no significant differences regarding age, sex, type of cardiopathy, EF, GRS duration, NYHA functional class, glucomer filteration rate, sinus rhythm, and comorbidities. By contrast, outcomes were dramatically different regarding ICD complications (OR=2.99, 95%CI 1.92-4.66, P<0.005), inappropriate shocks (12.2% vs. 11.3% vs. 5.4%, P<0.05), and overall mortality (32.0% vs. 17.2% vs.13.9%, P<0.05). Finally, we observed a much higher proportion of ICD-refractory sudden cardiac death among ES group (30.0% vs. 8.0% vs. 6.1%, P<0.001). In multivariate analysis, occurrence of an ES during follow-up independently predicted overall mortality (OR=2.99, 95%CI 1.92-4.66, P<0.005).

**Conclusion:** Overall, in the setting of primary prevention ICDs recipients, annual incidence of ES is relatively low (almost 1%). Although no clear differences in characteristics, we observed major differences in outcomes.

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**Clinical course of implantable cardioverter-defibrillator patients: prolonged follow-up in routine clinical practice**

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**Introduction:** Large randomized trials have demonstrated the beneficial effect of ICD treatment in selected patients. Data on long-term follow-up in patients outside the settings of trials are scarce.

**Methods:** All patients who underwent ICD implantation at our Medical Center since 1996 were evaluated. Implantations were based on international guidelines. Cumulative incidences were obtained from cumulative incidence curves correcting for the competing risk of all-cause mortality and ICD interventions.

**Results:** A total of 3055 patients (1967 (64%) primary; 1088 (36%) secondary prevention) were included. During a median follow-up of 5.1 years (25th-75th percentile 3.1-7.8) 842 (28%) patients died. The 12-year cumulative incidence for all-cause mortality was 55% (95% CI 51-59) which was similar for primary and secondary prevention patients (log rank p=0.92; Table 1). A total of 1081 (35%) patients received appropriate ICD therapy. The 12-year cumulative incidence for appropriate therapy in primary patients was 42% (95% CI 38-47) as compared to 63% (95% CI 59-67) in secondary patients (p<0.001). Table 1 demonstrates additively evaluated cumulative incidences.

#### Table 1. Overview of follow-up of ICD recipients.

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>1 year FU</th>
<th>6 years FU</th>
<th>12 years FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>Primary 6% (5-7)</td>
<td>30% (28-33)</td>
<td>53% (45-63)</td>
</tr>
<tr>
<td>Non-primary 4% (4-7)</td>
<td>27% (23-33)</td>
<td>56% (51-61)</td>
<td></td>
</tr>
<tr>
<td>Appropriate ICD therapy</td>
<td>Primary 11% (10-13)</td>
<td>34% (31-37)</td>
<td>42% (38-47)</td>
</tr>
<tr>
<td>Non-primary 24% (21-26)</td>
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<td>63% (59-67)</td>
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<tr>
<td>Non-primary 14% (12-17)</td>
<td>36% (33-39)</td>
<td>47% (43-51)</td>
<td></td>
</tr>
</tbody>
</table>

**Device related complications**

- Inappropriate ICD shock: 6% (5-7) | 14% (13-16) | 20% (18-22)
- Device infection: 1% (1-2) | 4% (3-5) | 6% (5-8)
- Lead failure: 1% (1-2) | 2% (2-3) | 4% (3-5)

**Conclusion:** After 12 year follow-up 55% of ICD recipients died. Of primary prevention ICDs recipients 42% required ICD intervention for potential life threatening arrhythmias as compared to 63% (95% CI 59-67) in secondary patients (p<0.001).

### 332 | BEDSIDE

**Co-morbidities in ICD-recipients and its importance for psychological outcomes: the results from a large cross-sectional study**

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**Purpose:** Determine the association of co-morbidity burden and psychological outcome in ICD-patients.

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>ICD-related concerns, %</th>
<th>Anxiety, %</th>
<th>Depression, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>Primary 6% (5-7)</td>
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**Device related complications**

- Inappropriate ICD shock: 6% (5-7) | 14% (13-16) | 20% (18-22)
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- Lead failure: 1% (1-2) | 2% (2-3) | 4% (3-5)

**Conclusion:** After 12 year follow-up 55% of ICD recipients died. Of primary prevention ICDs recipients 42% required ICD intervention for potential life threatening arrhythmias as compared to 63% in secondary prevention patients.
Method: 3,067 Swedish patients (80% male, age 66±12 years) completed the survey. Anxiety and depression were measured using the Hospital Anxiety Depression Scale, and ICD-related concerns with the ICD Questionnaire.

Results: Eight percent reported having none of the 14 co-morbidities (mean 2.7±1.9). Those with rheumatic diseases, intermittent claudication, and neurological disorders other than stroke, perceived the highest level of discomfort from their co-morbid condition. Seventeen percent suffered from anxiety, 9% depression, and 26% ICD-related concerns. Those with intermittent claudication reported the highest burden of anxiety (24%), depression (18%), and ICD-related concerns (31%), while those with cancer reported the lowest psychosocial distress; with 15% suffering from anxiety and 9% from depression (Table 1). In multiple regression, both greater number of cardiac co-morbidities as well as non-cardiac co-morbidities were independently associated with higher levels of depression controlling for age, gender, education, time since ICD-implantation, and having received ICD-shocks. Similarly, those two indicators of co-morbidity burden were associated with higher levels of anxiety, and higher levels of ICD-related concerns.

Conclusions: Most ICD-recipients have multiple co-morbidities. Higher co-morbidity burden is associated with worse psychological outcomes, suggesting that ICD-recipients with multiple co-morbidities should be targeted for management of psychological distress.
tion; however, some investigators assert that risk models have so far not been very successful. Thus, we examined whether the inclusion of dietary evaluation in a risk prediction model that already contained the classical CVD risk factors, increases the accuracy and reduces the bias in estimating future CVD events.

Methods: The database of the ATTICA study (that included information from 1514 men and 1528 women) was used. At baseline, the HellenicSCORE values (based on, age, gender, smoking, systolic blood pressure and total cholesterol) were calculated; while overall assessment of dietary habits was based on the Mediterranean Diet Score (MDS) that evaluates adherence to this traditional diet. In 2006, the 5-year follow-up was performed in 2101 participants and development of CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria.

Results: The MDS and the HellenicSCORE were significant predictors of CVD events, even after adjusting for various potential confounders (p < 0.05). However, estimating bias (i.e., misclassification of cases) of the model that included HellenicSCORE and other potential confounders was 13.8%. The MDS was associated with the estimating bias of the outcome (p < 0.001), and explained 6.1% of this bias. Other baseline factors associated with bias were increased body mass index, low education status and increased energy intake/BMR ratio.

Conclusion: The inclusion of dietary evaluation, as well as other lifestyle characteristic increases the accuracy and reduces estimating bias of CVD risk prediction models.

P376 | BEDSIDE
Carotid intima media thickness to reclassify individuals at moderate risk of cardiovascular disease: the Dublin Cardiohealth station study
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Purpose: The 5th Joint Task Force European guidelines on cardiovascular disease (CVD) prevention recommend measurement of carotid intima media thickness (IMT) in asymptomatic individuals at moderate risk (Class Ila). Using the Panatomic Cardiohealth station (CHS), a semi-automated ultrasound system which allows detection of carotid plaque and measurement of CIMIT, we aimed to evaluate the ability of CIMIT to further risk stratify patients attending a CVD prevention clinic.

Methods: Patients who were aged over 18 years who were free of known CVD and were classified as moderate, high or very high risk of CVD based on the 5th joint task force European guidelines on CVD prevention priorities were included. Information was collected on traditional risk factors for CVD including smoking status, diabetes, family history of premature CVD, blood pressure, heart rate, body mass index, waist circumference, lipid measurements and glucose. Three measurements of right and left IMT at the common carotid artery were taken; the highest of these was used in the analyses. Elevated CIMIT was defined as >0.9mm as recommended in the guidelines. We analysed the percentage of those at moderate risk reclassified after addition of CIMIT and used Fischer’s exact test to determine whether the percentage was statistically significant.

Results: 200 patients were included in the study (65% women). The mean age was 64 years and 58 years in women. 18% of both men and women were current smokers. 14% of men and 10% of women had diabetes. Of women, 72% were classified as moderate risk, 22% were classified as high risk and 8% were based as very high risk based on traditional risk factors and overall 24% had elevated CIMIT. Of men, 55% were classified as moderate risk, 24% were classified as high risk and 21% were based as very high risk based on traditional risk factors and overall 40% had elevated CIMIT. The reclassification from moderate to high risk based on the CIMIT measurement was 27% in men (p < 0.001) and 15% in women (p < 0.001).

Conclusions: CIMIT measurement reclassifies a considerable percentage of patients who are judged to be at moderate risk using traditional CVD risk factors alone. This supports the recommendation to use CIMIT for further risk stratification in those at moderate risk. It was possible to measure CIMIT quickly and easily during a routine cardiovascular risk factor clinic visit using the CHS.

P377 | BEDSIDE
Prevalence of high cardiovascular risk calculated by SCORE evaluation system in Russian population
S.A. Shalina1, A.D. Deev1, A.O. Konrady2, Y.A. Karpov1, O.P. Rotar2, J.V. Zhenghokova3, E.V. Shlyakhova2, S.A. Boytsov1 on behalf of the ESSE-RF study investigators. 1National Research Center for Preventive Medicine, Moscow, Russian Federation; 2Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation; 3Clinical Cardiology Research Center, Moscow, Russian Federation

Purpose: To estimate the high cardiovascular risk in a Russian population according to the SCORE evaluation system for regions of high cardiovascular risk.

Methods: Data came from multicenter epidemiological study called ESSE-RF in Russian Federation. Eight of regions from 41 participating (Ural), Orenburg (O), Saint Petersburg (SP), Tomsk (T), Tyumen (TYU), Volgograd (VGL), Voronezh (VOR) conducted survey in 2012-2013 with randomly selected subjects aged 35-64 years by a single core protocol. Total number of screened was 10405 (3239 men). Education, HDL cholesterol, triglycerides, hear rate, alcohol consumption for subject without CVD history were added into analysis. The estimated 10-year absolute risk for fatal CVD≥5% considered as a high (HCVDR). All data were age- adjusted according Euro Standard. Descriptive statistics and logistic regression were used.

Results: At age 40, 22.8% of men and 23.6% of women were at HCVDR. Corresponding numbers at age 50 were 53.7% and 33.9% and at age 60 were 93.5% and 60.5%. At age 40, one 5 men and one of 5 women would be classified at low risk for CVD, while at age 60 only 7% of men and 40% of women. Prevalence of HCVDR in entire cohort was 57.9% (men 67.3%; women - 54.0%, p < 0.001). The highest proportion of HCVDR had men in AL (75.1%) and women in VOR (64.5%), whereas the lowest one had men and women in TYU (52.2% and 41.5%), respectively. Large differences between regions remain after adjustment for age and sex differences.

Conclusion: According to SCORE system more than half of the adults Russian population is at high CVD risk The proportion of HCVDR substantially differ between regions, varying from 65.7% in VOR (Central Russia) to 45.1% in TYU (Ural).

P378 | BEDSIDE
Combined high sensitivity c-reactive protein and maximal exercise test as predictors of 10-year mortality among stable patients referred for diagnostic treadmill stress testing (2000-2001)
J. Shehadeh 1, O. Reges2, M. Heshen3, N. Yaniv1, D.A. Halon1, L. Morton2, 1Lady Davis Carmel Medical Center, Haifa, Israel; 2Clalit Research Center, Tel Aviv, Israel

Background: Cardiovascular disease remains the biggest cause of death worldwide especially in the western world including our country. Exercise capacity measured by peak metabolic equivalents (METs) and high sensitivity C-reactive protein (hsCRP) can improve the predictive capability of cardiovascular morbidity and mortality. Full evidence regarding the integrated predictive capability of these parameters is lacking.

Objective: To examine the independent and the integrated contribution of these functional and inflammatory parameters in predicting all cause mortality during 10 years of follow up.

Patients and methods: 385 stable patients were referred for diagnostic symptom driven treadmill stress testing for suspected/known coronary artery disease in the period between 15/8/2000 and 27/1/2002. Blood samples for hs –CRP were drawn before initiating exercise testing from all participants. Data regarding all cause mortality during 10 years of follow up after the index date was taken from the medical file and cox regression was performed for risk assessment.

In order to examine the integrated contribution of METS and hs CRP, categorical variable was identified expressing the combined profile of the two variables.

Findings: Univariate analysis uploaded significant contribution of the two parameters in predicting all cause mortality. Multivariate analysis taking into account the framingham risk score,gender,age,METS and hs CRP showed independent contribution of METS in predicting all cause mortality (HR=0.82, 95% CI: 0.73-0.93, P=0.001). Examining the combined contribution of METS and hs CRP when dividing the patients into four groups-(elevated METs, elevated hs CRP, decreased METs, decreased hs CRP), the mortality risk is the lowest in the group defined by elevated METS and decreased hs CRP. Compared to this group, the mortality risk is higher with change of any variable. Higher values of hs CRP increase the risk of death by 8.0 among people with low functional capacity compared to lower values of hs CRP among the same group.

Conclusions: It is recommended to combine hs CRP test as part of the regular monitoring cardiac patients even among those identified in exercise testing including those with high functional capacity.

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Impact of the genetic and conventional risk factors of ischemic heart disease on acute coronary syndrome prediction
D. Zaliunas1, 2, 3, O. Gustiene1, S. Maciulskyte1, V. Lesauskaite2, R. Zaliunas1, 1National Research Center for Preventive Medicine, Moscow, Russian Federation; 2Lithuanian University of Health Sciences, Academy of Medicine, Department of Cardiology, Kaunas, Lithuania; 3Lithuanian University of Health Sciences, Institute of Cardiology, Kaunas, Lithuania

Background: Matrix metalloproteinases (MMPs) and components of renin-angiotensin system (RAS) may be associated with atherogenesis, plaque rupture and pathogenesis of acute coronary syndromes (ACS) including different types of ACS such as ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI). Aim of the study was to evaluate the influence of traditional risk factors of ischemic heart disease (IHD) and genetic factors to predict different types of ACS.

Methods: Five hundred and twenty three patients with ACS (393 with STEMI and 130 with NSTEMI) comprised a study group. The control group involved 645 healthy individuals referred for diagnostic treadmill stress testing (ESSE-RF). 

Impact of the genetic and conventional risk factors of ischemic heart disease on acute coronary syndrome prediction

Appendix

Risk prediction in asymptomatic populations 51

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Results: Patients with ACS more often had ID or II genotype than DD genotype of ACE (p=0.04) and 5ASA or 5ASA genotype than 6ASA genotype of MPP-3 (p=0.02) in comparison to the control group. The genotypes and allele of other studied genes (MMP-2 (-735) C/T, MMP-2 (-1306) C/T, and MMP-3 (-1562) C/T) did not differ between the groups. 5ASA and 5ASA genotypes of MMP-3 (OR 1.9; p=0.061) and ID genotypes of MMP-3 (OR 1.7; p=0.006) along with traditional IHD factors such as smoking (OR 4.9; p<0.001), hypertension (OR 2.0; p=0.001), diabetes mellitus (OR 2.9; p=0.001) and dyslipidemia (OR 2.1; p=0.001) increased the risk of STEMI. However, polymorphism of MMP-3 5A/6A and ACE ID did not increase risk of NSTEMI (OR 1.1; p=0.9 and OR 1.5; p=0.1, respectively).

Conclusions: Genetic polymorphism of MMP-3 5A/6A and ACE ID along with conventional IHD risk factors increase the risk of occurrence of STEMI, however traditional IHD factors have a superior role.

P380 | BEDSIDE
Impact of adipose tissue composition on cardiovascular risk assessment
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Background: Visceral adipose tissue (VAT), unlike subcutaneous adipose tissue (SAT), has been shown to be highly correlated with cardiovascular risk factors. The aim of this study was to evaluate the predictive value of adipose tissue composition measured by computed tomography for cardiovascular outcome.

Methods: 369 consecutive patients without history of cardiovascular disease who underwent 64-slice computed tomography angiography (CTA) were recruited. The ratio of visceral adipose tissue to the total adipose tissue (%VA T) was calculated using CTA. Data were divided into two groups in accordance with tertiles of %VA T. In Cox analysis, the hazard ratio (HR) of %VA T (per tertile) for MACE was 1.39 (95% confidence interval [CI] 1.05–1.82, p=0.02). Among patients with tertile 3, HR for MACE was 1.81 (95% CI 1.01–3.23, p=0.045) compared to tertile 1 after adjustment for confounding factors.

Conclusion: %VA T is independently associated with MACE, indicating that adipose tissue composition is a useful predictor of cardiovascular outcome.

P381 | BEDSIDE
Mthfr c677t genotype is not associated with ischaemic heart disease and stroke in a large prospective study in China
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Purpose: The MTHFR C677T variant is associated with higher homocysteine levels, and previous studies have reported a 30% higher risk of stroke for the TT compared to CC genotype in Asian but not in Western populations. In Asian regions, where there is low dietary folate consumption, it has been suggested that randomized controlled trials of folic acid supplementation to reduce homocysteine, or Mendelian randomisation studies using the C677T variant, are required to investigate the causal relationship between homocysteine and cardiovascular disease.

Methods: We examined the associations of the C677T genotype with both stroke and ischaemic heart disease (IHD; defined as fatal coronary disease, fatal or non-fatal myocardial infarction) in men and women recruited from 10 diverse regions across China between 2004 and 2008 as part of the China Kadoorie Biobank (CKB) prospective study. Genotyping was carried out in a random subset of about a fifth of CKB participants using Illumina GoldenGate technology. After excluding individuals, data on MTHFR C677T (rs1801133) and A1298C (rs1801131) variants were available for 82,000 participants. This SNP pair were in high linkage disequilibrium (R-square=0.168, D-prime=0.99). Over a 6-year follow-up, there were 5794 incident strokes (3613 ischaemic, 912 haemorrhagic) and 649 incident IHD events in the genotyped subset.

The prevalence of TT homozygotes varied almost 10-fold between the ten regions (41.2% vs 4.8%) with a north to south gradient. With full adjustment for age, sex and region, the relative risks for TT vs CC were 0.95 (95% CI: 0.76, 1.24) for IHD and 1.05 (0.96, 1.15) for stroke, with similar results for ischaemic and haemorrhagic stroke. Without adjustment for region, the age and sex-adjusted relative risks for TT vs CC were 1.42 (95% CI: 1.14, 1.76) for IHD and 1.32 (1.23, 1.43) for stroke. The prevalence of the A1298C genotype also differed substantially across regions and was unrelated to IHD or stroke, irrespective of how the data were analysed.

Conclusion: This large study, with almost twice the number of stroke cases as a previously reported meta-analysis, does not support an association between the MTHFR genotypes and risk of stroke in Asian populations. Inadequate correction for the large geographic variation in MTHFR genotypes may account for the discrepancy with previous reports. Folic acid treatment is unlikely to have any clinically important beneficial effect on risk of IHD, or stroke.
CAC progression beyond estimated values in participants of the Heinz Nixdorf Recall (HNR) study cohort.

Methods: Participants of the HNR study received at the age of 45 to 75 years a first electron beam CT (EBCT) and were followed for 5 years, before a second EBCT (Imatron, GE, USA) was performed with the same scanning system, identical scanning protocols and evaluation algorithms. In 3481 participants a complete data set including risk factor profiles and CAC values > 10 Agatston score were available. Participants with coronary events or coronary revascularization before recruitment or during follow-up were excluded. From measured CAC values at baseline and after 5-years a model was derived for prediction of CAC progression. Odds ratios with 95% confidence intervals (CI) for measured exceeding predicted progression by a predefined threshold were calculated in a multivariable analysis.

Results: The following parameters were identified in men demonstrating an attenuation or accelerated CAC progression: age 0.71 (0.65-0.78), p < 0.0001; systolic blood pressure 1.13 (1.06-1.21), p = 0.0005; lipid lowering medication 1.89 (1.24-2.89), p = 0.0003; diabetes 1.90 (1.37-2.63), p < 0.0001; present smoking 1.99 (1.40-2.80), p < 0.0001, whereas antihypertensive agents, LDL-cholesterol, and former smoking were not significant. The following parameters were identified for women: systolic blood pressure 1.08 (1.01-1.14), p = 0.02; lipid lowering medication 1.40 (1.02-1.89), p = 0.02; lipid lowering medication 1.49 (1.02-1.91), p = 0.04; diabetes 1.56 (1.05-2.23), p = 0.03, and present smoking 1.98 (1.47-2.67), p < 0.0001.

Conclusion: Systolic blood pressure, lipid lowering medication, diabetes and present smoking in both men and women as well as younger age in men only are predictors of CAC progression beyond predictable levels.

P384 | BEDSIDE
Subclinical arterial wall damage in patients with low and moderate cardiovascular risk
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Background: Adults over 40 years of age often demonstrate atherosclerotic arterial damage without apparent clinical manifestation, so called subclinical atherosclerosis, that was shown to be sufficient for the development of advanced cardiovascular events such as myocardial infarction, stroke, or sudden death.

Aim: To study the degree of subclinical arterial wall damage in patients with low and moderate risk of cardiovascular death by SCORE scale using by instrumental research methods.

Material and methods: We enrolled 600 patients (mean age - 49±7.1) with low and moderate risk by SCORE scale, of them: 445 women and 155 men without atherosclerosis and diabetes mellitus-related diseases. Everyone passed carotid duplex ultrasonography with the measurement of intima-media thickness (IMT) and carotid plaque (CP) burden. In the study subjects computer sphygmography was also performed to determine ankle-brachial pulse wave velocity (abPWV) and ankle-brachial index (ABI).

Results: Using instrumental research methods, we detected 389 (64%) patients with subclinical signs of atherosclerosis. CPs were found in 359 patients (80%), thickened IMT (>0.9mm) in 28 patients (5%), increased abPWV in 227 patients (38%), and ABI of ≤ 0.9 in 29 patients (5%). Out of 28 patients with thickened IMT, only two didn’t have CP, and 331 patients with CP had normal IMT. Out of 227 patients with increased abPWV, 30 didn’t have CP, and 197 patients had both increased abPWV and CP. All 29 patients with ABI of ≤ 0.9 had CPs (Table 1). The presence of CP was the most sensitive parameter in the include patients in terms of atherosclerosis determination (92%).

Table 1. Arterial wall damage parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Carotid plaque *+ (n=357)</th>
<th>Carotid plaque *− (n=243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMT &lt;0.9 mm</td>
<td>26 (7%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>IMT ≥0.9 mm</td>
<td>331 (93%)</td>
<td>241 (99%)</td>
</tr>
<tr>
<td>Increased abPWV, m/s</td>
<td>197 (55%)</td>
<td>30 (12%)</td>
</tr>
<tr>
<td>Normal abPWV, m/s</td>
<td>165 (45%)</td>
<td>213 (88%)</td>
</tr>
<tr>
<td>ABI ≤0.9</td>
<td>29 (9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>ABI &gt;0.9</td>
<td>325 (91%)</td>
<td>243 (100%)</td>
</tr>
</tbody>
</table>

Conclusion: The study demonstrated high degree of subclinical arterial wall damage in patients with low and moderate risk by SCORE scale and high detection frequency of carotid plaques.

P385 | BEDSIDE
Differential value of left ventricular mass index and wall thickness in predicting cardiovascular prognosis: the Pamela study
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Aim: Data on the prognostic value of echocardiographic left ventricular hypertrophy (LVH) as defined by LV wall thickness rather than LV mass estimate are scanty and not univocal.

Thus, we investigated the value of LV mass index, wall thickness and relative wall thickness ( SWT) in predicting cardiovascular events in the PAMELA population.

Methods: At entry 17 165 subjects underwent an electrocardiographic examination and instrumental research methods including laboratory investigations, 24-hour ambulatory blood pressure (BP) monitoring, and echocardiographic studies. For the purpose of the present analysis all subjects were divided into quintiles of LV mass, LV mass/BSA, LV mass/h2.7, inter-ventricular septum (IVS), posterior wall (PW) thickness, LV-PW thickness, and SWT.

Results: Follow-up of 148 months, 139 non-fatal or fatal cardiovascular events were documented. After adjustment for age, sex, BP, fasting blood glucose, total cholesterol, and use of antihypertensive drugs, only the subjects stratified in the highest quintiles of LV mass indexed to BSA or height2.7 exhibited a greater risk for incident cardiovascular disease: relative risk 2.69 (CI: 1.05-6.96, p=0.04) and 4.62 (CI: 1.42-15.02, p=0.01), respectively, as compared to the first quintile (reference group). The same was not true for the highest quintiles of IVS, PW thickness, IVS-PW thickness and SWT. Similar findings were found when echocardiographic parameters were expressed as continuous variables.

Conclusions: The present study indicates that LV wall thickness, at difference from LV mass index, does not provide a reliable estimate of cardiovascular risk associated with LVH in a general population. From these data it is recommended that echocardiographic laboratories should provide a systematic estimate of LV mass index, which is a strong, independent predictor of incident cardiovascular disease.

P386 | SPOTLIGHT
Abnormal rise in blood pressure post exercise in asymptomatic normotensive subjects is associated with structural and functional cardiovascular abnormalities
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Purpose: To examine whether abnormal rise in blood pressure post mild exercise is correlated with cardiovascular disease risk in subjects with normal blood pressure at rest.

Methods: We evaluated 2230 subjects aged 23-80 years, who underwent screening for CVD risk using Early CVD Risk Score (ECVDRS), also known as Ras-mussen Risk Score. ECVDRS consists of 10 non-invasive tests including large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild ex- ercise (BP-PME), Carotid Intima Media Thickness (C1M), and left ventricular ul- trasound. In the presented study sub, we evaluate the subgroup of asymptomatic normotensive individuals at risk for cardiovascular, structural and functional (C1, C2, C1M) abnormalities. BP at rest is considered normal when it is below 140/systolic and 80/diastolic.

Results: Among the 2230 asymptomatic participants, we analyzed 1307 with normal resting BP taking no anti-hypertensive medication. We test the hypothesis that asymptomatic subjects with normal resting BP that have abnormal BP-PME have significantly higher cardiovascular risk that those with normal rise in BP-PME. We used 4 Chi-square tests to test the independence between the two groups: normal rise in BP-PME versus abnormal rise in BP-PME. Results revealed that in the group with abnormal rise in BP-PME, C1 = 1.91 (1--1.30) = 4.485, p = 0.0012; C2 = 1.62 (1.42-1.82), p = 0.0012; C1M = 1.72 (1.51-1.96), p < 0.0001; C2M = 1.41 (1.21-1.64), p = 0.0002. The proportion of abnormal C1 was 0.03 and 0.07 respectively with normal vs elevated BP-PME, x2 (1, N = 1307) = 6.842, p = 0.0089. Finally, the proportion of abnormal C1M was 0.18 and 0.23 respectively with normal vs elevated BP-PME, x2 (1, N = 1307) = 4.903, p = 0.0319.

Conclusion: We found significantly associated of echo-determined LVH and abnormalities in C1 and C1M among subjects with normal resting BP. Assessment of BP-PME could be beneficial in screening subjects with normal resting BP regarding cardiovascular structural and functional abnormalities for further cardiovascular risk stratification and initiating appropriate therapeutic interventions. Additionally, these preliminary findings warrants the need for further investigation of the etiology and subsequent morbidity associated with elevated BP-PME. BP-PME assessment could help identify early cardiac disease likely to progress to morbid events in low risk patients.

P387 | BENCH
Cumulative effect of axial, structural and repolarization ecg findings on long-term cardiovascular mortality in healthy individuals
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Purpose: Atherosclerotic cardiovascular disease (ASCVD) is a major burden...
around the globe. Traditional risk scores such as the Framingham risk score (FRS) have played a central role for early detection of high-risk individuals for ASCVD. However, these risk scores do not include findings from electrocardiograms (ECG) that are acquired easily and cost-effectively in everyday practice. Despite its long history, the prognostic implication of ECG findings remains unclear and no attempt to evaluate the cumulative effect of axial, structural, and repolarization ECG findings on ASCVD mortality in a Japanese cohort registry.

Methods: Community-dwelling Japanese individuals from the NIPPON DATA 80 and 90 groups included in this study. The office-based FRS and the cohort-driven NIPPON DATA score (NDS) were calculated for each individual. Baseline ECG findings were classified according to the Minnesota Code and categorized into axial (left axis deviation, clockwise rotation), structural (left ventricular hypertrophy, atrial enlargement), and repolarization (minor and major ST-T changes) abnormalities. Individuals were divided into three groups according to the number of ECG category: none, single, or more than two. The hazard ratios for each of the group were estimated with stratified Cox proportional hazard models adjusted for the FRS and the NDS.

Results: A total of 16,816 individuals were evaluated. The average age was 51.2 (95% confidence interval [CI], 37.7-65.7), 42.7% were male. The follow-up duration was 300,924 person-years with a mean of 17.9 (95%CI, 12.1-23.7) years. Follow-up per person: 4,203 participants (25.0%) had single or more ECG categories: 3,648 (21.7%) had single, 555 (3.3%) had more than two categories. The median for each risk score was as follows: FRS in male 13.20% (interquartile range, 5.6-25.3%), FRS in female 6.30% (interquartile range, 2.8-13.7%), and NDS 0.40% (interquartile range, 0.10-1.93%). After adjustment for FRS and the NDS, the hazard ratios for each ECG category were as follows: FRS for male (Single 1.33, 95%CI 1.20-1.47, More than two 1.84, 95%CI 1.55-2.19) and NDS (Single 1.26, 95%CI 1.18-3.6, More than two 1.81, 95%CI 1.61-2.03).

Conclusion: Cumulative ECG findings are independent predictors for long-term ASCVD risk in individuals with multiple ECG findings who possess intermediate risks according to traditional risk scores may benefit from intensive primary intervention.

P389 | BEDSIDE
Serum uric acid, arterial stiffness and total cardiovascular risk: is there a link?

Purpose: To analyze the relation between serum uric acid levels (UA), arterial stiffness and total cardiovascular (CV) risk in a large adult population using the data from SEPHAR II Romanian national representative survey.

Methods: A total of 2,273 subjects enrolled in the SEPHAR II survey (69.06% response rate, 52.6% females, age range: 18-80 years) were evaluated by means of a questionnaire, anthropometric, blood pressure (BP) and arterial stiffness measurements (PWVao, AIXao) by validated sfigmomanometric device, 12 lead ECGs and a number of laboratory tests (sex and BP values).

Results: Mean serum UA value was 4.93 ± 1.42 mg/dl (range 1.20-10.80 mg/dl), the prevalence of hyperuricemia being 12.9%. There was a significant correlation between UA levels and aortic and brachial BP values, independent of age and sex (r2=0.025, p<0.0001), the highest values being observed in brachial SBP 20.042, p=0.0001 for brachial DBP, r2=0.038, p=0.0001 for brachial SBP; r2=0.038, p=0.0001 for brachial DBP; after adjusting for SBP (r2=0.24, More than two 1.86, 95%CI 1.41-2.34). FRS for female (Single 1.33, 95%CI 1.20-1.47, More than two 1.84, 95%CI 1.55-2.19) and NDS (Single 1.26, 95%CI 1.18-3.6, More than two 1.81, 95%CI 1.61-2.03).

Conclusion: Serum uric acid levels as a cardiovascular risk factor. The novelty of our results is the link between serum UA, arterial stiffness and total CV risk. Our results suggest that increased UA levels promote endothelial dysfunction and atherosclerosis leading to arterial stiffness on one hand and contributes to the progression of renal failure independently of age and sex and BP values, on the other, therefore enhancing the total CV risk.

P390 | BEDSIDE
Reclassification improvement and discrimination by testosterone in hypertensive males

Purpose: Testosterone deficiency (TD) confers an independent risk for cardiovascular events and total mortality. Hypertension has been associated with increased prevalence of TD subjects. The purpose of this study was to determine net reclassification improvement (NRI) and discriminatory capability of total testosterone (TT) in comparison with traditional risk factors in middle-aged hypertensive men.

Methods: Major adverse cardiovascular events (MACE) in relation to TT were analyzed in 120 hypertensive males (mean age 56 years). The reclassification of MACE risk associated with TT was assessed using a method that quantifies NRI. The discriminatory capability of TT was examined using C statistics.

Results: During a mean follow-up of 44 months, 19/228 participants experienced a MACE. Compared to patients who did not experience MACE, hypertensive subjects who developed MACE had lower TT concentration (P=0.01) and a higher prevalence of TD (P=0.025). Data on the number of subjects according to Framingham CVD risk category based on an age-adjusted regression model, with reclassification of risk category after inclusion of TT in a multivariate statistical model are shown in Table. The overall NRI was 38.8% (2.94, P<0.05). The C statistic for the multivariate model including Framingham CVD factors was 0.774. Addition of TT to this model offered a statistically significant improvement in the resulting C statistic to 0.801 (P<0.05, for comparison between the area under the curve and the C statistic).

Conclusion: Testosterone improves risk prediction when added to standard risk prediction models and may represent a valuable biomarker of prediction of MACE risk in middle-aged hypertensive patients.

P391 | BEDSIDE
Risk prediction of cardiovascular adverse events in elective non-cardiac surgeries - a comprehensive nationwide study

Methods and results: From Danish nationwide registries we identified individuals ≥25 years undergoing elective non-cardiac surgery in 2005-11 (n=441,245). The total of 2,273 (0.52%) had a MACE within 30 days of surgery (387 [17.0%] non-cardiac myocardial infarctions, 680 [29.9%] non-fatal strokes, and 1,206 [53.1%] cardiovascular deaths). Surgery in the eye, ear-nose-throat, breast, neurologic areas, male and female reproductive organs, minor orthopedic, and venous or lymphatic vessels were not associated with increased risks (odds ratio [OR] <2), compared with the background population. RCRI had c-statistics of 0.757 and was not well-calibrated (p=0.0001). We suggested an extended and re-calibrated version of the RCRI (including age, sex, and more surgery subtypes), derived on two thirds of the surgery cohort and validated it in the last third (c-statistics 0.889, calibration p=0.09).

Conclusion: Risk prediction of cardiovascular adverse events in elective non-cardiac surgeries: is there a link? Risk prediction models and may represent a valuable biomarker of prediction of MACE risk in middle-aged hypertensive patients.
P393 | BEDSIDE
How do we explain the risk of sudden death caused by representative cardiovascular diseases diagnosed by the screening system for school children?

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Objectives: To clarify the epidemiological risk of sudden death (SD) due to representative cardiovascular diseases and electrocardiogram abnormalities that are diagnosed by screening system for school students, their prevalence and mortal-

Methods: This study enrolled 7 representative screening diseases including paroxysmal ventricular contraction and/or ventricular tachycardia (PVC/VT), complete right bundle branch block (CRBBB), ventricular septal defect (VSD), atrial septal defect (ASD), cardiomyopathy (CM), long QT syndrome (LQT) and WPW syndrome. Prevalence of these was estimated from the annual summary. This study enrolled 1,092 children between 1992 and 2009. Secondary analysis revealed prevalence of 1.4% for PVC/VT, 13.3% for CRBBB, 27.7% for VSD, 0.25% for ASD, 2.9% for cardiomyopathy, 1.8% for long QT syndrome and 0.14% for WPW syndrome.

Results: PVC/VT and CRBBB had the higher incidence of SD. The incidence of SD in PVC/VT was 0.25% and 1.25% in CRBBB.

Conclusions: These results show the additive effect of a number of risk alleles in several genetic markers independent from TRF, which is associated with an increased risk of CAD. This score can be very useful in the diagnosis of 15% of the individuals considered at low-risk and that develop CAD without or with few TRF.

P395 | BEDSIDE
The Framingham risk score and severity of coronary artery stenosis

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Purpose: Coronary artery Disease (CAD) is a leading cause of mortality world-
wide. Framingham risk scoring system is a simple, easy to perform and reliable parameters that currently used to predict the risk of developing cardiovascular disease and to determine the treatment goals for prevention of disease progression, but it is not used to predict CAD severity. The aim of this study is to investigate the correlation of Framingham Risk Score (FRS) with the severity of CAD.

Methods: This prospective study included patients who underwent coronary an-

Results: The number of risk alleles varied from 0 to 7. Before the median (3rd category), controls had a higher number of risk alleles while after the median the cases had more risk alleles. From the 2nd quartile there was an increased risk of CAD, initially with marginal statistical significance and then gradually higher.

Conclusion: These results show that FRS, based on the additive effect of a number of risk alleles in several genetic markers independent from TRF, is asso-

Association between GRS and CAD risk.

P394 | BEDSIDE
Determination of a genetic risk score in coronary patients from a population of our country

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Approximately 15% who develop coronary artery disease (CAD) have few tradi-
tional risk factors (TRF) and are considered low risk in the light of existing predic-
tive models. Genetic factors can explain 40-55% of this variability in the popu-
lation.

Objective: Evaluate the association between the genetic risk score (GRS) based on the number of risk alleles accumulated in a set of genetic variants independent of TRF, and the CAD risk.

Methods: A case-control study with 2473 individuals, 1312 with CAD and 1161 controls was performed. We selected 4 genetic variants associated to CAD, but independent from TRF: CDKN2B, ADAMTS7, GJA4 and KIF6. GRS was defined, based on the sum of the risk alleles (0, 1 and 2) accumulated in each variant with the possibility of each individual having 0 to 8 categories. The reference class was the median of the control population. A logistic regression was done to estimate the CAD risk, in which the OR was obtained in relation to the reference class for each category. GRS was divided into quartiles and a multivariate analysis was performed to obtain the regression coefficient (β) (ref class was the 1st quartile).

Results: The number of risk alleles varied from 0 to 7. Before the median (3rd category), controls had a higher number of risk alleles while after the median the cases had more risk alleles. From the 2nd quartile there was an increased risk of CAD, initially with marginal statistical significance and then gradually higher.
and specificity 77.3% (Area Under the Curve [AUC]: 0.882, 95% CI: 0.830-0.934, P = .001).

Conclusion: Framingham Risk Score is a simple method that can be used to predict the severity of coronary artery disease. Further large-scale studies are needed to confirm the finding of our study.

P396 | BEDSIDE
HEART score proposed modification for assessment of Indigenous Australians presenting with high risk chest pain
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Purpose: To examine the validity of use of the HEART score for the assessment of Indigenous Australian Aboriginal and Torres Strait Islander (ATSI) presenting with high risk chest pain.

Methods: The HEART score data was collected from consecutive patients admitted to our hospital with myocardial infarction over one year. The HEART score for both patients groups was calculated and analysed for validity and proposed modification.

Results: 441 patients were admitted to Cairns Hospital over a one year period with myocardial infarction – 120 of these patients were ATSI and 321 were non-Indigenous. The mean HEART score for ATSI and non-Indigenous patients was 6.43 ± 1.56 and 6.76 ± 1.48 respectively. The HEART score significantly underestimated the risk in ATSI patients (p <0.05). After analysis this difference was due to a lower score in the ATSI population for the “Age” component of the score (0.85 ± 0.68 vs. 1.48 ± 0.59 p <.001). There was a 12-year difference in the mean age between the two groups (Fig. 1). This difference is partially offset by a higher score in the “Risk Factor” component of the HEART score in the ATSI group (1.66 ± 0.56 vs 1.32 ± 0.64 p <.001). There were no significant differences in the History, ECG or Troponin components of the score. Assessment of ATSI patients with a modified version of the HEART score that assigns increased risk to ATSI patients at a younger age (adjusted age bracket 40-60 years) reconciles the difference between the two groups (6.75 ± 1.46 vs. 6.76 ± 1.48 p <.095).

Figure 1

Conclusion: The HEART score significantly underestimates risk in ATSI patients. Modification of the age component of the score is required in order to produce accurate risk assessment in this population.

P397 | BEDSIDE
Prediction of critical limb ischemia incidence in hemodialysis patients with peripheral artery disease
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Purpose: Hemodialysis patients with critical limb ischemia (CLI) suffer chronic inflammation, repeated infection, require intervention, and can have a protracted hospital stay. Early prediction is the most important for management of CLI in hemodialysis patients with PAD.

Methods: The HEART score data was collected from consecutive patients admitted to our hospital with myocardial infarction over one year. The HEART score for both patients groups was calculated and analysed for validity and proposed modification.

Results: 441 patients were admitted to Cairns Hospital over a one year period with myocardial infarction – 120 of these patients were ATSI and 321 were non-Indigenous. The mean HEART score for ATSI and non-Indigenous patients was 6.43 ± 1.56 and 6.76 ± 1.48 respectively. The HEART score significantly underestimated the risk in ATSI patients (p <0.05). After analysis this difference was due to a lower score in the ATSI population for the “Age” component of the score (0.85 ± 0.68 vs. 1.48 ± 0.59 p <.001). There was a 12-year difference in the mean age between the two groups (Fig. 1). This difference is partially offset by a higher score in the “Risk Factor” component of the HEART score in the ATSI group (1.66 ± 0.56 vs 1.32 ± 0.64 p <.001). There were no significant differences in the History, ECG or Troponin components of the score. Assessment of ATSI patients with a modified version of the HEART score that assigns increased risk to ATSI patients at a younger age (adjusted age bracket 40-60 years) reconciles the difference between the two groups (6.75 ± 1.46 vs. 6.76 ± 1.48 p <.095).

Figure 1

Conclusion: The HEART score significantly underestimates risk in ATSI patients. Modification of the age component of the score is required in order to produce accurate risk assessment in this population.

P399 | BEDSIDE
How can we improve attendance to cardiac rehabilitation after an acute coronary syndrome? A multifaceted intervention in our city
P. Sigaud1, B. Gencer2, S. Reverdin1, P. Meyer1, F. Mach1, 1Geneva University Hospitals. Cardiology Division. Geneva, Switzerland; 2Geneva University Hospital. Cardiology Division. Geneva, Switzerland

Introduction: Cardiac rehabilitation (CR) is strongly recommended after an acute coronary syndrome (ACS), but underused in clinical practice. Few studies assessed interventions to improve the accessibility and attractiveness of CR programs in Switzerland.

Methods: We designed a multifaceted intervention for patients admitted after an ACS at our university hospital, which consisted in 3 main areas of focus: (1) to fix systematic early appointment to CR within 7 days after hospital discharge, (2) to offer to all patients free bus passes for our city’s transport network during outpatient CR, and (3) to incorporate novel and more stimulating physical activities in the CR program, such as riding electric bicycles, Nordic walking and urban training. We compared two main outcomes based on medical records: (1) the CR referral time from hospital discharge to start of the CR program and (2) the number of patients who attended the CR program before (June-December 2012) and after (June-December 2013) the intervention. We also assessed the natural evolution before the intervention using data from 2010 and 2011.

Results: Before the intervention, the mean CR referral time gradually increased from 18 days in 2010 to 28 days in 2013 (before June 2013). During same period, the number of participants to our CR program progressively increased by 15.5% each year. After the implementation of the intervention (from June 2013), we observed a significant decrease of the CR referral time to 9.3 days and a significant improvement of the number of CR participants (130 in June-December 2013 compared to 96 in June-December 2012). 2/3 participants received a free bus pass at the start of the program, while others had already an available pass. No participants refused this offer.

Conclusion: Our intervention decreased successfully the CR referral time and increased CR attendance ensuring a continuum and coherence in the process of care of patients with ACS. This multifaceted approach might be cost-effective and should be evaluated in other settings.

P400 | BEDSIDE
Severe erectile dysfunction in coronary heart disease patients: a marker for poorer outcome

Erectile dysfunction (ED) prevalence is unsurprisingly high in coronary artery disease, reflecting similar vascular abnormalities. We aimed to evaluate the prognostic value of ED in patients enrolled to a cardiac rehabilitation program (CRP) after an acute coronary event. Methods: Retrospective cohort of 373 male patients enrolled in a cardiac CRP after an acute coronary event. Data regarding sociodemographic, clinical and risk factor profile was abstracted from clinical records. Erectile function was evaluated through the 5-Questions International Index of Erectile Function (IEF). We categorized patients in two groups: group 1 (mild to moderate ED, IEF <12) and group 2 (no or mild ED, IEF ≥12). Data on mortality and morbidity outcomes was analyzed. We used a composite outcome (all cause mortality, new hospital admission for ACS, stroke and CHF and/or revascularization procedures). Relevant variables identified in univariate analysis were included into a multivariate regression model using cox proportional hazards method to establish prognostic significance of severe erectile dysfunction.

Results: In this study 62 patients (16.6%) had moderate/severe ED. This group was older (G1:57.9±8.9 years vs G2:52.9±9.3 years; p<0.01) and showed higher prevalence of diabetes (G1:33.8% vs G2:13.4%, p<0.01), more extensive coronary vessel involvement (2.2 coronary vessel involved, G1:47.3% vs G2:33.8%, p<0.01), higher cumulative tobacco consumption (G1:57.9±8.6pack/year vs G2:47.3±9.3pack/year) and more severe heart failure (NYHA III/IV, G1:40.4% vs G2:18.5%, p<0.01). Furthermore, this group was more likely to suffer from dyslipidemia (G1:81.0% vs G2:67.7%, p<0.01). Multivariate regression analysis demonstrated a significant association between ED and mortality (HR: 2.95, 95% CI: 1.12-7.86, p<0.03) and new hospital admission for ACS (HR: 2.81, 95% CI: 1.14-6.92, p<0.02) after adjusting for age, gender, diabetes, dyslipidemia and heart failure.
P403 | BEDSIDE
Magnitude and etiology of muscle wasting after on-pump coronary artery bypass graft surgery: implications for rehabilitation
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Purpose: The magnitude and etiology (hormonal disturbances, inflammation, immobilisation, insulin resistance) of muscle wasting after coronary artery bypass graft surgery (CABG) is speculative. How to prevent muscle wasting after CABG surgery and/or whether muscle mass regain should be aimed at during rehabilitation remains thus uncertain.
Methods: Whole-body lean tissue mass was assessed before and 24±6 days after CABG surgery in 25 subjects. Blood testosterone, cortisol, insulin-like growth factor-1 (IGF-1), growth hormone, sex-hormone binding globulin (SHBG), glucose, insulin, c-peptide, c-reactive protein (CRP) content, and free androgen index, cortisol/testosterone ratio, HOMA-IR index were assessed before surgery, during the first three days after surgery, and at body composition re-assessment. Relations between changes in whole-body lean tissue mass and changes in blood parameters after surgery or subject characteristics were studied.
Results: After surgery, free androgen index and blood SHBG, testosterone and IGF-1 content decreased significantly, while HOMA-IR index, cortisol/testosterone ratio, blood CRP content increased significantly (p<0.0025). Whole-body lean tissue mass decreased significantly (-2.1±0.2kg, p=0.0025) after surgery. Amount of whole-body lean tissue mass loss after CABG surgery was independently related to younger age, greater increase in blood cortisol/testosterone ratio after surgery, and shorter time interval to body composition re-assessment (p<0.05).
Conclusion: Significant lean tissue mass loss is observed after CABG surgery. Especially in younger subjects and/or subjects with greater increase in blood cortisol/testosterone ratio after surgery and earlier re-assessment of body composition, rehabilitation interventions should be adapted to prevent muscle wasting and/or maximize muscle mass regain.

P404 | BEDSIDE
Improvement of cardiopulmonary exercise test parameters in patients affected by pulmonary arterial hypertension (PAH) after cardiorespiratory training in a day-care service
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Purpose: PAH is a rare disease characterized by a severe impairment of functional status and quality of life. Recent studies reported positive effects of rehabilitation on these aspects of PAH. Aim of this study was to evaluate the feasibility of a cardiorespiratory training program in a day-care service and the possible effects on exercise capacity in PAH patients.
Methods: Twelve patients (M/F 1/1, age 44±14) affected by PAH in WHO classes II and III and stable clinical conditions were enrolled in a 4 weeks cardiorespiratory training program as our day-care service, consisting in aerobic and resistance exercises, inspiratory muscles reinforcement, slow breathing and relaxation sessions. Patients were checked in occasion of a routine control (T0), one month later at the beginning of the training (T1), and at the end of training program (T2). Patients underwent to pulmonary function and exercise capacity evaluation by execution of spirometry, diffusion test for CO, 6-minute walking test (6-MWT) and maximal cardiopulmonary exercise test (CPET). Quality of life was examined by the EuroQuol-5D. Echocardiography and brain-natriuretic peptide measurement were also done. Primary end-point was the effect of training on peak VO2.
Results: No changes were observed from T0 to T1 as result of clinical status stability. After training, at T1, improvements of quality of life (from 0.7±0.2 to 0.88±0.12, p<0.012) and functional capacity (+37 m at 6MWT and +14 watt at CPET) were recorded, with an increasing of peak VO2 and pulse O2 (tab1). During training sessions no adverse events were observed.

<table>
<thead>
<tr>
<th>Time</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWT (m)</td>
<td>476±107</td>
<td>475±111</td>
<td>513±99&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.020</td>
</tr>
<tr>
<td>%Predicted 6MWT</td>
<td>78±14</td>
<td>78±13</td>
<td>84±10&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.034</td>
</tr>
<tr>
<td>Workload peak (W)</td>
<td>76±22</td>
<td>77±21</td>
<td>90±21&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.001</td>
</tr>
<tr>
<td>VO2 peak (m/min)</td>
<td>1137±243</td>
<td>1100±209</td>
<td>1305±302&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.003</td>
</tr>
<tr>
<td>CI2 peak (m/min/bpm)</td>
<td>1.8±0.3</td>
<td>2.0±0.3</td>
<td>8.2±2.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.019</td>
</tr>
</tbody>
</table>

<sup>a</sup>p<0.05 vs same variable at T0, <sup>b</sup>p<0.05 vs same variable at T1.

Conclusions: Cardiorespiratory training in day-service is feasible for PAH patients in class WHO II and III with an increase of exercise capacity due to a strengthened muscular performance and a better quality of life, without side effects. This improvement allows the patients to achieve better functional and prognostic classes.

P402 | BEDSIDE
Impact of cardiac rehabilitation on mortality and cardiovascular events after percutaneous coronary intervention
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Purpose: Although numerous studies have reported that cardiac rehabilitation (CR) is associated with reduced mortality after myocardial infarction, less is known about its association with mortality after percutaneous coronary intervention. The aim of this study was to examine the effects of cardiac rehabilitation (CR) on reinfarction, cardiac mortality and all-cause mortality after percutaneous coronary intervention.
Methods: We performed a retrospective analysis of data from a prospectively collected registry of 768 consecutive patients who underwent percutaneous coronary intervention in our university hospital from 2005 to 2008.
Results: During a median follow-up of 2.5 years, 106 deaths (65 cardiac) and 34 myocardial infarctions, occurred in the study subjects. Participation in CR, noted in 35.2% (277 of 786) of the cohort. CR was associated with a significant decrease in all-cause mortality (5.4% vs 17.8%, p<0.001) OR 0.264 [0.149-0.465]). A significant decrease in cardiac mortality was also observed (1.4% vs 12.1% p<0.001) OR 0.107 [0.038-0.296] in CR participants; however, no effect was observed for subsequent myocardial infarction.
Conclusion: We found that CR participation after percutaneous coronary intervention was associated with a significant reduction in cardiac mortality and in all-cause mortality rates.

P401 | BEDSIDE
Beneficial effect of cardiac rehabilitation on the endothelial function and arterial stiffness pronounced at 6 months after myocardial infarction (Forever study)
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Endothelial function and arterial stiffness have proved prognostic value for patients after acute coronary syndrome (ACS). Aim of the study was to investigate longstanding effect of early cardiac rehabilitation (CR) on endothelial function and arterial stiffness in prospective cohort of patient after ACS. Population of study consists 90 patients treated in study center during and after ACS. All the patients were offered participation in the program of early CR, 73 patients completed program. Follow up of all patients include 3 visits: first visit – before CR (2 weeks ± 2 days after ACS), second visit – after completed program of CR or the corresponding time for the group of 17 patients who didn’t participate in CR (control group), third (6 months ± 2 weeks after ACS). During each visit we determine arterial stiffness measuring pulse wave velocity (PWV) using Comploid device and endothelial function measuring reactive hyperemia index (RHI) using EndoPAT 2000 system. Table 1 presents PWV and RHI of rehabilitated patients compared with control group using t-Test.

<table>
<thead>
<tr>
<th>PWV</th>
<th>RHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I visit</td>
<td>10.8±3.14 vs. 11.5±2.71; NS</td>
</tr>
<tr>
<td>II visit</td>
<td>9.2±2.06 vs. 11.9±3.53; p&lt;0.0001</td>
</tr>
<tr>
<td>III visit</td>
<td>28.02±10.41 vs. 11.10±3.37; p=0.0036</td>
</tr>
</tbody>
</table>

Beneficial effect of CR program on arterial compliance appears soon after CR program and remain significant 6 month after ACS. Significant difference between rehabilitated and non-rehabilitated patients in endothelial function is evident in 6 month after ACS. At 6 month after ACS arterial compliance and endothelial function of rehabilitated patients were better than in control group.
**P406 | BEDSIDE**  
The effects of an aerobic exercise programme using video gaming on the fitness level of cardiac patients

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**Purpose:** There is incontrovertible evidence for the effectiveness of exercise in improving the fitness of persons with stable chronic heart disease. Active play video games are becoming increasingly popular for use in exercise for improvement of cardiovascular health, but little evidence exists for their effectiveness in improving fitness in cardiac patients. This study examined the effects of an aerobic exercise programme, using a video gaming system, on the fitness level of cardiac patients.

**Methods:** An experimental pre-test post-test design was used. Twenty-one (21) subjects referred for exercise training by cardiologists/cardiothoracic surgeons consented to participate in the study. Each individual was required to complete 40-minute sessions of aerobic exercise using a video gaming system (rhythm boxing, free step, obstacle course, free run, island run, super hula hoop, rhythm parade, advanced step) three times per week for 6 weeks. The outcomes assessed at baseline and post-intervention were: distance walked in 6 minutes (6MWD), peak oxygen consumption (VO2peak), resting blood lactate, resting blood pressure and resting heart rate. Participants were also asked to rate their overall enjoyment of the sessions using a visual analogue scale (VAS). 0 = not at all enjoyable and 10=extremely enjoyable. The paired t-test was used to examine differences in the outcomes pre- and post-intervention.

**Results:** Nineteen persons (9 females, 10 males), mean age 60.2±12.3 years old, completed the study. Two subjects were unable to complete the six weeks, one due to post-thoracotomy pain and the other, the development of angina resulting from an occluded coronary stent. There was a significant increase in the 6MWD (pre-test 477.9±114.1 metres, post-test 526.8±132 metres, p<0.001) and VO2peak (pre-test 14.4±4.6 mL/kg/min, post-test 15.9±5.2 mL/kg/min, p<0.001). Resting blood lactate was significantly reduced (pre-test 2.9±1.1 mmol/L, post-test 2.06±0.8 mmol/L, p<0.005). No significant changes were noted in resting systolic (p=0.07) and diastolic (p=0.81) blood pressures or in resting heart rate (p=0.17). The average enjoyment score using the VAS was 8.9.

**Conclusions:** Aerobic exercise using video games is effective in increasing the exercise capacity of cardiac patients and may be an enjoyable alternative to traditional modes of exercise.

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**P406 | BEDSIDE**

Statins impair exercise training induced strength gain in coronary artery disease patients

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**Purpose:** Statin use may be associated with adverse skeletal muscle effects. Since physical fitness is an important determinant of outcome of patients with coronary artery disease (CAD) and exercise training (ET) is the core component of cardiac rehabilitation, our objective was to determine if statins have effects on changes in muscle strength after a six-month exercise-based cardiac rehabilitation in patients with CAD. The study population belongs to a larger ARTEMIS-study (Clinical-Trials.gov, Record1539/31/06, Identifier NCT01426865).

**Methods:** Peak isometric strength of leg extenders (STPeak) and peak oxygen consumption (VO2peak) were measured for 36 patients with CAD (12 women and 24 men, age 63±5y, BMI 27.1±3, STPeak 3.6±1.0 kg/kg, VO2peak 25±7 mL/kg/min) before and after six-month home-based ET program according to current guidelines. Twelve patients were not on statin treatment (non-STAT). For this group 24 patients using statins (STAT) were matched (1:2) according to age, gender, diabetes status, baseline BMI, -STPeak and -VO2peak from the ARTEMIS database.

**Results:** STPeak increased by 17±22% (3.6±1.2 vs. 4.1±1.5 kg/kg) for non-STAT but did not change for STAT (0.1±7 vs. 3.6±0.9 kg/kg, p<0.0001 for interaction). Changes in VO2peak did not differ between the groups (non-STAT 5.1±9% vs. STAT 3.6±6%, p=0.178 for interaction). Furthermore, the groups did not differ from each other according to changes in BMI, other medication than statins, clinical status at baseline e.g. ejection fraction or realised exercise training (p ns for all).

**Conclusions:** Statins may attenuate increases in strength of leg extenders associated with exercise-based cardiac rehabilitation in CAD patients. Given the strong independent cardioprotective effects of statin therapy and evidence of increased muscle strength to improve functional capacity and well-being, the benefits and disadvantages of each should be considered in cardiac rehabilitation.

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**P407 | BEDSIDE**

Adherence to cardiac rehabilitation after acute coronary syndrome: Findings from a randomized controlled trial comparing shared municipal care vs hospital care

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**Purpose:** The aim was to compare shared care cardiac rehabilitation (SC-CR) to hospital-based CR (H-CR) in terms of adherence.

**Results:** CR suffers from underutilisation and lack of adherence, even though it is documented that cardiovascular mortality is reduced if CR is effectively implemented. CR attendance could potentially be improved if provided by the Municipal Health Care Centers (MHCC) in collaboration with the general practitioners (GP) thus offering both proximity and profound knowledge of the patients.

**Material and methods:** Patients were screened during admission for acute coronary syndrome (ACS) in 4 coronary units in the Central Region of Denmark from Oct 2011 till March 2013. Participants (18-80 years, EF>40%), no prior rehabilitation were randomized to phase II CR given either as SC-CR or H-CR. In SC-CR, the MHCC provided the lifestyle interventions while the GP was in charge of risk factor management and of the medical treatment.

The outcome was adherence to the CR-programme defined as a composite measure of adherence to the different elements of CR (smoking cessation course, dietary counselling, exercise training, clinical assessment, patient education and talks with health staff). Full adherence was defined as attending 50% or more of each of the elements.

**Results:** 212 patients were recruited. Data on patient reported adherence at 4 months follow-up is seen in the table.

<table>
<thead>
<tr>
<th>Adherence to cardiac rehabilitation</th>
<th>H-CR (n=97)</th>
<th>SC-CR (n=93)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full adherence</td>
<td>43</td>
<td>52</td>
<td>1.59 (0.86;2.94)</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>85</td>
<td>83</td>
<td>1.17 (0.43;3.21)</td>
</tr>
<tr>
<td>Vis at the GP</td>
<td>62</td>
<td>83</td>
<td>4.69 (2.06;11.36)</td>
</tr>
<tr>
<td>Dietary counselling</td>
<td>85/86</td>
<td>65/73</td>
<td>1.01 (0.00;7.05)</td>
</tr>
<tr>
<td>Deselectected</td>
<td>11</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>34/38</td>
<td>29/34</td>
<td>0.68 (1.32;5.52)</td>
</tr>
<tr>
<td>Exercise testing</td>
<td>60/73</td>
<td>49/67</td>
<td>0.59 (2.41;1.42)</td>
</tr>
<tr>
<td>Deselectected</td>
<td>24</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Patient education</td>
<td>33/53</td>
<td>50/82</td>
<td>0.95 (4.40;2.04)</td>
</tr>
<tr>
<td>Talks with health staff</td>
<td>51/72</td>
<td>52/82</td>
<td>0.68 (3.21;1.42)</td>
</tr>
</tbody>
</table>

**Conclusion:** Full adherence to CR among patients with ACS was seen more frequently in patients receiving SC-CR. Data on specific lifestyle changes regarding secondary prevention are underway.

**P408 | BEDSIDE**

Rehabilitation early after heart transplantation: modalities and feasibility

P. Meurin1, J-Y. Tabet1, S. Varnous2, C. Aubailly2, F. Gabin3, H. Weber1, S. Ouldamar2, S. Guendouz3, A. Ben Driss1, N. Renaud1. 1Les Grands Prés, Villeuneuve Saint Denis, France; 2Hospital Pitié-Salpetrière, Paris, France; 3University Hospital Henrion Mondor, Hospital Mondor, Creteil, France

**Background:** During the three first months following heart transplantation, patients still require close medical follow up and exercise training (because of major pre and post operative muscular wasting). The objective of this study was to assess the usefulness of an inpatients Cardiac Rehabilitation center (inCRC) in these two settings.

**Methods:** 100 consecutive patients (age 47±13.2, men: 79%) referred to our inCRC less than 3 months after heart transplantation were included. Acute events (AE) occurring during the inCRC stay, exercise training modality and results were assessed.

**Results:** Patients were hospitalized in the inCRC 33±9±21 days after the transplantation, for a 25±9±11 days duration on average. During this period, AE occurred in 49% (n=49) of the patients: 24 graft rejection, 19 bacterial or fungal infection requiring IV antibioticotherapy, and 6 other AE. Most of these events were managed by the inCRC but 22 patients were temporarily referred to the transplant unit for treatment of 4 severe AE (infection n=1, tamponade n=1, acute rejection requiring plasmapheresis: n=3, other: n=7). 17 patients (17%) were col-

**Ergonomic improvements after rehab**

<table>
<thead>
<tr>
<th>Post op day 33±21 (before rehabilitation)</th>
<th>Post op day 60±22 (after rehabilitation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO2 (mL/kg/min)</td>
<td>12.7±3.2</td>
</tr>
<tr>
<td>Ventilatory threshold (mL/kg/min)</td>
<td>9.9±2.5</td>
</tr>
<tr>
<td>VO2max (mL/kg/min)</td>
<td>42.7±4.4</td>
</tr>
<tr>
<td>Maximal workload (watts)</td>
<td>60±17</td>
</tr>
<tr>
<td>Resting heart rate (bpm)</td>
<td>91±14</td>
</tr>
<tr>
<td>Maximal heart rate (bpm)</td>
<td>107±16</td>
</tr>
</tbody>
</table>

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onized by a multiresistant bacterium which required contact precautions during the exercise training sessions. Moreover, patients underwent 2.8±1.4 endomyocardial biopsies.

Finally, due to all these event, 23% (n=23) of the patients underwent only 5 exercise training sessions or less.

The exercise capacity improvement after completion of a classical exercise training program (n=13±5 sessions) is given in the table below for For the 77 other patients (77%).

Conclusion: Early after heart transplantation an inCRC can be useful (i) to-at a lesser cost than in a classical hospital- safely treat subacute complications under the guidance of the referent transplantation center and (ii) to perform an exercise training program.

WHAT AFFECTS OUTCOMES FROM CARDIAC REHABILITATION?

P411 | BEDSIDE

A new formula for chronotropic incompetence in coronary disease: what will it add?

Background: Chronotropic incompetence (CI) is common in patients (pts) with cardiovascular disease and produces exercise intolerance that impairs quality of life. It is also an independent predictor of major adverse cardiovascular events and mortality. However, the importance of CI is underappreciated, and CI is often overlooked in clinical practice possibly due to multiple definitions and the medication's effect. The traditional equation to predict maximal heart rate (HR) (220 – age), is widely used regardless of patients' characteristics, namely known coronary heart disease and/or beta-blockers (BB) use, and may be inadequate in such pts. Consequently, an alternative formula from Brawner (164 – 0.7*age) is gaining acceptance. We sought to evaluate and compare CI in pts referred to a cardiac rehabilitation program (CRP) after an acute coronary syndrome using distinct criteria (traditional vs the Brawner formula).

Methods: We retrospectively analyzed records of 453 pts participating in CRP at our institution, under BB therapy, referenced to a CRP from December 2008 to August 2013. CI was defined by the presence of chronotropic incompetence (peak HR – HR at rest)/age-expected HR reserve) < 0.62 or < 0.80 using the traditional (TF) and Brawner formula (BF). We divided pts into three categories [chronotropic incompetence (CI) only with BF, group I, CI with both formulas – group II and CI with both formulas – group III] and compared CI to TF.

Results: Patients’ mean age was 54±10 years and 88% were male. All were on BB therapy. CI was present in 157 (35%) and 46 (10%) cases using TF and BF, respectively. Comparing groups, patients with group I were younger (51±9 vs 56±8 years; p<0.043) and had higher HR at rest and maximal HR (73±12 vs 68±10 bpm; p=0.032; 124±9 vs 104±11 bpm; p<0.001) than those in group III. No significant differences were found regarding cardiovascular risk factors, Duke Activity Status Index, left ventricular function and other severity indicators. After Cox-regression multivariate analysis, higher HR at rest was the only independent predictor of CC diagnosis with BF (OR 2.0, 95% confidence interval: 1.34-3.01; p<0.001).

Conclusion: In a coronary artery disease population under BB therapy, TF overestimates CI. The use of BF can unmask false positives particularly in those cases with higher rates at rest, perhaps on dependency of lower doses of BB. These data points out that CI (as a prognostic indicator) may be over diagnosed in coronary patients.
P413 | BEDSIDE
What variables predict participation in exercise-based cardiac rehabilitation in patients with coronary artery disease?

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Purpose: Despite the well-established positive effects of exercise-based cardiac rehabilitation (CR) participation has been shown to be sub-optimal. A significant association between kinesiophobia (fear of movement) and participation in CR has previously been found. Therefore, the aim of this study was to identify predictors of participation in CR in patients with coronary artery disease (CAD), with a special reference to kinesiophobia.

Methods: In all, 332 patients (75 women; mean age 65.9±1 years) with a diagnosis of CAD were recruited between 2007 and 2009 at our hospital. The patients were tested regarding muscle endurance, level of physical activity, health related quality of life, anxiety, depression and kinesiophobia. A path model with direct and indirect effects via kinesiophobia was used to predict participation in CR. An explorative selection of significant predictors was performed.

Results: Kinesiophobia (p<0.012), waist circumference (p=0.023), and a previous history of PCI (p=0.037) had direct negative effects on participation in CR, while current incidence of CAGB (p<0.001), PCI (p<0.005) and BMI (p=0.008) had positive effects. Compared to patients diagnosed with unstable angina, a diagnosis of myocardial infarction (p=0.004) had a positive effect on participation in CR. The following indirect effects on participation in CR were found: Anxiety (p=0.001) and previous PCI (p<0.025) increased kinesiophobia, while muscle endurance (p<0.003), perceptions of general health (p<0.001) and physical functioning (p<0.009) decreased kinesiophobia. Moreover, men had higher kinesiophobia compared to women (p=0.031) and smoking was found to reduce kinesiophobia (p<0.004).

Conclusions: Several important variables with an influence on participation in CR were identified and should be further analysed in relation to clinical practice. A reduction of kinesiophobia can be an efficient way to increase participation in CR and should thus be given priority in future research.

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A multicentre retrospective study on outcomes among patients attending home-based and hospital-based cardiac rehabilitation (CR) programmes

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Purpose: This study aims to verify if home-based cardiac rehabilitation programme can reduce complications and improve the outcomes in term of mortality, hospitalization, morbidity, bodily condition and quality of life.

Methods: This is a retrospective, descriptive, multicentre study aiming to analyse rehabilitation outcomes. A total of 164 patients, who attended cardiac surgery during years 2012-2013, where recruited for this study: among all the patients included in its study the eHealth unit of CCM, while the hospital-based programme had cardiac surgery. For patients with pericardial effusion medical records were searched for patients 18 years or older who had cardiac surgery. Patients with pericardial effusion medical records were reviewed to evaluate its manifestations and management. To identify risk factors for its development.

Results: Of 1,416 patients admitted to our in-hospital cardiac rehabilitation within last 18 month, 669 (47.2%) had cardiac surgery (by pass, valves or combine). Patients were admitted to our in –hospital three weeks cardiac rehabilitation program from forth postoperative day to day sixty. Pericardial effusion was detected in 58 patients (8.7%), of whom 98.3% had nonspecific symptoms. Clinical features of tamponade were documented in 1 patient. Effusion was evacuated by echocardiography-guided pericardiocentesis. The totals of 57 patients were treated conservatively. Independent risk factors for effusion were larger body surface area, hypertension, renal failure, urgency of operation, cardiac operation other than coronary artery bypass grafting

Conclusions: In our study, pericardial effusion occurred in 8.7% of patients, and symptoms were nonspecific. Several factors, mainly related to preoperative characteristics and type of operation, predispose patients to effusion.

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Importance of optimizing chronotropic response and reserve during cardiac rehabilitation and different chronotropic profiles with classical and new heart rate-lowering therapies

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Purpose: B-blockers may induce exercise intolerance during cardiac rehabilita- tion programs (CRP) due to negative inotropism. We wondered if Ivabradine may provide a better tolerance to exercise and better chronotropic profile during the program in intolerant participants to B-blocking agents.

Methods: We analysed our data from the cardiac rehabilitation unit in 2013, when 108 patients completed the program. 28 replacing prescriptions (from Bisoprolol to Ivabradine) were necessary due to intolerance to exercise, despite reductions to minimum doses. We assessed the chronotropic response (maximum heart rate- heart rate at rest (MHR-HRR) and chronotropic reserve (MHR-HRR/ (220-AGE-HRR) x100). We measured them, both at the time of the replacement and at the end of the program and compared both groups, correlating chronotropic profiles with increment in METs functional capacity.

Results: 80 participants were maintained with Bisoprolol 5 mg daily, whereas the other 28 were prescribed 5 mg Ivabradine b.i.d in substitution. The bisoprolo group (BG) mean age was 59.15 years, and mean ejection fraction (EF) 58.2% (95% CI 46.7-66.7%) versus 61.82 years and 56.12% (95% CI 47.15-67.25%) in the Ivabradine group (IG). Maximum heart rate (MHR) was higher among those patients taking Ivabradine at the end of the program, reaching a mean of 138.15 bpm, 11.4 bpm more than b-blocked patients (MHR 138.15 vs. 126.66 bpm p<0.05). On the contrary, no significant differences were found between both groups when analysing maximum METs functional capacity in the final exercise test (BG mean METs 9.72 vs. IG 10.38 p<0.05). However incremental METs were higher in the Ivabradine group due to lower basal METs in the preliminary exercise test just before the replacement therapy was prescribed.

Conclusions: Ivabradine represents a suitable alternative to those patients who complain for intolerance exercise due to B-blocking agents. Both Ivabradine and Bisoprolol allow reaching a remarkable increment of METs in the final exercise test of the CRP. However, although chronotropic response and reserve may be higher in patients taking Ivabradine than in those with Bisoprolol, Ivabradine must only be considered in exercise intolerant patients after excluding other pharmacological or clinical reasons.

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Incidence and characteristics of pericardial effusion after cardiac surgery in patients referred to in-hospital cardiac rehabilitation

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Background: We aimed to review recent experience at our institution in the diag- nosis and treatment of pericardial effusion in patient who were referred to our in-house cardiac rehabilitation program after cardiac surgery and to identify risk factors for its development.

Methods: We aimed to review the clinical data of patients 18 years or older who had cardiac surgery. For patients with pericardial effusion medical records were reviewed to evaluate its manifestations and management. To identify risk factors for its development, study patients were compared with patients after cardiac surgery without pericardial effusion.

Results: Of 1,416 patients admitted to our in-hospital cardiac rehabilitation within last 18 month, 669 (47.2%) had cardiac surgery (by pass, valves or combine). Patients were admitted to our in –hospital three weeks cardiac rehabilitation program from forth postoperative day to day sixty. Pericardial effusion was detected in 58 patients (8.7%), of whom 98.3% had nonspecific symptoms. Clinical features of tamponade were documented in 1 patient. Effusion was evacuated by echocardiography-guided pericardiocentesis. The totals of 57 patients were treated conservatively. Independent risk factors for effusion were larger body surface area, hypertension, renal failure, urgency of operation, cardiac operation other than coronary artery bypass grafting

Conclusions: In our study, pericardial effusion occurred in 8.7% of patients, and symptoms were nonspecific. Several factors, mainly related to preoperative characteristics and type of operation, predispose patients to effusion.

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Diastolic function during exercise: effects of a 12 week high-intensity exercise program in patients with a recent myocardial infarction


Purpose: Reduced left ventricular (LV) diastolic function is a negative prognostic marker after acute myocardial infarction. High-intensity interval training can improve functional capacity in myocardial infarction patients, but it is not known
whether it can improve diastolic function. Our aim was to study whether a twelve week high-intensity interval training program could improve diastolic function in patients with a relatively recent myocardial infarction.

Methods: Thirty patients (27 males, 3 females, mean age = 56 (8) years, mean time from infarction = 78 (45) days) performed high-intensity interval training twice a week for 12 weeks. Each training session consisted of four 4-minute intervals at 85-95% of peak heart rate, separated by 4-minute active breaks at 70%. A cardiopulmonary exercise test was performed to determine peak oxygen uptake (VO2peak). Echocardiography, including color tissue Doppler of the LV, was performed during supine rest and during an upright bicycle exercise test (peak load 75 Watt).

Results: There was a significant increase in VO2peak from baseline to follow-up (35 (7) vs. 39 (7) ml/kg/min, p<0.001). There was a significant correlation between improvement in VO2peak and early diastolic velocity (e) at rest (r=0.41, p=0.01) and the relationship was present both at baseline and follow-up (r=0.48, p=0.007, and r=0.41, p=0.03). There was a trend towards an increase of e’ at 75 Watt from baseline to follow-up (8.1 (1.6) vs. 8.5 (1.7) cm/s, p=0.06), but no change in e’ at rest (7.2 (1.9) vs. 7.3 (1.6) cm/s, p=0.43). There was no change in E/e’ at rest (10 (2) vs. 10 (2), p=0.84, E/e’ at 75 Watt (11 (3) vs. 11 (3), p=0.70) or E/A ratio at rest (1.2 (0.3) vs. 1.1 (0.3), p=0.41). There were no changes in variables describing left ventricular systolic function: mitral annular systolic velocity (s’) at rest (6.0 (1.0) vs. 6.0 (0.9) cm/s, p=0.93), s’ at 75 Watt (7.9 (1.1) vs. 8.0 (1.3) cm/s, p=0.83), or mitral annular plane systolic excursion at rest (13 (3) vs. 13 (1) mm, p=0.38). Heart rate was unchanged at rest (59 (7) vs. 57 (8), p=0.13) and at 75 Watt (94 (13) vs. 91 (11), p=0.12).

Discussion: The purpose of this study was to identify a cardiovascular condition that can affect diastolic function. The results demonstrate the importance of obtaining measurements during exercise when evaluating the effects of an exercise training intervention.

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The effect of education level on CR outcomes after primary PCI

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Purpose: Previous research has shown that higher education is related with more participation in cardiac rehabilitation (CR). However, little is known whether education level influences CR outcomes. This study investigated whether the effect of CR on quality of life is predicted by education level.

Methods: Between January 2009 and March 2011, 408 patients who underwent primary Percutaneous Coro operation (pPCI) after acute myocardial infarction (AMI) were included in this study. Patients were stratified into 3 education levels (left vs. middle vs. right) and intervention groups. Patients not participating in CR formed the control group. Education level was determined with a self-reported questionnaire and divided into low and high. Low education level was considered when the patient’s highest achieved education level was primary school or secondary school. High education level was considered when patients completed secondary vocational, a degree or university. Quality of life was measured using ShortForm-12 questionnaire (SF-12). This questionnaire distinguishes a physical component score (PCS) and a mental component score (MCS). Patients filled out the questionnaires at baseline (T0), after 12 weeks (T1) and after one year (T2).

Results: 253 patients participated in CR, 155 did not. In the CR-group, 73% was highly educated and only 62% in the control group (P<0.05). For both PCS and MCS, all patients in the CR-group showed larger improvements from T0 to T12 and from T0 to T25 compared to the control group (P<0.05). From baseline to twelve weeks, low-educated patients in the CR-group showed a non-significant higher improvement on PCS and MCS compared to highly-educated patients. However, from baseline to one year, the highly-educated patients in the CR-group showed non-significant larger improvements compared to low-educated patients.

Discussion: Patients who participated in CR had larger improvements in quality of life after twelve weeks and one year follow-up compared to patients who did not attend CR. Highly-educated patients did not benefit more from CR compared to low-educated patients.
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High intensity, interval exercise improves the quality of life, ventricular diastolic function, ergonomic capacity and psychological status of patients with chronic heart failure: A phase iii randomi

Background: The aim of this work was to evaluate the effect of high intensity, interval exercise on the quality of life (QoL) and diastolic function among chronic heart failure (CHF) patients.

Methods: A phase III clinical trial. Of the 100 consecutive CHF patients (NYHA class II-IV, age 18-70 years) that were randomly allocated to exercise treat-
ment or control, 72 (exercise group, n=33, 63±9 years; 88% men, 70% ischemic heart failure and exercise group, n=39, 56±11 years; 82% men, 70% ischemic heart failure) completed the study. The intervention group followed a high intensity, interval ergometric training (i.e., 30 sec at 100% of max workload, 30 sec at rest) for 30 min/day-by-12 weeks, whereas the control group received regu-
lar instructions. Echocardiographic assessment was performed before and after completion of the intervention. The pulsed tissue Doppler imaging (TDI) of the systolic and diastolic function of mitral annulus was characterized by the systolic wave Smv, and the diastolic waves: Emv and Amv. Furthermore the ratio E/Emv and the flow propagation velocity (Vp), left ventricular outflow velocity integral (VTI), and left atrial fraction were also calculated. QoL was evaluated using the validated and translated Minnesota Living with Heart Failure questionnaire (MLHFQ) and depression level decrease (p<0.05). Sim-
ilarly, intervention group improved 6-minutes-walk test by 13%; VO2 max level (p=0.06); decreased E to A ratio by 24% (p=0.004) and decreased E to Emv ratio by 8% (p<0.05), with no significant change on control group (all p>0.05). Sim-
ilarly, intervention group improved 6-minutes-walk test by 13%; VO2 max level by 12.5% (p=0.002;VC02 level by 21%; L/min (p=0.01); total power by 83% watts (p=0.04), as compared with the intervention group.

Conclusion: High intensity, systematic aerobic training, which was feasible to
both CHF patients, should be strongly encouraged by clinicians, since it seems beneficial improving their QoL, by increasing their fitness level, as well as their psychological status, in parallel with improvement in diastolic function.

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Positive effect of early combined physical training in patients after aortic prosthetic valve replacement
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Aortic stenosis is the most common valve disease due to a growing elderly popu-
lation, both the studies on post aortic prosthetic valve replacement (AVR) physical rehabilitation are rare. Cyclic training data in the AVR subjects are sporadic.

Purpose: To assess the effect of cycling sessions additional to routine physi-
cal training in patients after aortic prosthetic valve replacement (AVR). Subjects. 33 stable cardiovascular disease (CVD) patients after AVR: 52% women, age, 63±9.6 years.

Methods: 9:12 days after surgery all subjects started every day in hospital super-
novated combined physical training programme that involved 25 minutes of moder-
ate aerobic exercises for extremities, and additional cycle training including gradu-
ally increasing (from 6 to 14 minutes) working period with the baseline workload of 25W. The cycle training intensity increased gradually (SW every 2 days) in accord-
rance with the individual somatic condition and improvement. Also all patients were encouraged to attend everyday moderate unsupervised walking sessions for 6 -
20 minutes. At baseline and pre-discharge the 6-minute walk (6MW) test, Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS), the State-Trait Anxiety Inventory (STAI), the Mini–Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA) were used. Quality of life (QOL) was assessed by a 10-score Visual Analogue Scale (VAS).

Results: Baseline 6MW distance was fair (346±16 metres), QOL score was 6.9±2.2. At baseline most of the patients demonstrated affective disorders, a co-morbidity of depression and anxiety was registered (r=0.87, p<0.05). Mental status data were associated with 6MW distance and QOL (depression level and 6MW: r=0.77, p<0.05; level of sleep disorders and 6MW: r=0.8, p<0.05, state anxiety level and QOL: r = −0.712, p<0.05). The level of cognitive functioning was reduced, average MMSE and MoCA scores were normal (27±1.4 and 27±1.3, respectively). At discharge patients practiced 8±1 combined physical training sessions; no serious adverse events were registered. There was a sig-
nificant benefit in the 6-minute walk outcome (405±15 metres, p<0.03) and anxi-
ey reduction (p<0.05), and the level of cognitive functioning and QOL (7.1±2.4) did not change significantly.

Conclusions: Combined (aerobic exercises and cycle training) early physical re-
habilitation programme is safe, improves aerobic fitness, and demonstrates extra benefits in anxiety decrease in post AVR patients.

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Benefits of exercise on physical fitness in patients with pulmonary arterial hypertension: a systematic review and meta-analysis of controlled trials
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Background: Pulmonary arterial hypertension (PAH) is a progressive disorder characterized by hypertension in the pulmonary artery due to increased pulmo-
nary vascular resistance. PAH leads to symptoms such as shortness of breath, dizziness, leg edema and chest pain, impacting heavily on the patients' daily life and participation in physical activity. Information stating that exercise training might be beneficial for this specific patient population is emerging; however the level of evidence is low. Therefore the aim of this systematic review and meta-
analytic research was to summarize the existing evidence for the use of exercise training to improve physical fitness and functionality in patients with PAH.

Methods: A comprehensive search up to January 2014 identified controlled trials, lasting at least 3 weeks, that investigated the effect of exercise training on physi-
cal fitness in symptomatic PAH patients. The updated clinical classification of PAH presented with PAH as defined according to the updated clinical classification of pulmonary hypertension. Studies were reviewed for study quality, participant de-
tails, exercise intervention characteristics, and intervention outcomes. Data were pooled by using the generic inverse variance method using random effect models and were expressed as weighted means and 95% confidence intervals.

Results: Of 110 identified abstracts, a total of 5 studies and 103 patients (exer-
cise: 50; control: 53; mean age 49.7 years) met the inclusion criteria for review. Severity of pulmonary hypertension ranged from mild to severe, 91 patients suf-
furred from PAH, and 12 patients had chronic thromboembolic pulmonary hyper-
tension. Exercise training led to a significant increase in 6 minute walk distance (72.5 m; 46.0 m to 99.1 m; p<0.0001) and peak oxygen uptake (2.16 mL/kg/min; 2.16 to 3.93; p<0.02). No severe adverse events related to exercise training were reported.

Conclusions: The findings from this systematic review and meta-analysis sug-
gest that exercise training improves exercise tolerance and functional capacity in patients with PAH. However further well designed and larger randomized con-
trolled trials are needed to confirm these findings.

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Safety and effectiveness of cardiopulmonary rehabilitation in stable patients with severe pulmonary arterial hypertension
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Purpose: Although disease-targeted medication improved prognosis in arterial hypertension, these persistent limiting factors of physical activity that decreases quality of life of these patients. A purpose of this prospective study was to evaluate safety and effectiveness of cardiopulmonary rehabilitation in stable patients with severe pulmonary arterial hypertension (PAH).

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Methods: Patients with PAH in WHO functional class II-IV on stable therapies for at least 3 months were eligible for this study. The cardiopulmonary rehabilitation programme consisted of a 2-week in-hospital rehabilitation followed by a 10-week home-based rehabilitation monitored telemetrically. A 6-minute walking test (6MWT) and cardiopulmonary exercise tests were performed, and Borg scale, WHO functional class, and N-terminal pro-B natriuretic peptide were assessed at baseline and after 12 weeks of rehabilitation. Additionally SF-36 was used to assess the quality of life. No changes in medication were made within the study period and preceding 3 months.

Results: Ten patients with PAH (7 women; mean age, 49.5±12.8 years; idiopathic pulmonary hypertension, n=7; Eisenmenger’s syndrome, n=3) completed a 12-week rehabilitation programme. After 12 weeks of cardiopulmonary rehabilitation, there was no significant change in 6MWT distance (354.4±93.7 vs. 359.8±80.4; p=0.83), NT-proBNP level (137.6±289.3 vs. 172.8±401.9; A: p=0.507), and peak oxygen consumption (14.4±3.0 vs. 15.9±4.1; p=0.142). Nevertheless, we observed a significant decrease in Borg scale (4.8±2.1 vs. 3.1±2.2; p=0.044), improvement in WHO functional class (2.9±0.7 vs. 2.4±0.7; p=0.043) and improvement in scores of quality of life. Rehabilitation was generally well tolerated, however complications such as presyncopy episodes and haemoptysis occurred in two patients.

Conclusions: A 12-week cardiopulmonary rehabilitation programme in patients with PAH improved dyspnoea, functional class and quality of life which was not reflected, however, in objective measures of physical activity. Strict monitoring of patients is necessary to timely prevent and treat potential complications.

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Heart rate variability and QTC interval in patients with chronic obstructive pulmonary disease receiving 4-week rehabilitation
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Purpose: Chronic obstructive pulmonary disease (COPD) modulates autonomic nervous system activity, increasing risk of arrhythmias. Potentially protective effects of not yet thoroughly investigated and seemed to correlate heart rate variability (HRV) and QTC interval in patients with COPD and healthy individuals, and to study effects of rehabilitation in patients with COPD.

Methods: 20-minute electrocardiograms were recorded to compare HRV parameters (heart rate, NN, RMSSD, pNN50, TP, LF, HF, LF/HF) and QTC interval (1) between 31 patients with COPD and 31 age- and sex-matched healthy controls. Rehabilitation intervention group consisted of a 2-week in-hospital rehabilitation followed by a 10-week home-based rehabilitation monitored telemetrically. A 6-minute walking test (6MWT), and incremental shuttle walking test (ISWT) were performed.

Results: Compared to healthy individuals, patients with COPD had higher heart rate (p<0.05), reduced NN, SDNN, RMSSD, pNN50, LF, HF, LF/HF and QTC interval (1) between 31 patients with COPD and 31 age- and sex-matched control patients with COPD. Before and after rehabilitation, electrocardiogram, St. George’s respiratory questionnaire (SGRQ), 6-min walk test (6MWT), and incremental shuttle walking test (ISWT) were performed.

Conclusions: Patients with COPD have reduced HRV in comparison with healthy controls. Rehabilitation improved HRV parameters that correlated with patient perception of COPD.

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Functional independence measure score predicts amputation-free survival in patients with critical limb ischemia following endovascular therapy
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Purpose: Non-ambulatory status is known to impact on the prognosis of patients with critical limb ischemia (CLI). However, whether the activity of daily life (ADL) status affects the prognosis of CLI patients following revascularization therapy has not been systematically explored. We investigated if the Functional Independence Measure (FIM) score for ADL is related to the prognosis of CLI patients after EVT.

Methods: Clinical outcomes were retrospectively evaluated in 79 consecutive patients (74±9 years; 61% male) with CLI who underwent successful endovascular therapy (EVT). ADL score was assessed at hospital discharge. Cox proportional hazard regression analysis was performed to explore the independent amputation free survival (AFS) determinants.

Results: Baseline ADL characteristics included 7% self-walking, 44% assisted walking and 49% wheelchair-dependent status. Average FIM score at discharge was 81±22. Chronic heart failure and FIM score at discharge were chosen as the independent predictors of AFS (Table). According to the receiver operating characteristic curve, the cut-off value of FIM score was 75 (sensitivity, 72%; specificity, 53%). AFS rate at 1 year was higher in the high (> 75) FIM group than in low (< 74) FIM group (82.3% versus 54.1%, p=0.020).

Conclusions: FIM score at discharge was independently associated with AFS after EVT in patients with CLI.
DRUG TREATMENT OF HYPERTENSION

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Comparison of Exforge HCT single pill combination and amlopidine/valsartan/hydrochlorothiazide free combination: health resource utilization and costs.

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Purpose: Single pill combinations (SPC) are associated with improved adherence and persistence and reduced healthcare resource utilization and costs in adult hypertensive patients with comorbidities. Recent evidence is available showing improved persistence and adherence for the SPC Exforge HCT, but its impact on resource use and costs has not yet been studied. This study investigated if Exforge HCT is associated with reduced healthcare resource utilization (HRU) and costs in adult hypertensive (HTN) patients compared to amlopidine/valsartan/hydrochlorothiazide free combination (FC).

Methods: The study included adults (18 yrs. or older) covered by commercial and Medicare Supplemental insurance in the Truven MarketScan database with an HTN diagnosis between October 2009 and December 2011. At least two filled prescriptions for Exforge HCT or two periods of at least 15 days of concurrent use of amlopidine, valsartan and hydrochlorothiazide (FC cohort) were required. Patients were continuously enrolled at least 12 months before and 12 months after the index prescription and had valsartan initial dose of 160 or 320 mg/day. Outcomes of interest included all-cause and HTN specific HRU, all-cause and HTN specific healthcare costs at 12 months. Chi-square tests and independent sample t-tests were used after adequate propensity score matching (PSM) (absolute standardized differences (ASM) <0.1) using demographics, comorbidities, pre-index HRU index costs and valsartan initial dose.

Results: From 9,221 Exforge HCT patients, 1,884 patients were successfully matched after PSM adjustment. All key variables such as demographics and comorbidities performed well within the threshold of ASM. Exforge HCT patients exhibited reduced all-cause and HTN specific ER visits and outpatients visits (difference: 7% to 25% decrease) (all p < 0.05). Exforge HCT patients also had a statistically significant (p < 0.05) lower proportion of patients with ≥1 all-cause hospitalization (15% vs 18.1%) and ≥1 all cause ER visit (25.7 vs 31.4%) and ≥1 ER HTN specific visit (9.7% vs 14.1%). The costs incurred by Exforge HCT patients were 3 to 44% numerically lower compared to the FC patients although not statistically significant except for all cause ER costs ($431 vs $549, p = 0.05).

Conclusion: Real-world data indicate that Exforge HCT is associated with reduced HRU compared to amlopidine/valsartan/hydrochlorothiazide FC.

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Clinical evidence of efficacy and safety of calcium channel blocker/thiazide combination therapy

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Objective: Combination therapy is increasingly common in the management of even uncomplicated hypertension. Most combinations are either based on a thiazide diuretic or on a dihydropyridine calcium channel blocker (CCB). No formal combinations of a CCB and a thiazide diuretic are available and there seems to have been some reluctance to use this combination. The following summarizes clinical evidence of efficacy and safety of the combination of a CCB with a thiazide diuretic.

Design and method: We searched PubMed and identified 345 abstracts, of which 45 articles were retrieved and reviewed for possible inclusion. Five studies (ELSA, VALUE, FEVER, CHOP, and CHIEF) with a total of 31’105 patients fulfilled the inclusion criteria and were included in the analysis. We calculated risk ratios (RR) as measures of treatment effects for all-cause mortality, cardiovascular mortality, myocardial infarction, and stroke at maximum available follow-up.

Results: The combination of CCB with a thiazide diuretic was similarly effective than the comparator in reducing all-cause (RR 0.89, 95% confidence interval [CI] 0.75-1.06) and cardiovascular mortality (RR 0.89, CI 0.71-1.10). CCB combined with a thiazide diuretic was more effective in preventing myocardial infarction (RR 0.83, CI 0.73-0.95) and stroke (RR 0.77, CI 0.64-0.92) than the combined combinations.

Conclusions: The present data document efficacy and safety of the CCB/thiazide diuretic combination in reducing cardiovascular morbidity and mortality. Elderly patients with isolated systolic hypertension may particularly benefit from CCB/thiazide combination, since both drug classes, have been shown to confer cerebrovascular protection.

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Efficacy and safety of LCZ696 add-on to amlopidine in patients with systolic hypertension uncontrolled with amlopidine monotherapy

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Purpose: A large proportion of patients with hypertension remain uncontrolled with currently prescribed combination therapies. This is the first study to evaluate the efficacy and safety of LCZ696 (Japanese Adopted Name [JAN]: Sucacetiril Val- sartan Sodium Hydroate), a first-in-class angiotensin receptor neprilysin inhibitor, plus an antibiotic (Aml) in adult hypertensive (HTN) patients with systolic hypertension (SH) who had uncontrolled blood pressure (BP) with Aml monotherapy in Asia.

Methods: In this multicenter, double-blind, parallel-group and active-controlled study, Asian patients who were inadequately responsive to Aml 5mg after a 4-week run-in period, with mean sitting (ma) systolic BP (SBP) >145mmHg and ≥180mmHg, were randomized to receive LCZ696 200mg add-on to Aml 5mg (LCZ696/Aml) or remain on Aml 5mg for an additional 8 weeks. Primary assessment was to test the superiority of LCZ696/Aml versus Aml in lowering 24-hour mean ambulatory (ma) SBP from baseline to Week 8.

Results: Of the total 371 patients screened, 266 (71.7%) patients who were not adequately responsive to Aml 5mg after 4 weeks were randomized (mean age, 55.4 years; maSBP/maDBP, 153.7/89.7/64.0mmHg; maSBP/maDBP/maPP, 139.0/86.1/52.8mmHg; males, 58.6%; body mass index, 26.3 kg/m²; mean duration of hypertension, 8.8 years). LCZ696/Aml versus Aml resulted in superior (p <0.001) least squares mean reduction in maSBP (Table) with a between-treatment difference of -13.1mmHg. LCZ696/Aml also showed significantly (p <0.001) greater reductions in ambulatory DBP and PP and office SBP/DBP and PP compared with Aml (Table). Overall incidence of adverse events (AEs) was similar with LCZ696/Aml (20.0%) and Aml (21.3%), and most of AEs were mild in severity.

Conclusion: This study demonstrated that adding LCZ696 to Aml provided significantly greater BP reductions and was generally well-tolerated compared with Aml alone. This combination, therefore, could be an effective treatment for Asian patients with SH uncontrolled with Aml monotherapy.

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Evaluation of a novel, fixed-dose combination of perindopril 3.5 mg/amlopidine 2.5 mg as a first-step treatment in hypertension with 24-hour ambulatory blood pressure monitoring

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Objective: To evaluate the efficacy over 24 hours of perindopril 3.5 mg/amlopidine 2.5 mg once daily, a novel fixed-dose combination with doses selected to achieve approximately equal blood pressure-lowering effects for each component, as a potential first-step treatment in patients with hypertension.

Methods: An international, randomized, double-blind, placebo-controlled substudy with 6 parallel treatment arms and an 8-week randomized treatment period,
whose design, clinical significance, and noninferiority criteria were in accordance with European guidelines.

**Results:** 1297 patients with mild-to-moderate uncomplicated hypertension, mean age 51.9 years, were randomized and 94.9% completed the study. The combination was statistically and clinically superior to placebo (between-group difference in mean change in SBP: -2.25 mm Hg, mean change in DBP: -3.99 mm Hg, P < 0.001 for both). The decrease in mean 24 h SBP/DBP were greater than with perindopril 5 mg (-3.82/-2.40, 95% CI [-5.84; -1.79]/[-3.84; -0.97], respectively and similar to amlopidine 3.5 mg (-0.03/0.26, 95% CI [-2.10; 2.04]/[-1.73; 1.21], respectively). These results were also supported by blood pressure measurements obtained over the daytime, nighttime, last 6 hours, and morning periods. Adverse events related to peripheral edema were less frequent with the combination compared to amlopidine 3.5 mg.

**Conclusions:** The optimized efficacy/tolerability ratio of the combination of perindopril 2.5 mg/amlopidine 3.5 mg as demonstrated by blood pressure lowering efficacy over 24 h and a favorable safety profile make it a suitable option for use as first-step treatment in uncomplicated hypertension.

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**Different angiotensin-converting enzyme inhibitors and mortality in patients with hypertension**

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**Background:** Despite the widespread use of angiotensin-converting enzyme (ACE) inhibitors, the comparative effectiveness of different ACE inhibitors in reducing cardiovascular morbidity and mortality in hypertensive patients is seldom reported.

**Methods:** Hypertensive patients who started captopril, enalapril, lisinopril, fosinopril, perindopril, ramipril, or imidapril therapy between January 1, 2004 and December 31, 2009 were identified from Taiwan’s National Health Insurance database. Overall, cardiovascular, cerebrovascular, and cancer mortalities were linked through Taiwan’s National Death Registry. Patients were followed from beginning ACE inhibitor therapy until death, disenrollment, or study termination (December 31, 2010). A Cox proportional hazard regression model was used to calculate the hazard ratio and 95% confidence interval, using ramipril as the reference group.

**Results:** A total of 989,489 hypertensive patients were included, with a mean follow-up ranging from 3.52 years for imidapril to 4.49 years for enalapril. Captopril initiators had the highest overall mortality rate (117.8 per 1,000,000 person-days) as compared to other ACE inhibitors (54.3 to 79.4 per 1,000,000 person-days). Patients who started captopril therapy had a significantly increased risk of overall mortality (adjusted hazard ratio 1.28, 95% confidence interval 1.24 to 1.31) when compared with the reference therapy ramipril. Enalapril (1.08, 1.05 to 1.11) and fosinopril (1.08, 1.05 to 1.12) were also associated with a modestly increased risk. No difference in mortality was found for lisinopril, perindopril, and imidapril, and comparable with ramipril.

**Conclusions:** There are substantive differences in the mortality risk associated with different ACE inhibitors. However, potential residual confounding effects might still exist.

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**Efficacy of LCZ696, an angiotensin receptor neprilysin inhibitor (ARNI), in obese and overweight subjects with hypertension**

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**Purpose:** This study assessed the efficacy of LCZ696 (Japanese Adopted Name [JAN]: Sucabitril Valsartan Sodium Hydrate), a first-in-class angiotensin receptor neprilysin inhibitor, versus valsartan in overweight and obese subjects with hypertension (HTN).

**Methods:** Data from two 8-week, multicenter, randomized, double-blind, placebo- and active-controlled studies in subjects with HTN were pooled to evaluate treatment effects. In two separate studies, baseline characteristics were comparable with fasting lipids (BMI) as normal (BMI <25 kg/m²), overweight (BMI 25–30 kg/m²), or obese (BMI ≥30 kg/m²).

**Results:** Overall, there were 133 (15.7%), 388 (43.4%), and 347 (40.9%) normal, overweight, and obese subjects. In LCZ696-treated subjects, baseline characteristics of normal (BMI 23.4 kg/m²), overweight (BMI 27.7 kg/m²), and obese (BMI 35.0 kg/m²) HTN subjects were similar (mean age: 59.3, 57, and 54.5 yrs; <65 yrs: 39%, 29%, and 19%; mean duration of HTN: 6.5, 7.0, and 7.6 yrs; msSBP: 157.3, 157.9, and 158.0 mmHg; msDBP: 93.8, 95.7, and 97.3 mmHg; msPP: 63.5, 62.2, and 60.7 mmHg, respectively). After 8 weeks of treatment, LCZ696 was more effective than valsartan in lowering ms and ms SBP and ms PP in the overall patient population. Specifically, the reductions in ms SBP and ms PP and LCZ696, compared with placebo, were similar in overweight and obese subjects (Table).

**Conclusions:** LCZ696 is effective in reducing ms and ms SBP and ms PP in normal, overweight, and obese subjects with HTN. The BP lowering efficacy of LCZ696 is not affected by BMI.
incidence of hospitalization in patients with heart failure with preserved ejection fraction (EF). However, it is not elucidated whether ARB or ACEI has the beneficial effect on left ventricular (LV) diastolic function in hypertension (HTN). The aim of this study was to examine the impact of ARB or ACEI on diastolic function using the novel one-best real-time 3-dimensional speckle tracking echocardiography (3D ST) that enables to evaluate phasic LV global strain rate (SR) with high volume rate.

Methods: We examined LV diastolic function by the 3D-ST in 58 normal controls and 87 consecutive patients with HTN and preserved EF (LVEF>50%). Patients with HTN were divided into 2 groups: AA group treated with ARB or ACEI and BCD group with Beta-blocker, Ca-antagonist or Diuretics. We examined LV global SR during diastolic relaxation (IVR) as SR and LV strain assessed as SR during IVR using 3D-STE -0.65 ± 0.41* BCD; -0.45 ± 0.35*, control; -0.15 ± 0.15 vs. AA SR during IVR: AA; -0.65 ± 0.41*, BCD; -0.45 ± 0.35*, control; -0.15 ± 0.15 vs. AA. There was no significant difference in age, blood pressure and cardiac function between 2 groups. This suggested that inhibitors of renin-angiotensin-aldosterone system (ARB or ACEI) may have a beneficial effect not only on systolic function but on diastolic function.

Conclusions: LV relaxation assessed by LV global SR during IVR using 3D-STE -0.65 ± 0.41* BCD; -0.45 ± 0.35*, control; -0.15 ± 0.15 vs. AA. There was no significant difference in age, blood pressure and cardiac function between 2 groups. This suggested that inhibitors of renin-angiotensin-aldosterone system (ARB or ACEI) may have a beneficial effect not only on systolic function but on diastolic function.

Results: There was no difference in age and LVEF among 3 groups (LVEF: control; 67.6±8, AA; 68.7±8, BCD; 66.7±7%). There was no difference between the 2 groups. This suggested that inhibitors of renin-angiotensin-aldosterone system (ARB or ACEI) may have a beneficial effect not only on systolic function but on diastolic function.

Conclusions: LV relaxation assessed by LV global SR during IVR using 3D-STE -0.65 ± 0.41* BCD; -0.45 ± 0.35*, control; -0.15 ± 0.15 vs. AA SR during IVR: AA; -0.65 ± 0.41*, BCD; -0.45 ± 0.35*, control; -0.15 ± 0.15 vs. AA. There was no significant difference in age, blood pressure and cardiac function between 2 groups. This suggested that inhibitors of renin-angiotensin-aldosterone system (ARB or ACEI) may have a beneficial effect not only on systolic function but on diastolic function.
Effects of antihypertensive treatment with a combination of telmisartan and amloidipine on various cardiovascular biomarkers Results from the randomized and double-blind TEAMSTA protect I Study A. Jagodzinski1, M. Karakas1, T. Zeller1, S. Appelbaum1, T. Muenzel2, P. Wild2, F. Simko1, O. Pechanova2, K. Repova Bednarova1, K. Krajcirovicova1, N. Kamodyova3, S. Zorad4, J. Kucharska5, A. Gvozdjakova5, M. Adamcova6, L. Paulis 7, 1 Comenius University, Faculty of Medicine, Dept. of Pathophysiology, Bratislava, Slovak Republic; 2 Slovak Academy of Sciences, Institute of Normal and Pathological Physiology, Bratislava, Slovak Republic; 3 Comenius University, Faculty of Medicine, Institute of Molecular Biomedicine, Bratislava, Slovak Republic; 4 Slovak Academy of Sciences, Institute of Experimental Endocrinology, Bratislava, Slovak Republic; 5 Comenius University, Faculty of Medicine, 3rd Clinic of Medicine, Bratislava, Slovak Republic; 6 Charles University Prague, Faculty of Medicine in Hradec Kralove, Dept. of Physiology, Hradec Kralove, Czech Republic Exposure of rats to continuous light attenuates melatonin production and results in hypertension development. This study investigated whether hypertension induced by continuous light (24 hours/day) exposure induced heart and aorta remodeling and if these alterations are prevented by melatonin or angiotensin converting enzyme inhibitor captopril. Four groups of 3-month old male Wistar rats (10 per group) were treated as follows for six weeks: untreated controls, exposed to continuous light, light-exposed and treated with either captopril (100 mg/kg/day), or melatonin (10 mg/kg/day). Exposure to continuous light led to hypertension, left ventricular (LV) hypertrophy and fibrosis, and enhancement of the oxidative load in the LV and aorta. Increase in systolic blood pressure by continuous light exposure was prevented completely by captopril and partially by melatonin. Both captopril and melatonin reduced the wall thickness and cross sectional area of the aorta and reduced the level of oxidative stress. However, only captopril reduced LV hypertrophy development and only melatonin reduced LV hydroxyproline concentration. Both captopril and melatonin prevented LV remodeling. In conclusion, captopril prevented LV hypertrophy development in the continuous light-induced hypertension model, while only melatonin significantly reduced fibrosis. This antibiotic action of melatonin may be protective in hypertensive heart disease.

This work was supported by: VEGA 1/0227/12, 2/00183/12; and APVV-0742-10.
In this study, we evaluated registry data to determine whether ACEI treatment or ARB treatment would better lead to outcome for patients who underwent PCI after AMI at the 30-day follow-up and at 1-year follow-up stages.

Methods and results: A total of 11,968 eligible AMI patients were finally enrolled into the present analysis. According to the medical treatments, patients were divided into 2 groups as follows: ACEI group (n = 9,847) and ARB group (n = 2,121). After propensity score matching, the n number for each of the two groups became 2034. The ACEI group when compared to the ARB group showed decreased risk and increased benefit in target vessel revascularization (TVR) (0.62 (0.4-0.96), p = 0.0326). Subanalysis showed the ACEI group had increased benefit in TVR in female, age < 70, non-diabetic, non-hypertensive, and non-dyslipidemia patients [p = 0.0378, 0.0158, 0.0188]. Recurrent MI risk was uniquely increased for male patients in the ACEI group (3.47 (1.05-11.4), p = 0.0411). Total MACE was decreased for patients between the ages of 60 and 70 in the ACEI group [0.58 (0.36-0.94), p = 0.0283].

Conclusions: The main message from our study is that ACEI therapy leads to better outcome at the 1-year follow-up, especially for low risk patients.

NEW ASPECTS IN ACUTE PULMONARY EMBOLISM

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Clinical presentation and outcome in patients with pulmonary embolism with and without cancer
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Background: Pulmonary embolism (PE) is a common event in patients with cancer. Aim: To assess whether the clinical presentation and the clinical outcome of PE differ in patients with cancer compared to patients without cancer.

Patients: 1702 patients with acute PE included in the Italian Pulmonary Embolism Registry for whom presence/absence of cancer was reported.

Results: Overall, 451 patients had cancer at time of acute PE (26.5%), of whom 365 had a history of cancer and 86 a cancer diagnosed during the admission for PE. Patients with newly diagnosed cancer, history of cancer and no cancer were similar concerning age, hemodynamic status at presentation, chest pain, onset, of dyspnea. Patients with newly diagnosed cancer were more frequently females and had significantly higher D-dimer compared to either patients with history of or no cancer. Recent trauma was less common in patients with newly diagnosed or history of cancer compared to patients without cancer while recent surgery was more common in patients with history of cancer compared to patients with newly diagnosed or no cancer. Patients with history of cancer less commonly received thrombolytic therapy compared to either patients with newly diagnosed or no cancer.

The severity of PE in terms of shock, hypotension, right ventricle dysfunction or injury and central localization of PE was similar in patients with newly diagnosed cancer, history of and no cancer. In-hospital death occurred in 10.5, 7.9 and 5.9% of patients with newly diagnosed, history of or no cancer. Newly diagnosed cancer patients had higher risk of death, compared to those with no cancer [HR 2.23 (95% CI 1.33-3.75; p = 0.002), age over 75, hemodynamic impairment, right ventricle dysfunction, dyspnea onset <24 hours and recent bed-rest were independent predictors of in-hospital death. Hemodynamic impairment, right ventricle dysfunction, dyspnea onset <24 hours and recent bed-rest were independent predictors of in-hospital death due to PE.

Conclusions: In patients from the IPER Registry, history of and newly diagnosed cancer were independent predictors of in-hospital death but not of death due to PE.

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Can we safely discharge low risk acute pulmonary embolism patients home?
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Introduction: ESC prognostic tool classifies APE patients into 3 risk groups (high, intermediate and low risk). Previous studies have shown that short term mortality in low risk patients is below 1% and these patients may be safely treated at home. Low risk classification by the ESC prognostic tool needs both echocardiographic evaluation and analysis of clinical data. Only if both evaluations show no myocardial injury is the patient classified as low risk. Echocardiography is not readily available in emergency departments of most hospitals.

Objective: We aimed to compare 30 day all-cause mortality between APE patients classified as low risk by an adapted ESC prognostic tool using only analytical variables (no echocardiography) and APE patients classified as low risk by the SPESI tool.

Methods: Retrospective, observational study that included all patients with APE discharged from our hospital between January 2010 and December 2011. The primary endpoint was 30 day all-cause mortality. Low risk patients by the adapted ESC prognostic tool were defined as those having TAPSE equal or above 90 mmHg and Troponin I below 0.04 ng/mL and BNP below 100 ng/mL. Low risk patients by the SPESI prognostic tool were defined as those having score 0.

Results: Between January 2010 and December 2011, 436 patients (205 males, mean age 72 years) were diagnosed with APE. All patients were admitted to hospital wards. 46 (10.6%) patients died during hospital stay. 120 (27.5%) patients were classified as low risk with the adapted ESC prognostic tool (73.4% vs 46% and 16.4% vs 60%, p<0.001). Low risk patients classified by the SPESI tool also had lower 30 day all-cause mortality (9.4% vs 22.6%, p<0.01). Negative Predictive Value (NPV) of low risk in adapted ESC prognostic tool was 0.92 and NPV of low risk in adapted SPESI tool was 0.97. Patients classified as high risk by adapted ESC tool was 3.084 (95% CI 1.278 – 7.443) for adapted ESC tool and 5.1615 (95% CI 1.838 – 17.147) for SPESI tool.

Conclusion: Adapted ESC prognostic tool should not be used to decide adequacy of ambulatory treatment as patients in the low risk category still have high mortality (7.4%). SPESI performed better but still 4.9% patients in the low risk category died during the first 30 days after diagnosis.

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Elevated circulating platelet microparticles during in vitro fertilization (IVF): a possible prothrombotic effect of an estrogen surge
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Purpose: Pregnant women conceived by in vitro fertilization (IVF) have a sevenfold increased incidence of pulmonary embolism (PE) during the first trimester of their pregnancy. Indeed, PE is the major cause of maternal mortality. It is therefore of utmost importance to understand the underlying pathophysiology. IVF seems to be associated with an increased coagulability, including increased thrombin generation. However, the influence of IVF on platelet function has been less investigatated, partly due to methodological difficulties. Assessment of platelet derived microparticles (PMPs) in frozen plasma samples by flow cytometry provides an opportunity to measure platelet function in large clinical studies. Thus we studied PMPs which are released from the platelets upon activation, and thus reflect platelet activation. Notably, PMPs also boost thrombin generation and fibrin formation through expression of molecules that interact with coagulation.

Methods: Venous blood samples were drawn at two occasions from 31 women by a gonadotropin releasing hormone (GnRH) agonist, and 2. during high level stimulation (HLS) achieved by follicle stimulating hormone (FSH). PMPs were analyzed by flow cytometry in samples prepared from platelet poor plasma. Plasma was incubated with lactadherin-FITC and CD42a-PE (platelet antigen GPIX), and CD62P-APC (P-selectin) or CD154-APC (CD40 ligand).

Results: Plasma estradiol increased from 154 pg/mL to 5889 pg/mL at HLS. PMPs (CD42+) constituting 60% of total micro vesicle population. PMPs were decreased in plasma from patients who underwent PCI after myocardial infarction (MI) at the 30-day follow-up and at 1-year follow-up stages.

Conclusions: We find a major increase in PMPs in parallel with the profound estradiol surge that occurs during IVF. Thus we studied PMPs which are released from the platelets upon activation, and thus reflect platelet activation. Notably, PMPs also boost thrombin generation and fibrin formation through expression of molecules that interact with coagulation.

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Drug therapy in hypertension / New aspects in acute pulmonary embolism
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Objective: Right ventricular dysfunction (RVD) is an indicator of poor prognosis in normotensive patients with acute pulmonary embolism (APE). However, variability in RVD in RVD in pregnant women has been recently reported. Recently, right ventricular function relates to left ventricular function (LV-LV) at echocardiography, decreased TAPSE was reported to be of prognostic value. The aim of this study was to compare RV/LV at echocardiography and multidetector computed tomography (MDCT) with TAPSE for 30 days pulmonary embolism related mortality in initially normotensive APE patients.

Methods: We examined 76 patients (35M, mean age: 64; 61±18yr) with confirmed APE hemodynamically stable at admission (RRs ≥90mmHg). The prognostic value of RVD in pregnant patients with confirmed APE was identified in the apical 4 chamber view and tricuspid annulus plane systolic excision (TAPSE) measured at echocardiography and MDCT (RV/LV) ratio were evaluated.

Results: Intermediate risk APE was diagnosed in 54 pts, while in 22 pts low
risk APE. Thirty-day APE-related mortality was 10.5% (8 pts) and all-cause mortality was 13% (10 pts). In ROC analysis APE-related mortality of TAPSPE was higher (p<0.0001) (0.905, 95% CI: 0.828 to 0.983) than AUC of echo RV/LV ratio (0.427, 95% CI: 0.183 to 0.672) and MDCT RV/LV ratio (0.371, 95% CI: 0.145 to 0.598). At univariable and multivariable Cox analysis, TAPSPE was the only significant mortality predictor with HR = 0.62 to 0.87, p=0.0004 and (HR: 0.73, 95% CI: 0.62 to 0.87; p=0.0003) respectively, while RV/LV ratio at echo or MSCT were nonsignificant. TAPSPE <15 mm was a significant predictor of APE-related mortality with HR: 26.2, 95% CI: 3.2 to 214; p=0.002, with PPV of 44% and NPV: 88%. HR: >18 mm had a 100% NPV. All patients with TAPSPE >18 were in low-risk group with good prognosis.

Conclusions: TAPSPE, easily measurable echocardiographic parameter is preferable to echo and MDCT RV/LV ratio for risk stratification in initially normotensive patients with APE. TAPSPE <15 mm identifies patients with an increased risk of 30-day APE-related mortality.

P453 | BEDSIDE
Efficacy and safety of novel oral anticoagulants in patients with pulmonary embolism: a systematic review and meta-analysis

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Purpose: Novel oral anticoagulants (NOACs) have been shown to be as effective as conventional anticoagulation for the prevention of recurrences in patients with venous thromboembolism (VTE). Whether their effect is confirmed in patients as conventional anticoagulation for the prevention of recurrences in patients with recurrent VTE.

Methods: We performed a systematic review and a meta-analysis of phase III randomized controlled trials aimed at assessing the efficacy and safety of NOACs in patients with acute PE. MEDLINE, EMBASE, and CENTRAL were searched up to December 2013 without restrictions. The primary outcome of the analysis was recurrent VTE. Other outcomes were major bleeding (MB) and the composite of major or clinically relevant non major bleeding (CRB: clinically relevant bleeding). Data were pooled and compared by ORs and 95% CIs.

Results: Overall, 6 studies (2 rivaroxaban, 2 dabigatran, 1 apixaban, 1 edoxaban) patients receiving NOACs with conventional anticoagulation (low-dose (25mg) prolonged administration (in 6 hours) of tissue type plasminogen activator (tPA) and conventional treatment respectively (OR fixed 0.92, 95% CI 0.79-1.06; I-squared 0%). Bleedings were less frequent in patients receiving NOACs respect to conventional treatment in terms of both major bleeding (OR random 0.61, 95% CI 0.44-0.85; I-squared 53%) and CRB (OR random 0.70, 95% CI 0.54-0.91; I-squared 87%). Five studies (11559 patients) reported on separate data in patients presenting with acute PE. VTE recurrence occurred in 2.4% and 2.6% patients treated with NOACs and conventional anticoagulant, respectively (OR fixed 0.89, 95% CI 0.71-1.2; I-squared 0%). CRB occurred in 8.4% and 9.8% patients with acute PE treated with NOACs and conventional anticoagulant, respectively (OR random 0.73, 95% CI 0.48-1.09; I-squared 81%). Data were confirmed after heterogeneity was solved.

Conclusions: NOACs are as effective as and probably safer than conventional anticoagulant treatment when given in patients with acute PE for prevention of recurrent VTE.

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Low dose prolonged infusion of tissue type plasminogen activator therapy in massive pulmonary embolism

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Aims: Pulmonary embolism (PE) is life threatening disease requiring early diagnosis and treatment. The aim of the present study was to assess the effects of low-dose (25mg) prolonged administration (in 6 hours) of tissue type plasminogen activator (tPA) on in hospital mortality and outcomes in patients with massive PE.

Methods: A total of 27 consecutive patients with massive PE were included in this study. The primary end point consisted of in hospital all cause mortality, major complications, pulmonary hypertension and right ventricular dysfunction. Secondary points are all cause mortality, pulmonary hypertension and right ventricular dysfunction at 6 month. This study is registered to Clinical Trials with the number of NCT02029456.

Results: The mean age of the patients was 66.19±15.72 and 14 of the 27 patients were older than 70 year. Echocardiographic outcomes of the patients are demonstrated in Table-1. The mean pulmonary artery systolic pressure (PASP), tricuspid annular plane systolic excursion (TAPSE), right atrium/left ventricle (RA/LV) diameter and right ventricle/ left ventricle (RV/LV) diameter were significantly decreased after TT. The myocardial performance index (MPI) and s′ were significantly increased after the TT. No major bleeding was observed. None of the patients had stroke, transient ischemic attack or cardiopulmonary arrest during hospitalization. Over all none of the patients died in the hospital or during follow up. Pulmonary hypertension was not developed during follow up. All patients reached primary and secondary outcomes.

Conclusion: Low dose prolonged infusion of tPA is an effective and safe therapy in patients with massive PE. This protocol is also effective in decreasing PASP and restoration of RV functions.
groups (16.2% vs. 22.5% vs. 16.7% vs. 13.3%; p=0.557). PO/CA were present in 233 patients (44.0%), whereas 54.4% did not have PO/CA. 30-day mortality was significantly different between these two groups [22.9 vs. 13.3%, unadjusted OR=1.945 (95% CI: 1.116–3.391), p=0.024]. When we considered the presence of PO/CA and troponin level together, they significantly predicted 30-day mortality (OR=3.040; p<0.001). The presence of both PO/CA significantly contributed to the prediction model (PO/CA adjusted OR 2.319 (95% CI: 1.115–4.820), p=0.024, troponin level adjusted OR=1.499 (95% CI: 0.993–2.262), p=0.054).

Conclusion: Although we did not find a significant relation between the location of pulmonary emboli and 30-day mortality, the presence of PO/CA was associated with twice the mortality. Therefore, imaging aspects related to pulmonary parenchyma can provide significant prognostic value in APE patients.

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Prognostic value of renal dysfunction in patients with acute symptomatic pulmonary embolism: a multicenter validation study
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Purpose: Current risk stratification of acute pulmonary embolism (APE) is based on the assessment of clinical status, right ventricular dysfunction and myocardial infarction. Furthermore, an estimated glomerular filtration rate (eGFR) <35 ml/min/1.73m2 was shown to predict 30-day mortality in normotensive patients. In normotensive patients, 208 (9%) had an eGFR ≥35 ml/min/1.73m2. The eGFR differed between 573 (22%) patients with low- and 1768 (70%) patients with intermediate- and 191 (7%) patients with high-risk of death APE (66 [4-177] vs. 73 [4-297] vs. 62 [9-236] ml/min/1.73m2, p=0.0001). Two hundred twelve (8.3%) patients died during the 30-day observation period; these patients had a lower eGFR compared to survivors (58 [8-175] vs. 72 [4-297] ml/min/1.73m2, p=0.0001). In multivariable analysis, eGFR and heart rate were identified as independent predictors of mortality. Of 2399 normotensive patients, 208 (9%) had an eGFR <35 ml/min/1.73m2 and associated with an increased risk of death during 30-days follow-up (HR, 2.03 [95% CI, 1.34-3.06], p=0.0001). Troponin-positive patients with an eGFR <35 ml/min/1.73m2 had a 30-day PE-related mortality rate of 9% and troponin-negative patients with an eGFR <35 ml/min/1.73m2 of 4%, while troponin-positive patients with an eGFR ≥35 ml/min/1.73m2 had a PE-related mortality rate of 2% (p=0.003).

Conclusions: Impaired renal function was present in 36% APE patients and related to 30-day all-cause mortality. In normotensive patients, an eGFR <35 ml/min/1.73m2 doubles the risk of death. Moreover, eGFR assessment can improve troponin-based risk stratification of APE.

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Heparin or no heparin in the initial treatment of venous thromboembolism
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Purpose: The key remaining question in the treatment of venous thromboembolism (VTE) with new oral anticoagulants is whether initial (LMWH)heparin therapy is really needed. Earlier studies indicated that treatment with rivaroxaban or apixaban alone might be as effective as standard therapy with LMWH and a vitamin K antagonist (VKA). In two VTE study arguments against omitting heparin in patients with severe pulmonary embolism (PE), in these patients LMWH/edoxaban was superior to standard therapy. Here, we present the robustness of the concept of severe PE and explore the possible reasons for the lower efficacy of LMWH/VKA.

Methods: Hokusai-VTE was a randomized, double-blind, trial of the oral Xa inhibitor edoxaban versus warfarin for long-term anticoagulant therapy in 8,292 patients with acute symptomatic deep vein thrombosis or PE, all patients received initial LMWH treatment. The primary efficacy outcome was recurrent symptomatic VTE (i.e., DVT, fatal and non-fatal PE). Severe PE was assessed at entry as NT-proBNP ≥500 pg/ml (also at >400 pg/ml and ≥600 pg/ml) and by CT pulmonary angiography (CTPA) RV/LV diameter ≥0.9. Investigated factors for lower efficacy of standard therapy included patient characteristics, comorbidity, VKA quality and bleeding.

Results: Severe PE was present in 28 and 44% of all PE patients based on BNP ≥500 pg/ml and CTPA, respectively. Recurrent VTE in patients with severe PE defined by BNP ≥500 pg/ml was 3.1% versus 6.2% (HR 0.50; p=0.031). Similar differences (p=0.003) were observed for the other BNP thresholds and consistent across all components of the efficacy outcome. For severe PE by CTPA the recurrent VTE rates were 2.7% and 4.7% (HR 0.57; p=0.126). The higher recurrence rate in severe PE-patients treated with LMWH/VKA could not be explained by any of the investigated factors.

Conclusion: In patients with severe PE, regardless of the definition used, initial LMWH followed by edoxaban was more effective than LMWH/VKA. The failure of standard therapy was not explained by differences in comorbidity or the quality of VKA therapy. Hence, the regimens of LMWH/edoxaban is the treatment of choice in these patients and therefore initial (LMWH) heparin should not be omitted. NT-proBNP is an independent marker of both fatal and non-fatal VTE.

P459 | BEDSIDE
Time course of plasma lactate levels in patients with acute symptomatic pulmonary embolism
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Purpose: To investigate the time course of plasma lactate in patients with acute pulmonary embolism (PE).

Methods: We studied adult outpatients with symptomatic, objectively confirmed pulmonary embolism (PE). From the large cohort of the ThromboEmbolism Lac-tome Outcome Study (TELOS) (540 patients) we selected 47 (8.7%) patients that had at least three different determination at 0, 6, 12, 24 or 48 h. To investigate which marker increases earlier, time course of plasma lactate was compared with that of high sensitive (Hi) Troponin I. Moreover we investigated whether patients with persistently high values had different 30-day PE-related mortality than patients without.

Results: The mean age at admission was 77 years (range 42-97 years), 59.6% patients were females. Five patients (12.2%) died within 30 days because of PE. Mean HS-Troponin I levels (expressed as fold increase versus baseline values) peaks after 6 hours (+5.2 folds) and normalized within 48 hours (Figure). Differently, the time course of plasma lactate levels largely differed among the population. We identified two main categories; patients that showed constantly normal plasma lactate levels (n=31, 65.9%), who were used for baseline value determination (0.98±0.13 mmol/L), and those that showed abundantly high (>2 mmol/L) levels at time 0 (n=16, 34.1%, 4.5±3.5 mmol/L) (Figure). Among these, patients with persistently high lactate values (n=8, 12.7%) had a significantly higher PE-related mortality (30%, 95% CI 15.4-76.3%) than patients with different time course (4.9%, 95% CI 1-9.9%) (P=0.02).

Conclusions: In patients with acute PE, plasma lactate levels increases earlier than HS-Troponin I. Patients with persistently high lactate values are at increased risk of 30-day PE related mortality.

P460 | BEDSIDE
Accuracy and prediction of adverse course of hospitalization for acute pulmonary embolism in regional intensive care centre
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Background: Adequate knowledge of acute pulmonary embolism (PE) is crucial for early diagnosis and prognosis-improving therapy. The aim of this study was to observe the impact of an educational campaign on the incidence of PE and 2. to analyse the potential of various imaging modalities to identify pts with high risk of adverse course (AC) of hospitalization.

Patients and methods: In 2010 we started an educational activity focused on PE management. We fully revised admissions for PE in the years 2010-2012 in our regional ICU serving a population of 81,000 inhabitants. Clinical and imaging data were retrospectively analysed with the aim to identify predictors of AC of hospitalization. AC was defined by one the following criteria: 1. Need of...
pulsed Doppler (ECHO 2D, ECHO Doppler). The results showed that tissue Doppler imaging (TDI) was a useful tool to identify patients with CTEPH. The combination of TDI and other clinical parameters could be used to stratify patients according to their risk of complications. The study results indicated that patients with CTEPH have a high mortality rate, and the identification of high-risk patients is crucial for optimal management. The study further suggested that TDI could be a valuable tool in the preoperative assessment of patients with CTEPH to guide surgical planning and improve patient outcomes.

In conclusion, tissue Doppler imaging (TDI) is a valuable tool in the preoperative assessment of patients with CTEPH to identify high-risk patients who may benefit from surgery. The results of this study suggest that TDI could be used to improve patient outcomes and reduce mortality in patients with CTEPH.
cluded in this double-blind, placebo-controlled, cross-over trial (NCT01246037). Limited scleroderma was one of the exclusion criteria. Bisoprolol or placebo was administered to the maximum tolerated dose (maximal 10 mg Bisoprolol or placebo 4 tablets). Patients were treated during 6 months, followed by a wash-out period and another 6 months treatment after cross-over. At baseline, after 6 months and at the end of the study all patients underwent CMR, echocardiography, heart rate variability measurement, PET scans, cardiological exercise tests and invasive pressure measurements. Every 4 weeks physical examination, ECG, 6MWD and Minnesota quality of life questionnaire were performed.

Results: The achieved dose of Bisoprolol was 4.4 mg (±3.2), placebo 2.7 tablets (±1.4). Mean heart rate significantly decreased from 83 bpm at baseline to 71 bpm during beta-blocker therapy (p<0.001). There were 5 SAE’s reported, 4 with no relation to the study-drug. One patient had to be treated with intravenous diuretics after starting beta-blocker therapy because of fluid retention. Two patients were intolerant for beta-blocker therapy due to hypotension and tiredness. No collapses were reported.

Right ventricular ejection fraction, measured with CMR, show a non-significant improvement of 2.93% in the whole group (p=0.121). However, during follow-up two patients who had Raynaud’s syndrome at inclusion in this group were diagnosed with limited scleroderma (an exclusion criterion of this study). These two patients showed a substantial decrease in right ventricular function. When these patients are excluded from the analysis, right ventricular function shows a significant and clinically relevant improvement of 3.5% (p=0.022), in the pure iPAH group.

Conclusions: Beta-blocker therapy seems to be safe and well tolerated in patients with PAH. Our results suggest that, in patients with Raynaud’s syndrome beta-blocker therapy is deleterious, but a significant improvement in RVEF is achieved in the iPAH group.

P466 | BEDSIDE
Left ventricular end diastolic eccentricity index predicts mortality in pulmonary arterial hypertension
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Purpose: Right ventricular pressure and volume overload result in interventricular septal shift towards the left ventricle in patients with pulmonary arterial hypertension (PAH). The aim of our study was to examine the predictive role of septal curvature as expressed by left ventricular (LV) eccentricity index in adult patients with PAH.

Methods: All patients underwent cardiac magnetic resonance (CMR). A routine set of LV and RV short-axis cines of 6mm slice thickness, were acquired from base to apex using a breath-hold retroscopic vector cardiography-gated balanced steady state free precession (SSFP) gradient echo sequence. LV eccentricity index in end diastolic (LVEDei) and end-systolic (LVESei) were assessed in the short axis view, at the mid-papillary level.

Results: Overall, 48 consecutive patients (28 women, mean age 46.9±13.1 years) (30 idiopathic PAH, 5 PAH associated to connective tissue disease and 13 PAH associated to congenital heart disease) were included. Over a median follow up period of 17.0 months (IQR 7.0-38.7 months) 8 patients died. In univariate Cox proportional hazard analysis only baseline LVEDei was significantly related to mortality (HR 1.65, 95% CI 1.04-25.82). ROC curve analysis showed that the optimal cut-off value of LVEDei to predict survival was 1.52. Kaplan-Meier survival analysis showed that LVEDei ≥ 1.52 is associated with a 12-fold (95% CI 2.03-71.0) increase in the risk of death (figure).

Conclusions: Interventricular septal shift as expressed by LVEDei is a strong predictor of mortality in PAH.

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Impact of insurance status on survival in pulmonary hypertension
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Purpose: In light of the current healthcare reform, elucidating the impact of insurance status on outcomes is imperative. The effect of insurance status on outcomes in pulmonary hypertension (PH) has not been well studied, and the aim of this investigation was to address this gap.

Methods: We examined an incident cohort of 259 consecutive PH patients referred for initial hemodynamic assessment. Demographics, echocardiographic parameters, hemodynamic data and insurance status were collected at the time of initial catheterization.

Results: 84 of 259 patients (32%) died during a median follow-up time of 2.7 years. Those who died tended to be older (63.3 ± 12.8 vs. 54.7 ± 15.5, p<0.001) and had more advanced WHO function class (6/40/45/9% vs. 1/10/31/28%; p<0.001) at presentation. They also had higher right atrial pressure (12.5 ± 6.3 vs. 10.1 ± 5.9, p<0.004). Patients who died were less likely to have private insurance (48% vs 66%, p=0.006). No differences were noted in demographics, right heart function by echo or right heart pressures by catheterization based on insurance status; however, mortality was significantly higher in the group without private insurance (p=0.018).

Conclusions: Lack of private insurance predicts poor outcome in pulmonary hypertension, despite similar right heart function and pulmonary pressures. This suggests an opportunity for public health interventions to narrow this disparity among pulmonary hypertension patients.

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Purpose: Riociguat, an oral soluble guanylate cyclase stimulator, is approved for the treatment of pulmonary arterial hypertension and persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment or inoperable CTEPH. This analysis was performed to characterize the pharmacokinetics (PK) and the pharmacokinetic/pharmacodynamic (PK/PD) relationship of riociguat in patients (pts) in the Phase III PATENT-1 and CHEST-1 studies and their long-term extension (LTE) studies PATENT-2 and CHEST-2.

Methods: Blood samples were collected from all pts in PATENT-1/2 and CHEST-1/2. All studies included male and female pts aged 18–80 years. In PATENT-1 (12 weeks) and CHEST-1 (16 weeks), pts were randomized to placebo or riociguat administered according to a dose-adjustment regimen (starting dose: 1 mg three times daily [tid]; range: 0.5–2.5 mg tid). Former placebo pts entering the LTE studies received riociguat. A nonlinear mixed-effects modeling approach was used to develop a population PK model to describe PK characteristics of riociguat in the studied population. The PK/PD relationship was investigated by comparing derived PK parameters and changes in pharmacodynamic parameters. Covariate analyses were performed including smoking status, co-medication with bosentan, bilirubin levels, and baseline creatinine clearance.

Results: A total of 5245 riociguat plasma samples were collected. The PK of riociguat in patients (pts) in the Phase III PATENT-1 and CHEST-1 studies and their long-term extension (LTE) studies PATENT-2 and CHEST-2 were 2.17/h, 1.81 L/h and 32.3 L, respectively. Inter-individual variability in the PK parameters was moderate for riociguat. There was no evidence of time- or dose-dependent changes in riociguat PK during the studies. Total CL of riociguat was used to develop a population PK model to describe PK characteristics of riociguat in the studied population. The PK/PD relationship was investigated by comparing derived PK parameters and changes in pharmacodynamic parameters. Covariate analyses were performed including smoking status, co-medication with bosentan, bilirubin levels, and baseline creatinine clearance.

Conclusions: Riociguat was described by a one-compartment model. The influence of pre-specified covariates on riociguat PK was established and a PK/PD relationship was achieved.
P469 | BEDSIDE
Pulmonary hypertension and pregnancy: a referral center 14 years experience
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Aims: Pregnancy in pulmonary arterial hypertension (PAH) patients has been related to maternal mortality rate between 30%-56%. Accumulated experience and introduction of specific therapy could have changed prognosis.

Methods and results: 16 pregnancies in 15 PAH patients (7 idiopathic, 6 congenital, 1 connective tissue disease and 1 chronic thromboembolic PH) were registered between 1999 and 2013. We studied baseline characteristics, progress and conclusion of pregnancy, maternal and foetal complications and mortality. Average mean pulmonary pressure and arterial resistance was of 53.1±19 mmHg and 11.5±9.9 WU respectively. 9 cases were diagnosed prior pregnancy, 4 during and 3 in postpartum. 10 pregnancies progressed, 4 therapeutic abortions were performed and 2 occurred spontaneously. One patient died in the sixth postpartum month due to refractory heart failure and another one during therapeutic abortion practice. Of the 10 pregnancies that progressed, 7 were complicated with heart failure and 5 had functional class III 3 months postpartum.

Conclusions: Pregnancy in severe PAH still associates with high maternal morbidity and mortality. The early detection of PAH patients avoiding pregnancy and interrupting it early in case it occurs.

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Influence of pulmonary arterial occlusion pressure on the diagnostic accuracy of echocardiographic pre-tetralogy of Fallot (PFO) measurements during exercise for the detection of scleroderma-associated pulmonary arterial hypertension
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Purpose: Pulmonary arterial hypertension (PAH) is a well-known complication in patients (pts) with scleroderma (SSc), harbouring a bad prognosis. While the di- agnosis of PAH is confirmed by right heart catheterization (RHC), the initial sus- picion for the presence of PAH is raised by non-invasive methods. The diagnosis of PAH my be challenging, as SSc pts may additionally show an SSc-associated left- sided heart involvement. Pathophysiologial considerations suggest that end-tidal pCO2 (PETCO2) measurements during exercise correlate with pulmonary hemo- dynamics and the extent of pulmonary ventilation-/perfusion mismatch, making this parameter useful for PAH detection.

We hypothesized that the reliability of PAH detection by PFO measurements is influenced by the pulmonary arterial occlusion pressure (PAOP). Diagnostic accuracy might be higher in pts with a low PAOP (<12 mmHg) compared to pts with a PAOP of 12-15 mmHg.

Methods: In a multi-center approach we analyzed 171 consecutive SSc pts None of the pts had been previously diagnosed with PAH. All pts underwent cardiopul- monary exercise testing (CPET) and RHC. All exercise tests were interigated in a blinded manner. PAH was diagnosed according to current guidelines. The pts were classified into two groups according to PAOP:
– Group 1: PAOP <12 mmHg (n=127)
– Group 2: PAOP 12-15 mmHg (n=34)

All pts with postcapillary pulmonary hypertension (n=10) were separately ana- lyzed.

Results: In 48 pts, a diagnosis of PAH was confirmed. In 113 pts, pulmonary arterial mean pressure (PAPmean) was lower than 25 mmHg. In a “receiver oper- ating characteristics” (ROC) analysis, PFCO2 measurements for the detection of PAH showed a higher “area under the curve” (AUC) in pts with a low PAOP (AUC = 0.896) compared to pts with a PAOP of 12-15 mmHg (AUC = 0.797).

Conclusion: Diagnostic accuracy of exercise PFCO2 measurements for the detection of PAH is influenced by PAOP. There is a higher congruence between PFCO2 measurements and the diagnosis determined by RHC in pts with a PAOP <12 mmHg, compared to pts with a PAOP of 12-15 mmHg. This might be a methodological limitation for PFCO2 measurements. On the other hand, this might also indicate that pts with a higher PAOP may have a combined pre-and postcapillary limitation, pathophysiologically being reflected by exercise PFCO2.

P471 | BEDSIDE
Incidence and impact of patent foramen ovale among patients with pulmonary hypertension
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Background: Atrial septostomy is an accepted therapy for advanced pulmonary hypertension (PH), reducing right ventricular (RV) work-load at the expense of cyanosis. Patent foramen ovale (PFO) is a “natural” septostomy, occurring in up to 25% of the general population, the impact of which in PH is uncertain.

Methods: We examined the echocardiograms of an incident cohort of 259 PH patients referred for initial hemodynamic assessment. A patient selection criteria included technically adequate images and the performance of saline contrast injection with repeat injection following Valsalva maneuver if the initial injection showed no shunt. Congenital shunt lesions other than PFO were excluded.

Results: PFO was identified in 26% of the 109 patients. Patients with PFO were younger (53±15 vs. 60±14 years, p=0.01) than those without PFO, but otherwise had similar demographic features. Mean pulmonary artery pressure was higher in PFO patients (50±14 vs 42±15, p=0.02), though cardiac index was similar (2.4±1.0 vs 2.4±0.7, p=NS). Systolic flattening of the interventricular septum suggestive of RV pressure overload was more common in PFO patients (56% vs. 28%, p=0.007). Among patients with moderately or severely dilated RVs, PFO was present in 45% compared to only 8% of patients with normal or mildly dilated RVs, p<0.001. Similarly PFO was present in 38% of patients with moderate or se- verely dilated RVs, and 14% normal or mildly dilated RVs, p<0.006. No impact of PFO on survival was seen among the entire cohort, though patients with NYHA function class III and IV with PFO actually trended toward worse sur- vival than those without PFO, p=0.09.

Conclusion: PFO is common in PH patients, with rising incidence among patients with more dilated and dysfunctional RVs. This suggests that PFO in ad- vanced PH may be stretched open and not congenital. Patients with advanced functional impairment do not appear to benefit from the presence of PFO.

P472 | BEDSIDE
Mortality of patients with HIV-associated pulmonary hypertension in a densely populated, peri-urban township in South Africa
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Purpose: The prevalence of pulmonary hypertension (PH) in HIV-infected indi- viduals varies between 0.5% and 5.0%; 1000-fold higher than in the general pop- ulation. Since estimated one and three-hundred one and three-hundred pre-antiretroviral therapy (ART) era and 90% and 70% since the advent of ART . We aim to describe the clinical presentation and mortality of patients with HIV- associated PH (HIV-PH).

Methods: We base present data from an infectious diseases referral clinic in South Africa, which is one of the 13 specialist centres participating in the Pan African Pulmonary Hypertension Cohort (PAUPCOO) study, a prospective multina- tional cohort registry. PH was diagnosed by Echocardiography and defined as right-ventricular systolic pressure (RVSP) ≥35 mmHg. Functional tests included WHO-Functional Class and 6-Minutes Walk Test. Pulmonary function tests, ra- dio nucleotide perfusion scans, CT-Chest/CT-PA were performed if clinically indicated.

Results: 28 patients were diagnosed with HIV-PH between July 2011 and November 2013. Median age was 37 years (range 25 to 62), 71% were female, 57% lived in informal settlements, and 71% had prior history of tuberculosis. Me- dian CD4 count was 323 cells/μL (IQR 159-574) and 82% were on ART at the time of diagnosis. SOB (92%), palpitations (88%), fatigue (77%) were the common- monest symptoms and 75% were WHO FC III-IV at baseline. Median baseline RVSP was 61 mmHg (IQR 53 to 73) and TAPSE 14mm (IQR 11-16). Survival rate at 6-month (n=27) and 12-month (n=23) follow-up was 67% and 61%, re- spectively. Median time from presentation to death was 103 days (IQR 50 to 132). No impact of PFO on survival was seen in patients with normal or mildly dilated RVs. Functional tests included WHO-Functional Class and 6-Minutes Walk Test. Pulmonary function tests, ra- dio nucleotide perfusion scans, CT-Chest/CT-PA were performed if clinically indicated.

Conclusion: The highest recruitment rate of patients with HIV-PH within two years at a large PH centre reflects the high overall HIV prevalence. One-year survival of our patients seems to be lower compared to data from high-income countries. Low socio-economic status, late presentation and limited access to echocardiographic services and tertiary care, limited awareness of PH in HIV by primary care doctors and underreporting of PH-specific symptoms and signs are plausible reasons for the lower survival in our setting. Practitioners at primary care level should be aware of the increased risk of PH in HIV-positive patients, since early detection and referral may improve survival.
P473 | BEDSIDE
Exercise capacity is related with impaired endothelial glycosalix and increased aortic stiffness in patients with idiopathic pulmonary arterial hypertension under treatment: a pilot study
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Background: Reduced exercise capacity is the main symptom referred by patients diagnosed with idiopathic pulmonary arterial hypertension (IPAH). Pulmonary arterial endothelial function is known to be impaired in those patients while recently there is also evidence of peripheral systemic arterial dysfunction. This study evaluated if endothelial glycosalix plays a vital role in vascular permeability, inflammation and elasticity. Aortic stiffness is an important determinant of cardiovascular risk. We aimed to explore the relationship between exercise capacity, endothelial glycosalix and aortic stiffness in patients with IPAH under treatment.

Methods: We studied 30 patients with pulmonary arterial hypertension under treatment (mean age 53±17 years, 25 females), 18 with IPAH (mean age 51±17 years, 15 females) and 12 with other causes of PAH i.e. portopulmonary hypertension, scleroderma, hemolytic anemia, (mean age 57±16 years, 10 females). All patients were evaluated with echocardiogram, right heart catheterization, six minute walk test (6MWT), maximal oxygen consumption (VO2 peak) after cardiopulmonary exercise test (CPET). Aortic stiffness was evaluated by pulse wave velocity (PWV) while increased perfusion boundary region (PBR) of the sublingual arterial microvessels (ranged from 5-25 micrometers) using Sideview Darkfield imaging (Microscan, Glycocheck) was measured as a non-invasive accurate index of reduced endothelial glycosalix thickness.

Results: In total PAH population, 6MWT was related with PBR (r=-0.40, p<0.05 and r=0.45, p<0.01) and PWV (r=-0.55, p<0.05 and r=0.70, p<0.05). Aortic PWV was related with PBR (r=-0.56, p<0.05) and PWV (r=-0.48, p<0.05). In other PAH patients, VO2max was related with PBR (r=0.97, p<0.05) and 6MWT with PWV (r=0.60, p=0.05).

Conclusions: This is the first study showing an existing relationship between reduced exercise capacity, an index of severity and survival in PAH, with impaired non-invasive indices of the peripheral circulation (aortic stiffness, endothelium) in PAH patients. It also gives evidence that IPAH is not an isolated pulmonary disease but a systemic one. Further studies are needed to confirm our results showing in different groups of pulmonary arterial hypertension.

NEW ASPECTS IN PULMONARY HYPERTENSION – 2

P474 | BEDSIDE
New echocardiographic indexes for the evaluation of cardiac function of idiopathic pulmonary arterial hypertension using three dimensional echocardiography

Objectives: The evaluation of cardiac function of patients with idiopathic pulmonary arterial hypertension (IPAH) is very important in the management and prognosis of this disease. But it usually assessed by an invasive cardiac catheterization. The aim of this study was to explore new indexes of severity of IPAH using noninvasive real-time three-dimensional echocardiography (RT3DE).

Methods: RT3DE was performed in 24 patients with IPAH (1males, aged 25±10 years, mean pulmonary systolic pressure 68.8±25.5mmHg) and 25 normal controls (1males, aged 32±9years). End-systolic volume (EDV) and end-diastolic volume (ESV), ejection fraction (EF) of right ventricle (RV) as well as left ventricle (LV) were measured using four-dimensional RV and L V quantity method. Right heart catheterization was performed in IPAH patients within one day of RT3DE examination to obtain pulmonary vascular resistance (PVR). The correlations between RT3DE parameters and PVR were also analyzed.

Results: Biventricular volumes and systolic function data could be analyzed in the same loop with different software. RV diastolic volumes and LV volumes were compressed by RT3DE in IPAH patients as compared with normal controls (P<0.05). The relation of RV end-diastolic volume index (RVEDVi) with PVR (r=0.734, r<0.05, respectively) was significant only in IPAH patients while compared with normal controls (P<0.001), respectively. LV EF was significantly lower in IPAH patients compared with normal controls (P<0.001).

Conclusions: This is the first study showing an existing relationship between RT3DE parameters and PVR. The modality could unravel RA, RV mechanical dysfunction, otherwise not shown by echocardiography.

P477 | BEDSIDE
The impact of nutritional status on survival in pulmonary arterial hypertension

Objectives: The impact of nutritional status on survival in patients with pulmonary arterial hypertension (PAH) has not been studied. The objective of this study was to determine whether the nutritional status in PAH patients, as measured by Body Mass Index (BMI), Lean Body Mass (LBM), Percent of Ideal Body Weight (% IBW), serum albumin (SAlb) and hemoglobin (Hb), has an impact on survival.

Methods: Records of 82 patients with PAH (Group1) treated at our institution were reviewed. Data obtained included: age, gender, weight, SAlb, Hb, and nutritional parameters (EER, PBR, EER/PBR, MPA, PAH). Spearman's rho correlation analysis, receiver operating characteristic (ROC) analysis, univariate and multivariate logistic regression models were used to determine the impact of nutritional parameters on survival.

Results: Mean age was 64±11 years; 75% patients were females. Mean mPAP was 42.3±13 mmHg; 2% were overweight (BMI<18); 32% had normal BMI; 32% were overweight (BMI 25-30); 34% were obese (BMI>30); 16% had albumin<32gm/l; 7% were anemic with Hb<10gm/dl. During follow-up of 3-5 years, 28% expired. Studied parameters in the surviving and expired patients are tabulated below. On multivariate analysis, BMI and %IBW were significantly higher in survivors. LBM, SAlb, and Hb did not have a significant effect on survival.

Table 1. Nutritional parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Alive (n=59)</th>
<th>Expired (n=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>29.4±5</td>
<td>25±5</td>
<td>0.014</td>
</tr>
<tr>
<td>% SAlb</td>
<td>36.3</td>
<td>36.3</td>
<td>0.9</td>
</tr>
<tr>
<td>% IBW</td>
<td>126.6±1.7</td>
<td>126.6±1.4</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Conclusions: Anemia and hypoalbuminemia are uncommon in patients with PAH. The proportion of patients with PAH are overweight (32%) and obese (34%). A higher BMI and %IBW are associated with survival. Larger studies are needed to confirm these findings and determine the impact of nutritional status on mortality in patients with PAH.
Prognostic value of exercise ventilatory parameters in patients with pulmonary arterial hypertension

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Purpose: The aim of the study was to evaluate the ventilatory parameters obtained from cardiopulmonary exercise test (CPET) and to determine their prognostic value in patients with pulmonary arterial hypertension (PAH).

Material and methods: We prospectively studied 22 pts with PAH in II-IV WHO functional class, treated with specific pulmonary vasodilators. Exercise capacity (peak VO2), ventilatory response to exercise (VE/VCO2slope, VE/VCO2) and oxygen uptake efficiency slope (OUES) were obtained during CPET on using ramp protocol. Pts were followed up for 24 months, noting the endpoint of clinical deterioration (change of WHO class, the need for escalation of therapy) or death.

Results: Mean age of pts was 51.1±18 years, the majority of women (69%). WHO class II in 6 pts, III in 11 and IV in 5 pts. Average peak VO2 was 15.9±1.6 ml/kg/min, OUES was 1.09±0.44, VE/VCO2 was 49±13, VE/VCO2slope 50.8±15. After 6 months the end point occurred in 7 pts, in 2 years after 11 pts. In whom the endpoint occurred during 6-month follow-up, compared to stable pts (n=15), showed lower baseline peak VO2 (12.3±7 vs 17.7±1.6 ml/kg/min, p=0.03) and more enhanced ventilatory response to exercise: basic line VE/VCO2 (57.4±12.2 vs 45.3±12.5, p=0.04), VE/VCO2slope (62.1±14.5 vs 45.5±12.2, p=0.02), OUES (0.76±0.26 vs 1.23±0.43, p=0.01). Similarly showed pts in whom the endpoint occurred in 2-year follow-up (n=11 vs n=11): baseline peak VO2: 12.3±3.8 vs 18.6±1.67 ml/kg/min, p=0.03; OUES: 0.88±0.3 vs 1.28±0.48, p=0.04; VE/VCO2slope: 55.9±11.4 vs 45.6±16.6, p=0.04. Parameters: VE/VCO2slope > 45.7 (91% sensitivity, 73% specificity), OUES < 1.18 (sensitivity 90%, specificity 64%), peak VO2 <19.2 ml/kg/min (sensitivity 100%, specificity 54%) identified pts with worse clinical course. These parameters showed similar predictive value: VE/VCO2slope and OUES have prognostic value regarding clinical worsening in pts with pulmonary arterial hypertension, while the concentration of this protein in circulating plasma is similar to serum and in plasma.

Conclusion: Cardiopulmonary exercise test (CPET) in patients with PAH can provide important information about functional status and clinical deterioration. The combination of exercise and ventilation parameters increased the diagnostic sensitivity of PAH.

P479 | BEDSIDE Platelets in patients with pulmonary arterial hypertension have diminished TWEAK storage capacity what may affect vascular remodelling

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Pulmonary arterial hypertension (PAH) is a progressive disease characterized by proliferative changes in pulmonary arteries that produce a gradual increase in pulmonary vascular resistance and lead to right-heart failure and premature death. There is a growing evidence suggesting that soluble tumor necrosis factor (TNF) α (sTNFα) is released from platelets and induces plasma and vascular inflammation. The prognostic role of this phenomenon requires further investigation.

Methods: In a rapid release of sTWEAK and the amount of sTWEAK release is significantly lower in patients (pts) with pulmonary arterial hypertension (PAH) in comparison with healthy (H). Assessment of sTWEAK release was performed using ELISA. Platelets were isolated from citrate plasma by repeated centrifugation and homogenized in PBS for analysis of sTWEAK content.

Results: In the group of PAH pts, the concentration of sTWEAK in homogenates of isolated platelets was lower compared to control subjects (204.6±184.8 vs 97.9±55.7 pg/ml in PAH vs 91.2±26.7 pg/ml in controls). The concentration of released sTWEAK during clotting (difference between concentration in serum and in plasma) was lower in PAH patients (106.6±51 vs 194.7±85.7 pg/ml, p=0.002). Simultaneously PAH group presented lower number of platelets (196.9±63 vs 270.6±80.2 *10^10/ml, p=0.04), but within this population the number of platelets did not correlate with the release of sTWEAK. We were able to confirm by ELISA that homogenates of isolated platelets contain sTWEAK. Platelets from PAH patients had diminished sTWEAK capacity, while the concentration of this protein in circulating plasma is similar to the controls. Local platelet activation associated with thrombus formation results in a rapid release of sTWEAK and the amount of sTWEAK release is significantly smaller in PAH patients what may affect local vascular remodelling. Platelets are likely to be a major source of sTWEAK and thus may affect inflammation, healing and angiogenesis.

Conclusion: There is a growing evidence that the release of sTWEAK is decreased in PAH patients compared to healthy controls which may affect vascular remodelling. The role of sTWEAK in the PAH pathogenesis should be further investigated.
index, a direct linear correlation between distance walked in 6 minutes and CDi, RVWT, RVEDV, LVEDv and LVED面积 was observed. Multivariate regression analysis showed that CDi was an independent predictor of 6 minute walking distance (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Significant predictors of 6MWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>6MWD (m)</td>
</tr>
<tr>
<td>CDi (%)</td>
</tr>
<tr>
<td>RVWT (cm)</td>
</tr>
<tr>
<td>LVEDv (mL)</td>
</tr>
</tbody>
</table>

6MWD, distance walked in 6 minutes walking test.

Conclusion: CDi is a potential non invasive simple marker for the evaluation of functional capacity in patients with PAH. Its prognostic significance remains to be established in future studies.

P482 | BESIDE
Independent predictors of non-response to long-term sildenafil therapy in pulmonary arterial hypertension patients
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Purpose: Prognostic factors in pulmonary artery hypertension (PAH) patients receiving long-term sildenafil therapy, including markers of endothelial dysfunction, were not analyzed yet. Purpose of our study was to identify independent predictors of PAH patients, non-response (NR) to long-term sildenafil therapy (fetal outcome) among clinical, ECHO-CG, 6-minute walk test (6MWT) parameters and markers of endothelial dysfunction.

Methods: Our prospective observational study included 61 PAH patients NYHA II-III who had undergone right heart catheterization before the onset of long-term sildenafil therapy. There were 44 women and 17 men with a mean age 32.3 ± 3.7 years with mean pulmonary artery pressure 104.1 ± 10 mm Hg. At baseline, before prescription sildenafil 50 mg pd, and at 6 months 6MWT, ECHO-CG and plasma levels of endotheline-1 (ET-1) and von Willebrand factor WF were assessed with ELISA. In 21.4 ± 3.3 months patients retrospectively were divided into responders (alive) and NR (those who died from cardiovascular cause). For independent NR predictors’ identification 27 factors (demographic, clinical, ECHO-CG, 6MWT, ET-1 and WF) were assessed with a multivariate stepwise discriminant analysis procedure.

Results: The cumulative survival rate was 72.6% for PAH patients as a whole. Baseline WF in responders (n=45) vs NR (n=16) was 2.01 ± 0.24 vs 2.05 ± 0.28 IU/mL (p=0.05) while baseline ET-1 was 1.82 ± 0.04 vs 2.09 ± 0.12 fmol/mL (p=0.05). NR was associated with baseline plasma ET-1 > 2.0 fmol/mL (x1), its lowering by 6 months < 0.5 fmol/mL (x2), duration of symptoms for > 8 years (x3), syncope episodes (x4), 6MWT distance increase > 10% by 6 months (x5). Their presense was assessed by “1” and absence – by “0”.

Linear discriminant functions equations Y1 and Y2 had following appearance:

Y1 = -4.73917 + 5.54821 x1 + 0.91234 x2 + 6.7135 x3 + 4.43194 x4 + 1.17077 x5
Y2 = -0.23306 + 0.80601 x1 + 1.42072 x2 + 0.92134 x3 + 0.75671 x4 + 0.722805 x5

If Y1 > Y2, probability of NR associated with fatal outcome was 86.7%. If x2 > x3 were “0” or unknown, and x1>1, Y1 - Y2 (eg NR risk was 86.7%). Others are duration of symptoms > 8 years, syncope episodes, suboptimal ET-1 and 6MWT changes by 6 months but not plasma WF.

Conclusions: 1. 3 and 5-year incidence of PAH, as confirmed by right heart catheterism, did not differ between the two groups (Group A: 1.9%, 3.8%, and 7.5% vs Group B: 3%, 3.8% and 5.3%; p= n.s.).

The mean interval between SSc diagnosis and PAH diagnosis was 6.8 years in group A and 6.1 years in group B (p= n.s.). Survival of patients with development of PAH during follow-up was comparable at 3 years from diagnosis in group A and B (80% vs 66.6%; p= n.s.). Incidence of intestinal lung disease (ILD) was not significantly different (Group A 25.2% vs Group B 20.1%; p= n.s.). Mortality at 5 and 7 year in ILD patients was slight inferior in group A (5.3% vs 11.1%, p=0.055 and 5.3% vs 14.8%; p=0.06). The use of Iloprost was associated with a greater survival advantage both at 5 (Group A: 97.4% vs Group B: 86%; OR 6.175; p=0.04) and 7 years (Group A: 96.8% vs Group B: 72.4%; OR 7.14; p=0.036).

Implications: Our study suggests that Iloprost infusion for treatment of digital ulcers might be responsible of a slight but significant increase of survival in SSc patients. Incidence and mortality rates of pulmonary complications among groups A and B were comparable; the higher survival rate observed in group A were not related to a lower risk of PAH or ILD development. Iloprost therapy for digital ulcers didn’t affect the natural history of PAH.

P484 | BESIDE
Carbon dioxide output kinetics during early recovery from exercise are specifically altered in scleroderma patients with pulmonary arterial hypertension
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Purpose: Pulmonary arterial hypertension (PAH) is a well-known complication in patients (pts) with scleroderma (SSc), harboring a bad prognosis. While the disease is diagnosed by right heart catheterization (RHC), the follow-up evaluation is primarily based on non-invasive diagnostic procedures. Pathophysiologically considerations suggest that gas exchange measurements during early recovery after exercise contain information on the pulmonary ventilation-perfusion relationship.

We hypothesized that carbon dioxide output kinetics (VCO2) in the early recovery phase might be specifically altered in SSc patients with PAH.

Methods: We analyzed 48 consecutive SSc pts with dyspnea. Each patient underwent right heart catheterization (RHC) and cardiopulmonary exercise testing (CPET). PAH was diagnosed according to current guidelines. The pts were categorized into 3 groups: pts without PAH (group 1), pts with PAH and mild pulmonary artery pressure (PAP) elevation (25-35 mmHg, group 2), and pts with advanced PAP elevation (>35 mmHg, group 3).

In the recovery phase, VCO2 kinetics were expressed as percentage of peak VCO2 during exercise.

Results: In 23 out of 46 cases, PAH was diagnosed by RHC and could be ruled out in the remaining 23 cases. The PAH pts showed a significantly delayed decrease in VCO2 during recovery, compared to the pts without PAH. There was no significant difference in the VCO2 recovery kinetics between PAH pts with moderate PAP elevation and PAH pts with advanced PAP elevation (>35 mmHg).

In the early recovery phase, VCO2 kinetics were expressed as percentage of peak VCO2 during exercise.

Conclusions: In the early recovery phase after exercise, VCO2 recovery kinetics show characteristic alterations in SSc pts with PAH. The early recovery phase may contain important clinical information for the non-invasive work-up of PAH pts.
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Plasma microRNA as a new potential biomarker of irreversible pulmonary hypertension associated with congenital heart disease

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Purpose: The pulmonary arterial pressure (PAP) of some patients of severe pulmonary arterial hypertension (PAH) associated with congenital heart disease (CHD) remain high level or even continued to rise after surgery. However, according to the hemodynamic data before surgery, the reversibility of PAH is often difficult to predict. Recent studies demonstrated that microRNAs (miRNAs) are involved in pulmonary vascular remodeling. However, little is known about the roles of miRNAs in irreversible PAH.

Methods: 98 consecutive CHD patients with severe PAH who underwent cardiac surgery were enrolled in between October 2011 and September 2012 at our children’s medical center. Patients were retrospectively separated into 2 groups based on mean PAP 6 months after surgery. We compared 168 miRNA expressions in the plasma specimens of 10 patients (3 cases in the control group, 3 cases in reversible PAH group, 4 cases in irreversible PAH group). The expressions of selected miRNAs were validated independently in plasma samples from 10 cases in the control group, 12 cases in reversible PAH group and 8 cases in irreversible PAH group.

Results: Among the 98 patients, 86 patients had reversible PAP and 12 still had irreversible PAH. Preoperative clinical examination can not distinguish reversible PAH and irreversible PAH. The microarray chip analysis showed miR-301a-3p, mir-45, mir-26a, mir-374a were up-regulated, and miR-20b, mir-500a, mir-501-3p were down-regulated in irreversible PAH group. The expression levels of miR-301a-3p, miR-145, mir-126, mir-26a, and miR-374a were further detected and the expression of miR-145 and miR-126 in irreversible PAH group were twice higher than that of PAH.

Conclusions: 145 and miR-126 were significantly higher in the patients with irreversible pulmonary vascular remodeling, miR-145 and miR-126 may distinguish reversible PAH and irreversible PAH. The mechanisms and implications of the elevated miR-145 and miR-126 remain to be investigated.

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Reversal right ventricular remodeling in patients with pulmonary hypertension undergoing bilateral lung transplantation

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Bilateral Lung Transplantation (BLT) is an option for patients with severe Pulmonary Hypertension (PHs) who remain in advanced heart failure (HF) despite optimal treatment. Acute reduction of RV afterload after BLT leads to a right ventricular reverse remodeling (RVRV) with progressive normalisation of Right Ventricular (RV) structure and function. More data concerning recovery are needed.

Objective: To assess early RVRR patients with severe PH and RV failure who undergo BLT.

Methods: Observational retrospective study of patients with PHs (group 1 & 3) who underwent bilateral lung transplantation (BLT). Right heart catheterization (RHC) was done in pre-BLT evaluation. Structural, functional and ventricular interdependence parameters derived from echocardiographic (ETT) studies performed pre- & post-BLT were analyzed. Wilcixon & Chi Square tests were used to compare variables.

Results: From Jan’10 to Sep’13 18 patients (46±14 yrs, 56% male) with PHs in end stage RVHF were included. Etiology: 72% Pulmonary Arterial Hypertension (10 idiopathic, 2 veno-occlusive (VOD), 1 Congenital Heart Disease) and 28% PAH related to lung disease (4 idiopathic pulmonary fibrosis, 1 bronchiectasis). RHC showed: mean pulmonary artery pressure 55±20 mmHg, Cardiac Index 2.6±0.7 L/min/m2. All PAH patients (excluding VOD), received systemic prostacyclins and right ventricular support. Right ventricular systolic dysfunction was evaluated by pre- & post-BLT TTE. More data concerning recovery are needed.

Conclusions: To early RVRR in patients with severe PH and RV failure who undergo BLT.

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Microvolt T-Wave alternans profile in patients with pulmonary arterial hypertension


Background: Pulmonary arterial hypertension (PAH) is a life-limiting condition of different etiologies. Microvolt T-wave alternans (MTWA) has been demonstrated as a significant predictor of arrhythmic and cardiovascular death, however data on MTWA in PAH is limited. The study aimed to evaluate the profile of MTWA testing in PAH patients and clinical characteristics associated with MTWA results.

Methods and results: MTWA testing, echocardiography, 6-minute walk test, cardiopulmonary exercise test and laboratory measurements were performed. Among 33 patients MTWA test was positive in 22 (67%), negative in 8 (24%), and intermediate in 3 (9%) patients. When compared to patients with a negative result, those with positive MTWA presented larger left ventricular (LV) end-diastolic diameter (44±4 vs. 38±5 mm, p=0.04), lower LV ejection fraction (LVEF 56±9% vs. 65±5%, p=0.007), abnormal LV global longitudinal strain (LV GLS -15±3% vs. -20±2%, p=0.03), and higher plasma BNP (222±183 vs. 46±40 pg/ml, p<0.01). A cut-off value of -17.6% of LV GLS showed a sensitivity and specificity of 81% and 86% to predict positive MTWA result. By univariate logistic regression analysis LV GLS and LV GLS showed a significant association with positive MTWA result, and LV GLS was an independent predictor of MTWA analysis.

Conclusions: There is high incidence of positive MTWA tests in patients with PAH. Despite normal LVEF, the LV GLS is significantly reduced in patients with a positive MTWA result.

P490 | BEDSIDE

A comparison of rapid and slow initiation of intravenous epoprostenol infusion in patients with advanced pulmonary arterial hypertension

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Purpose: Pulmonary arterial hypertension (PAH) is a rare, progressive, and fatal disease. Intravenous infusion (IV) of epoprostenol is an effective treatment of
for patients with advanced PAH. However, there is no widely accepted standard for initiating such IVI therapy and it is unknown whether rapid or slow IVI epoprostenol initiation is superior for achieving improvement in PAH. In this study, we evaluated the hemodynamic changes in PAH patients treated with IVI epoprostenol to determine the optimal protocol for initiating this therapy.

Methods and results: We retrospectively analyzed 42 consecutive PAH patients who underwent IVI of epoprostenol in our hospital. The study group comprised 30 women with a mean age of 34.3 ± 12.5 years. The etiology of PAH was idiopathic PAH (IPAH) in 33 patients, heritable PAH (HPAH) in 5 patients, PAH associated with connective tissue disease (CTD-PAH) in 3 patients, and Eisenmenger syndrome (ES) in 1 patient. We divided the patients into a rapid-initiation therapy group and slow-initiation therapy group according to the cumulative epoprostenol dose for 180 days after the initiation (median cumulative dose of 617 ± 706 μg/kg and 3900 ± 815 μg/kg epoprostenol, respectively), and compared hemodynamic data between the groups. Follow-up right heart catheterization (RHC) was performed 217 ± 80 days after the initiation of IVI epoprostenol. There were no significant differences in mean pulmonary artery pressure (mPAP) or mean cardiac index (CI) between the rapid and slow initiation of therapy groups before starting the IVI epoprostenol (P = 0.134, P = 0.151, respectively). On the other hand, at follow-up RHC, both mPAP and pulmonary vascular resistance (PVR) were significantly decreased, and CI was significantly improved, in the rapid-initiation therapy group compared with the slow-initiation therapy group (P < 0.005, respectively), suggesting a significant improvement in hemodynamic parameters with the rapid initiation of IVI epoprostenol therapy.

Conclusions: Compared with slow initiation of IVI epoprostenol therapy, rapid initiation significantly improved the hemodynamics of patients in this study, suggesting that rapid initiation of such therapy could also improve long-term prognosis in such patients.

Conclusions: This study supports the use of iloprost to treat children with PH following surgery to correct CHD.

P492 | BEDSIDE
Biventricular dysfunction and their consequences predict mortality in pulmonary arterial hypertension
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Background: In pulmonary arterial hypertension (PAH) the right heart dysfunction is a strong predictor of adverse clinical outcome, while the role of the left heart is not fully determined. The aim of this study is to identify predictors of mortality in PAH including measures of both right and left heart function.

Methods: We studied 41 patients (mean age 66 ± 15, range 25-82 years, 27 females) with PAH, all of whom underwent detailed Doppler echocardiographic examination of the right and left heart function using conventional and speckle tracking echocardiography. Patients were followed up to 8 years.

Results: At follow up, (mean time 4.7 ± 3.2 years) only 18 patients survived. After correcting for age difference between groups, E/E' showed a trend to be higher (p = 0.07) but LV filling time remained significantly shorter (p = 0.032), PALS lower (p = 0.012), RA area larger (p = 0.036), tricuspid regurgitation (TR) severer (p = 0.006) and pericardial effusion present (p = 0.024) in the deceased patients compared to survivors. ROC-analysis showed LV filling time < 355 ms as the most accurate predictor of mortality with the largest area under the curve (AUC) (0.78) followed by - m mild TR (AUC=0.77), left atrial strain -23% (AUC=0.72) and right atrial area > 36 cm² (AUC=0.70).

Conclusion: In PAH, the strongest predictors of mortality indirectly reflect both left and right ventricular dysfunction as well as their consequence on respective atrial structure and function.

P493 | BEDSIDE
Relation of the novel pulmonary hypertension EMPHASIS10 quality of life score to BNP and exercise capacity: early results

Background: Pulmonary hypertension (PH) is a debilitating condition, characterised by exercise intolerance due to dyspnea and/or fatigue and is associated with a lower than normal life expectancy. Modern PH management is, thus, aimed at improving prognosis and quality of life (QoL). While previous generic and PH-specific QoL questionnaires exist, the EMPHASIS10 score was very recently developed as a short easily administered/scoring/interpreted PH-specific questionnaire. We report our early experience in using the EMPHASIS10 score in a general PH clinic and its relation to markers of disease severity, such as 6MWT distance, BNP, TAPSE.

Methods and results: The EMPHASIS10 score was provided to 34 consecutive PH patients. This consists of 10 questions, each graded semantic differential six-point scale (0 – 5), for a maximum achievable (worse possible) score of 50. Mean age was 45.5 ± 14 years and 10 (29.4%) were male. Diagnoses included 5 (14.7%) patients with IPAH or heritable PAH, 19 (55.9%) with PAH related to CHD, 4 (11.8%) patients with PAH due to connective tissues disease and 6 (17.6%) with other types of PH.

Average EMPHASIS10 score was 20.6 ± 11.9. The EMPHASIS10 score was not different between sexes and no relation to resting oxygen saturations was observed. Patients with a higher WHO functional class had significantly higher EMPHASIS10 scores (16.1 ± 10.5 in FC I-II versus 27.8 ± 10.7 in FC III-IV; p = 0.004).

A strong correlation between EMPHASIS10 score and log-transformed BNP (R = 0.42, p = 0.02), as well as 6MWT distance (R = 0.64, p = 7e-04) was found.

Conclusion: The EMPHASIS10 QoL score correlates well with established predictors of exercise intolerance and prognosis. Further studies are needed to establish its ability to monitor these patients.
P494 | BESIDE
Influence of bone morphogenic protein receptor 2 (BMPR2) mutation on haemodynamic parameters in pulmonary hypertension: a systematic review and meta-analysis
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Purpose: To assess the influence of BMPR2 mutations on age and haemodynamic parameters in patients diagnosed with idiopathic or heritable pulmonary hypertension (PH).

Methods: A systematic literature search was performed to identify all observational studies comparing haemodynamics in adult patients with PH with and without BMPR2 mutations. Pooled mean±SD values were calculated and mean difference (95% CI) calculated using a random effects model.

Results: Nine studies were included in the analysis reporting a total of 1624 patients, 458 BMPR2 mutation carriers (BMPR2+) and 1166 BMPR2 mutation non-carriers (BMPR2-). The frequency of BMPR2 mutations was 18.6% (range 3.5-30%) in those with idiopathic PH and 77% (range 53.3-86.6%) in those with heritable PH. BMPR2 mutations were present in 36% of males and 29.1% of females. Age and haemodynamic parameters at diagnosis are shown in Table 1. Those with a BMPR2 mutation presented younger with higher pulmonary artery pressures, higher pulmonary vascular resistance and a lower cardiac index. Mutation carriers were less likely to respond to acute vasodilator testing, 2.8% vs 16% (OR 0.16 [0.06-0.41], p<0.0001).

<table>
<thead>
<tr>
<th>Age and haemodynamics at diagnosis</th>
<th>BMPR2+</th>
<th>BMPR2-</th>
<th>Mean difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>41.6±11.3</td>
<td>41.6±11.3</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>35.6±14.8</td>
<td>35.6±14.8</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>RVR (mmHg/L/min)</td>
<td>12.3±7.4</td>
<td>12.3±7.4</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>PVR (mmHg/L/min)</td>
<td>13.3±7.4</td>
<td>13.3±7.4</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>RVSP (mmHg)</td>
<td>14.5±7.4</td>
<td>14.5±7.4</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>368±109</td>
<td>371±118</td>
<td>23.7±3.3, P&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: BMPR2 mutations are present in 18.6% of cases of idiopathic and 77% of familial PH. These patients present younger with more severe haemodynamic derangements and less frequent response to acute vasodilator testing.

P495 | BESIDE
Persistently elevated pulmonary arterial pressure in patients successfully undergone percutaneous transvenous mitral commissurotomy (PTMCT)
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Background: Pulmonary arterial pressure (PAP) is known to regress after successful percutaneous transvenous mitral commissurotomy (PTMCT). Data of persistent pulmonary artery hypertension (PPAH) following PTMCT is not consistent.

Methods: We analyzed the clinical, echocardiographic, and hemodynamic data of 50 PAT who have undergone successful PTMCT in our center from 2002 to 2013. Data of 31 patients who had PPAH (defined by pulmonary artery systolic pressure [PASP] of ≥40 mmHg at one year following PTMCT) were compared to the data of 39 patients who did not have PPAH.

Results: Patients who had PPAH were older (50.9±4.7 years vs 23.6±6.5 years, P<0.005). They had higher prevalence of atrial fibrillation (AF; 40 vs 15%, P<0.005), moderate or severe pulmonary artery hypertension (PAPH) defined as PASP more than 50 mmHg (43.5 vs 33.6%, P<0.005), anatomically advanced mitral valve disease as assessed by Wilkin’s echocardiographic score >8 (31.8 vs 21.2%, P<0.001). Those patients with PPAH had comparatively lower immediate postprocedure mitral valve area (MVA). On follow-up of more than two years, the occurrence of restenosis (40.3 vs 11.1%, P<0.0001), new onset heart failure (15% vs 5%, P<0.05) and need for repeat interventions (9.5% vs 2.8%, P<0.05) were higher in the PPAH group.

Conclusions: Patients with PPAH were older, with more co-morbidity, and had advanced rheumatic mitral valve disease. They had higher incidence of restenosis post PTMCT, new onset heart failure, and need for repeat interventions on long-term follow-up. PPAH represents an advanced stage of rheumatic valve disease and poor hemodynamics of the disease, which may be the reason for the poorer prognosis of these patients. Patients with PPAH requires intensive and more frequent follow-up.

P496 | BESIDE
Apical traction: a motion pattern associated with outcome in patients with pulmonary hypertension
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Purpose: Pulmonary hypertension (PH) leads to right ventricular (RV) remodeling and dysfunction. We observed that some PH patients show a specific motion pattern where the RV apex is pulled towards the left ventricle (LV) during systole, caused by traction from the LV ("apical traction", AT). This study was set up to characterize patients with AT and investigate the prognostic significance of this new marker.

Methods: Echoangiograms from 62 PH patients (42 females, age 61±16 y, PH 83±21mmHg) were retrospectively analyzed. AT was assessed visually by three readers and was confirmed by quantitative speckle tracking. RV dimensions, fractional area change (FAC), tricuspid annular planar systolic excursion (TAPSE), global longitudinal strain (RV GLS) as well as LV ejection fraction (LVEF) and LV GLS were measured. Primary outcome was death or heart/lung transplantation.

Results: AT was found in 31 PAT. Patients with AT had larger RV end-diastolic area (35.9±7.5cm2 vs 26.3±6.2cm2, P<0.001) and PH (82±15 vs. 75±23mmHg, P=0.002), and lower FAC (20.6% vs. 33.7%, P<0.001), RV GLS (10.6±3.0% vs -17.9±4.1%, P<0.001) and TAPSE (13.1±3mm vs 19.4±mm, P<0.001). LVEF and LV GLS were similar in both groups (62.4% vs. 62.5% and -19.2±4.5 vs. -20.7±3.7, resp., both P>NS). Primary end-point was reached by 24 patients. AT was associated with outcome in univariate (HR=2.35, 95%CI=1.44-30.74, P=0.040) and multivariate analysis (HR=2.70, 95%CI=1.70-129.64, P=0.015).

Conclusion: Apical traction is a novel echocardiographic marker in patients with PH which is associated with severely impaired RV function and bad prognosis. It can be visually-assessed without the need of complex measurements, making it an easy-to-use parameter for the clinical routine.

P497 | BESIDE
Static lung hyperinflation and increase of right ventricular volume reduce LV mass and volume in patients with COPD
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Purpose: To assess the impact of lung hyperinflation and the size of right ventricle (RV) on the left ventricle (LV) in patients with stable COPD, where LV cardiovascular disease was thoroughly excluded in advance.

Methods: 112 outpatients with stable COPD in GOLD stages I-V and 34 controls were included. The COPD patients were divided in two groups by mean pulmonary artery pressure (PAP): <25 mmHg: those with pulmonary hypertension (COPD-PH) and those without (COPD-non-PH). RV and LV end-diastolic volumes were measured by magnetic resonance and 3D echo imaging. To evaluate the importance of hyperinflation, residual volume (RV % predicted) was predicted by body plethysmography.

Results: There was a marked and significant increase in RV end-diastolic volume in the controls, 57.7±7.1 to COPD-non-PH, 71±15 and to COPD-PH, 74±14 mm3 (p<0.01 for all), but no change in LV volumes. The end-diastolic L/V RV ratio decreased significantly (p<0.01 for all) from the controls, 1.03, to COPD-non-PH, 0.88, and to COPD-PH, 0.78. Linear regression showed that one standard deviation (1SD) increase in RV % predicted (62%) was significantly associated with a 5.5 g decline in LV mass, (95% CI 8.5-2.4, p<0.001). In the same way, an increase of 1SD of RV volume (1.35 l) was related to a decline in LV mass of 5.4 g. Both regression analyses were adjusted for hypertension, diabetes, total cholesterol level and pack years of smoking. Body size and age, gender and height were adjusted for by means of BSA for LV mass and by use of predicted values of RV (accounting for height, age, and gender). Systolic blood pressure was not associated with LV mass change.

Conclusion: The present study has demonstrated that both static lung hyperinflation and RV volume have an adverse impact on LV mass and structure in stable COPD patients, where LV cardiovascular disease was excluded. These findings might be mechanisms for the observed subclinical impairment of LV function in these patients.
THE RIGHT VENTRICLE AND BASIC SCIENCE

P499 | BEDSIDE
Specific features of the right ventricle in Eisenmenger syndrome (pre-tricuspid versus post-tricuspid defects), MRI and ECHO evaluation

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Purpose: Right ventricle (RV) in Eisenmenger syndrome - severe pulmonary arterial hypertension (PAH) due to congenital heart defects - shows specific features compared to other types of PAH. Crucial influence for better patients (pts) survival is the long-term preservation of RV function. An important role in this seems to play the shunt location. Aim of this prospective study was to compare RV characteristics in pts with pre-tricuspid vs post-tricuspid defects (pre-TD/post-TD) by echo- and magnetic resonance imaging (MRI).

Methods: Consecutive pts (42±15 yrs) with Eisenmenger syndrome, with complete follow-up of 3-years. ECHO and MRI were performed within 24 hours; evaluated were RV dilatation, hypertrophy and function. RV measurements by ECHO: RV diameter (long-axis view, RVD, mm) and RV end-diastolic area (EDA, cm²), RV wall (RWW, mm), RV mass (g/m²) (by Simpson method), RV function (fractional area change [FAC, %] and TAPSE; mm); and by MRI: RV end-diastolic volume (EDV, ml/m²), RV mass (g/m²), RV ejection fraction (EF, %).

Results: ECHO: Pre-TD/post-TD – RVD 44.27/mm (P<0.0001), EDA 29.20/cm² (P<0.0007); RVW 8.9/5.0-mm (P<0.04), RV mass 46.56/g/m² (n.s.), RV/LV mass 0.77/0.85 (n.s.); TAPSE 20.24/mm (P<0.05). RV dilatation was present in 9.7±1.7% pts (P=0.0001), RV hypertrophy (RVW>5-mm) in all and RV dysfunction (FAC<36% and TAPSE-18 mm) in 22±4.7% (P<0.05) pts. MRI: Pre-TD/post-TD – RV dilatation (EDV>87-ml/m²) in 75.16.7% pts (P<0.009), RV EDV 123.364/ml², RV/LV EDV 2.30.86 (P<0.0004), RV mass 50.707/g/m², RV/LV mass 0.720.82 (n.s.), RV EF 48.53% (n.s.), RV dysfunction (EF<36%) found in 16.7±4.2% (P<0.03), RV hypertrophy – RV mass vs RV mass (P<0.05), but no correlation with RVW, RV function – ECHO FAC vs MRI EF (P<0.006), but no correlation with TAPSE.

Conclusions: Our study showed that severe RV hypertrophy was present in both groups (reaching up to 80% of systemic left ventricular mass), with hypertrophy slightly more prominent in post-TD. On the contrary in pre-TD group dominant RV dilatation and more frequent RV systolic dysfunction was present. RV estimation by ECHO and MRI is comparable in patients with RV symmetric dilatation/hypertrophy and global systolic impairment, like it is in Eisenmenger syndrome (or in PAH generally). RV assessment by ECHO is therefore feasible for complex RV evaluation in these patients and in serial follow-up for establishing possible progressive functional deterioration.

P500 | BEDSIDE
Association of apical longitudinal rotation with right ventricular performance in patients with pulmonary hypertension: insights into overestimation of tricuspid annular plane systolic excursion

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Purpose: Current guidelines recommend the routine use of tricuspid annular plane systolic excursion (TAPSE) as a simple method for estimating right ventricular (RV) function. However, when ventricular apical longitudinal rotation (apical-LR) occurs in pulmonary hypertension (PH) patients, it may result in overestimated TAPSE.

Methods: We studied 105 patients with PH defined as mean pulmonary artery pressure >25 mmHg at rest measured by right heart cardiac catheterization. TAPSE was defined as the maximum displacement during systole in the RV-focused apical 4-chamber view. RV free-wall longitudinal speckle-tracking strain (RVFSE) was calculated by averaging three regional peak systolic strains. The apical-LR was measured at the peak rotation in the apical region including both left and right ventricle. The eccentricity index (EI) was defined as the ratio of the length of two perpendicular minor-axis diameters, one of which bisected and was perpendicular to the interventricular septum, and was obtained at end-systole (EI-sys) and end-diastole (EI-di). Twenty-age-, gender- and left ventricular ejection fraction-matched normal controls were studied for comparison.

Results: The apical-LR in PH patients was significantly lower than that in normal controls (-3.4±2.7° vs. -1.3±1.9°; p<0.001). Simple linear regression analysis showed that gender, TAPSE, EI-sys, and EI-di/EI-sys were associated with apical-LR, but RVFSE was not. Multiple regression analysis demonstrated that gender, EI-di/EI-sys and TAPSE were independent determinants of apical-LR.

Conclusions: TAPSE may be overestimated in PH patients with clockwise rotation resulting from LV compression. TAPSE should thus be evaluated carefully in PH patients with marked apical rotation.

P501 | BEDSIDE
The effect of pulmonary hypertension on right ventricular function in acute myocardial infarction

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Background: Right ventricular (RV) dysfunction may accompany inferior wall infarction and is not uncommon in patients with acute anterior infarction. Pulmonary hypertension (PH) may exacerbate RV dysfunction (RVD). However, there is no data on the prognostic implications of both RVD and PH in acute myocardial infarction (AMI).

Methods: Echocardiography was performed in 1076 patients with AMI. RV function was assessed both visually and by measuring the RV fractional area change (RVFAC). Patients were classified into 4 groups according to the presence or absence of pulmonary hypertension (pulmonary artery systolic pressure >35 mmHg) and RVD (RVFAC<35%). The primary endpoint was all-cause mortality with complete follow-up of 3-years.

Results: Patients were classified as normal RV function without PH (n=477), normal RV and PH (n=436), RVD without PH (n=62), and RVD with PH (n=102). The Kaplan-Meier plots show that absolute mortality was highest in patients with both RVD and PH (Figure), with increased mortality predominantly in the first year. In a multivariable Cox regression model, compared with patients without RVD or PH, the adjusted HR for mortality were 1.54 [95% CI 1.14-2.12, p=0.005] in patients normal RV and PH, 1.45 (95% CI 0.72-2.94, P=0.029) in patients with RVD without PH, and 1.98 (95% CI 1.29-3.04, P<0.002) in patients with both RVD and PH.

Conclusion: The results of the current study suggest that PH adversely affects the clinical outcome of patients after AMI, especially when RVD is present. The ability to consider both RVD and PH together is essential for proper identification of patients at risk.

P502 | BEDSIDE
Right ventricular diastolic impairment, more than systolic, is common in Systemic Sclerosis

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Background: Cardiac involvement both of intrinsic or secondary origin is a critical complication favouring mortality in systemic sclerosis (SSc). If left ventricular (LV) involvement has been a matter of several studies, very scarce data are available regarding the right ventricle (RV).

Methods: We examined LV and RV systolic and diastolic function, in a large cohort of 212 consecutive SSc patients seen during a 9 month-period at two institutions and 50 healthy controls. Echocardiography and tissue-Doppler echocardiography (TDE) was used to measure systolic mitral annular velocity (SM), lateral annulus...
early diastolic velocity (Ea), tricuspid systolic annular velocity (ST) and tricuspid annular early diastolic velocity (ET). RV reduced contractility was defined as the existence of a ST < 0.10 cm/s. RV diastolic dysfunction was defined as impaired relaxation (tricuspid E/A ratio < 0.8), pseudonormal RV filling (tricuspid E/A ratio of 0.8 to 2.1 together with a tricuspid E/ET ratio > 6), or restrictive filling in case of tricuspid E/A ratio > 2.

Results: When compared to controls, SSC patients had consistently impaired RV indexes that include reduced RV contractility (p < 0.001), right atrial area (p = 0.027) and overall RV diastolic dysfunction identified in 25% of SSC patients as compared to 0% in the controls (p = 0.001). SSC patients also exhibited alterations in LV contractility and diastolic function but with less extent. In multivariate analysis, RV contractility as expressed by the Tissue Doppler echocardiography ST parameter was associated with SM (p = 0.030), DLCO (p = 0.013) whereas RV diastolic impairment and diastolic function but with less extent. In multivariate analysis, RV disease and pulmonary hypertension contribute to such impairment.

Conclusion: Our data show that RV is commonly affected in SSC with mainly impact on diastolic function and that several factors related or not to lung vascular disease and pulmonary hypertension contribute to such impairment.

P503 | BEDSIDE

Right ventricular end diastolic wall stress correlates with plasma B-type natriuretic peptide level in patients with pulmonary hypertension


Background: The level of plasma B-type natriuretic peptide (BNP) is a prognostic factor of patients with pulmonary hypertension (PH). Recent investigations have demonstrated that plasma BNP level strongly reflects left ventricular wall stress in patients with left heart failure. However, the relationship between right ventricular wall stress and BNP was still unclear. The purpose of this study is to assess the relationship between plasma BNP level and right ventricular wall stress in patients with right heart dysfunction due to pulmonary hypertension.

Methods: We enrolled 46 patients with PH. All patients had transthoracic echocardiographic examinations and pulmonary hemodynamic studies by right heart catheterization. We calculated right ventricular (RV) wall stress as the following formula: wall stress = 1.35*r*p/4*r; {r= RV basal dimension in apical 4 chamber view, p= RV pressure, r= thickness of RV free wall}, and compared RV wall stress and plasma BNP level.

Results: Plasma BNP level correlated with RV end diastolic wall stress significantly (p < 0.0001, r = 0.85), although it didn’t correlate with mean pulmonary artery pressure, pulmonary vessel resistance and cardiac output. Multivariate analysis showed that RV end diastolic wall stress was the independent parameter influencing BNP (p < 0.0001).

Conclusions: Our study showed that the elevation of plasma BNP level reflects increasing of right ventricular end diastolic wall stress in patients with pulmonary hypertension.

P504 | BEDSIDE

Acute changes in right ventricular synchrony and function post inhaled iloprost in pulmonary artery hypertension patients: a myocardial deformation imaging study

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Introduction: Inhaled prostanooids have demonstrated an improvement in clinical outcomes in pulmonary artery hypertension (PAH) patients. Right ventricular (RV) function is an important prognostic factor. The objective was to evaluate RV function and dyssynchrony indexes using myocardial deformation imaging post iloprost inhalation.

Methods: Fifteen idiopathic PAH patients with no prostanooid use were included. In all patients an echocardiographic study using strain analysis derived from speckle tracking, at baseline and 30 minute post iloprost inhalation were performed. RV peak systolic strain dyssynchrony (PSSD) index was calculated using

a six RV segments model from four chambers view (standard deviation of the times from QRS beginning to peak systolic strain of the six segments). Interventricular dysynchrony (IVD) were measured (difference in times, between QRS beginning to ejection phase of RV and left ventricle). Paired T-test was used.

Results: 73% were female, 44.1±8years and baseline six-minute walking test was 430.3±35m. Echocardiographic studies are shown in Table 1.

Table 1

| Heart rate (bpm) | 67±3.1 | 65±1.7 | 0.26 |
| SAP (mmHg) | 117±12 | 111±7 | 0.29 |
| DA (mmHg) | 67±9 | 65±8 | 0.40 |
| PSAP (mmHg) | 82±18 | 79±12 | 0.04 |
| PVR (Wood Units) | 3.9±0.5 | 2.3±0.6 | <0.01 |
| RV PSSD (max) | 16.2±3.5 | 7.0±2.7 | 0.02 |
| RV PSSD (min) | 5.3±2.0 | 2.2±1.6 | 0.00 |
| RV fractional area change (%) | 35±14 | 53±18 | 0.01 |
| RV output (lts/min) | 4.48±1.04 | 6.94±1.01 | 0.04 |
| RV GLS (%) | 13.8±3.1 | 17.0±3.6 | 0.04 |

Conclusions: Iloprost inhalation induces an acute reduction in RV PSSD and IVD indexes. This resynchronization response is related to a better RV performance and to a reduction in PVR. The magnitude of this behaviour and its impact in clinical outcomes must be studied in larger cohorts.

P505 | BEDSIDE

Role of right ventricle and pulmonary hypertension on determining delta VO2/delta work rate flattening: insights from cardiopulmonary exercise test combined with exercise echocardiography

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Background: Several cardiovascular diseases are characterized by an impaired VO2 kinetic during exercise. The lack of a linear increase of VO2/ΔWR relation, as assessed by expired gas analysis, is considered an indicator of abnormal cardiovascular efficiency. We aimed at describing the frequency of ΔVO2/ΔWR flattening in a symptomatic population of cardiac patients, characterizing its functional profile and testing the hypothesis that dynamic pulmonary hypertension and right ventricular contractile reserve play a major role.

Methods and results: We studied 136 patients, with different cardiovascular diseases, referred for dyspnoea during effort. Cardiopulmonary exercise test (CPET) combined with simultaneous exercise-echocardiography were performed using a symptom-limited protocol. ΔVO2/ΔWR flattening was observed in 36 patients (Group A, 26.5% of population) and was associated with a globally worse functional profile (reduced peak VO2, anaerobic threshold 11.4±3.3 vs 13.8±4.4 mL/kg/min, O2 pulse 8.2±2.3 vs 10.9±3.1 mL/beat, impaired VE/VCO2). At univariate analysis, exercise EF, exercise mitral regurgitation, rest and exercise TAPSE, exercise systolic pulmonary artery pressure (SPAP) and exercise cardiac output (7.7±2 vs 9.0±2.8 L/min) were all significantly (p < 0.05) impaired in Group A. The multivariate analysis identified exercise SPAP (OR 1.06; CI 1.01–1.11; p = 0.041) and exercise TAPSE (OR 0.88; CI 0.8–0.97; p = 0.013) as main cardiac determinants of ΔVO2/ΔWR flattening.

Table 1

| Rest | Peak | Rest | Peak | Rest | Peak |
| Peak VO2 | mL/kg/min | – | 13.4±3.9 | 18±6.6 | <0.0001 |
| ∆VO2/∆WR | – | 32±8.8 | 28.9±6.8 | 0.02 |
| LV EF, % | 47±14 | 47±17 | 52±16 | 55±17 | 0.12 |
| Mitral regurgitation ≥3+, % | 14 | 39 | 14 | 20 | 0.09 | 0.025 |
| TAPSE, mm | 37±17 | 61±19 | 33±14 | 51±18 | 0.22 | 0.0009 |
| Mitral regurgitation ≥3+, % | 14 | 39 | 14 | 20 | 0.09 | 0.025 |
| TAPSE, mm | 37±17 | 61±19 | 33±14 | 51±18 | 0.22 | 0.0009 |

Conclusions: In patients symptomatic for dyspnoea, the occurrence of ΔVO2/ΔWR flattening reflects a significantly impaired functional phenotype whose main cardiac determinants are the impaired SPAP response and the reduced peak RV longitudinal systolic function.

P506 | BENCH

LR11 gene deletion prevents pulmonary hypertension and vascular remodeling under hypoxia condition

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Introduction: Pathological feature of pulmonary hypertension is increased medial thickening of pulmonary artery due to hypertrophy and hyperplasia of pulmonary artery smooth muscle cells (VSMCs). LR11 as a member of LDL receptor
family is highly expressed in intimal VSMCs of atherosclerosis. However the role of LR11 gene regulation in pulmonary hypertension has not been explored.

Objective: To determine the role of LR11 deletion in pulmonary vascular remodeling under hypoxic condition.

Methods and results: Ten weeks old of LR11−/− (KO) and C57Bl/6 mice (WT) were placed in 10% hypoxic chamber. Two weeks after exposure of 10% hypoxia LR11−/− showed significantly lower (28±2±3 mmHg) in RVSP compare to control (33±2±0 mmHg) respectively (p<0.001). Specific staining for elastic fiber (EVG) and evaluation of medial wall thickness of pulmonary arterioles showed significantly less in LR11−/− (3.7±0.53%) compare to control (5.7±0.40%; p<0.001). Western blot analysis shows that LR11 expression is increased in lung of WT mice with hypoxia compared with normoxia.

Conclusion: This study demonstrated that deletion of the LR11 gene has prevented the development of pulmonary hypertension and vascular remodeling under hypoxic condition. This finding reveals a novel regulation of LR11 signaling in vascular remodeling.

P507 | BENCH Parenteral treprostinil upregulates fibrocyte BMPRII expression in pulmonary hypertension patients

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Introduction: Pulmonary hypertension (PH) is characterized by remodeling of pulmonary resistance vessels with fibrosis and thrombosis, eventually causing right heart failure. Fibrocytes are progenitor cells derived from monocytes and have been implicated in wound repair, atherosclerosis and fibrotic diseases. Circulating fibrocytes have been found to be increased in children and young adults with PH. Prostacyclin analogues, e.g. treprostinil, an established treatment for PH, were shown to inhibit adhesion and differentiation of fibrocytes in a murine model. We aimed to investigate fibrocytes in PH patients treated with treprostinil.

Methods: Peripheral blood samples from PH patients (n=9, female=66.6%, age=70±10.7y) were obtained at baseline, one week and one month after initiation of treatment with treprostinil. Flow cytometry was employed to characterize circulating fibrocytes based on the expression of CD45, CD34, Collagen I, CD11b and BMPRII.

Results: Treprostinil significantly increased BMPRII expression on fibrocytes (baseline mean fluorescence intensity (MFI) = 26495±55988, one month MFI = 40595±12074, p<0.001). Total numbers of fibrocytes were decreased (baseline = 0.27±0.16% of CD45+ cells, one month = 0.13±0.03% of CD45+ cells, p=0.004), and also CD34 expression (baseline 4470±36124, one month 20173±12074, p<0.001).

Conclusions: The restoration of the BMPRII pathway may normalize a pro-inflammatory state and thus inhibit recruitment of fibrocytes to the circulation.

P508 | BENCH Angiotensin II, angiotensin 1-7, and angiotensin converting enzyme 2 in patients with pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is a chronic and lethal disease that has no cure. The angiotensin converting enzyme type 2 (ACE2) has been recently described as a protein that converts Angiotensin II into Angiotensin 1-7. In vitro and in animal models of PAH, ACE2 and ACE1 have been implicated in the development of pulmonary hypertension. Disturbed lymphatic drainage due to elevated right ventricular pressures is blamed for PE. In this study we aimed to evaluate the prognostic value of PE in COPD.

Methods: The study cohort consisted of 488 COPD patients. Mean follow-up time was 12 months (IGR: 9-13 months). 37 patients (%7.5) had PE. The clinical, spirometric and echocardiographic data were compared between patients with PE group (n=37) and patients without PE group (n=451).

Results: Right ventricular functions were more depressed and pulmonary arterial pressure was more elevated in patient with PE group. Also, Kaplan-Meier survival curve analysis showed that at one year follow up mortality was higher in patients with PE group (long-Rank p value: 0.009). Age, male gender, presence of PE and oxygen usage were independent predictors of mortality on multivariate analysis.

Conclusion: Presence of PE predicted mortality in COPD patients at one year follow up.

P511 | BEDSIDE Fischer ratio as a predictor for severity and adverse cardiac events in pulmonary hypertension

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Purpose: Plasma amino acid concentrations (aminograms) show distinct patterns under various pathological conditions. But, the pattern of plasma amino acids in patients with pulmonary hypertension (PH) has not been elucidated. We sought to examine whether aminograms could have ability to predict clinical severity and adverse cardiac events in PH patients.

Methods: Fasting plasma aminograms of 140 consecutive patients with pulmonary hypertension were measured. Their plasma amino acid levels were compared with those of the age- and gender-matched healthy control subjects.

Results: Aminograms revealed that the plasma concentrations of many amino acids were significantly different between patients with pulmonary hypertension and healthy control subjects. Fischer ratio (branched-chain amino acids/aromatic amino acids) was focused as an integrated parameter. In all enrolled patients, Fischer ratio was negatively correlated with New York Heart Association functional class (p<0.001), plasma B-type natriuretic peptide (p<0.001), pulmonary vascular resistance (p<0.002), and positively correlated with venous oxygen saturation (p=0.002) and 6-minute walk distance (p=0.016). Time-course changes in Fischer ratio and those in cardiac output were significantly correlated (p=0.024).

Conclusions: In patients with PAH there are significant abnormalities in the AT1-ACE2-AT1-7 axis. These abnormalities may play a significant role in the pathogenesis of the disease, and might be therapeutically manipulated.
P512 | BEDSIDE
Characterization of patients with borderline pulmonary hypertension
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Purpose: According to the current guidelines for pulmonary hypertension (PH) normal mean pulmonary artery pressure (mPAP) at rest is defined by 14-13 mmHg, with an upper limit of normal of 20 mmHg. Pulmonary hypertension is defined by a mPAP >25 mmHg). The significance of mPAP between 21 and 24 mmHg is unclear. We sought to characterize patients presenting with “borderline” PH.

Methods: 4363 patients undergoing right heart catheterization (RHC) between 1996 and 2006 were analyzed. 393 data sets were from patients with “borderline” PH. Of those 22 underwent follow-up RHC.

Results: 

- **Table 1**

<table>
<thead>
<tr>
<th>Category</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA/WHO functional class</td>
<td>1 (29.7), 2 (46.8), 3 (3.6), 4 (1.9)</td>
</tr>
<tr>
<td>Coronal artery disease</td>
<td>163 (41.5)</td>
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<tr>
<td>Arterial hypertension</td>
<td>183 (46.3)</td>
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<td>Atrial fibrillation</td>
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<td>Systolic dysfunction</td>
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<td>Diastolic dysfunction</td>
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<tr>
<td>Aortic stenosis</td>
<td>111 (28.2)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>34 (8.7)</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>39 (9.7)</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>101 (25.7)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>55 (14)</td>
</tr>
<tr>
<td>Intrapulmonary shunt</td>
<td>7 (1.9)</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>21 (5.0)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>53 (13.5)</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>42 (10.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>‘Borderline’ PH</th>
<th>mPAP 21-24 mmHg (n=393)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA I/II/III/IV</td>
<td>156 (39.7), 184 (46.8), 34 (8.6), 19 (4.9)</td>
</tr>
<tr>
<td>Coronal artery disease</td>
<td>163 (41.5)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>183 (46.3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>116 (29.5)</td>
</tr>
<tr>
<td>Systolic dysfunction</td>
<td>136 (34.6)</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>148 (37.6)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>111 (28.2)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>34 (8.7)</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>39 (9.7)</td>
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<td>53 (13.5)</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>42 (10.7)</td>
</tr>
</tbody>
</table>

Conclusion: The data demonstrate that a significant proportion of reassessed patients with “borderline” PH develop ‘manifest’ PH. Valvular heart disease and left heart disease occurred in the majority of patients with “borderline” PH.

P513 | BEDSIDE
Different pulmonary arterial remodeling in chronic obstructive pulmonary disease and diffuse parenchymal lung disease awaiting lung transplantation
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Purpose: Pulmonary vasculopathy is common in chronic obstructive pulmonary disease (COPD) and diffuse parenchymal lung disease (DPLD) patients awaiting lung transplantation (LTx). However, the pathogenesis of pulmonary hypertension (PH) is likely to be different in both chronic lung diseases. We compared pulmonary vasculopathy in advanced COPD and DPLD candidates for LTx.

Methods: We studied 116 patients (p), 106 pre-LTx, NYHA 3-4, 41 COPD (59.5±3 years, 9 females), 65 DPLD (60.7±19 years, 16 females), and 10 healthy controls (51±18 years, 6 females). All patients were submitted to left and right heart catheterization, and intravascular ultrasound (IVUS) in medium sized pulmonary arteries (PAs). We assessed the mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), aortic pressure, cardiac index (CI), pulmonary vascular resistance (PVR), local pulmonary arterial elastic modulus (EM: diastolic lumen area x pulse pressure/systolic-diastolic lumen area) and relative wall fibrosis (%Fib: area of Fib/PA cross sectional area = 100).

Results: 16% of p had PCWP >15 mmHg and were not analyzed. PA EM and %Fib were increased even in non-PH p. DPLD p showed a significant higher EM and lower %Fib than COPD p (p<0.05). In COPD, both EM (r=0.75) and %Fib (r=0.6) significantly increased together with the worsening mPAP. By contrast, in DPLD only EM worsens with increasing mPAP (r=0.4).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Chronic obstructive pulmonary disease (n=106)</th>
<th>Diffuse parenchymal lung disease (n=41)</th>
<th>Control (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPAP, mmHg</td>
<td>20±5.0</td>
<td>21±3.0</td>
<td>25±1.0</td>
</tr>
<tr>
<td>CI, l/min/m²</td>
<td>2.4±1.0</td>
<td>2.8±0.6</td>
<td>2.3±0.5</td>
</tr>
<tr>
<td>PVR, Wood units</td>
<td>6.3±2.6</td>
<td>3.5±1.4</td>
<td>2.9±1.1</td>
</tr>
<tr>
<td>EM, mmHg</td>
<td>108±19</td>
<td>61±29</td>
<td>51±18</td>
</tr>
<tr>
<td>%Fib</td>
<td>27±6.0</td>
<td>24.6±8.5</td>
<td>19.8±6.6</td>
</tr>
</tbody>
</table>

Conclusion: COPD and DPLD showed different anatomical (%Fib) and functional (EM) pulmonary vasculopathy beyond the presence of PH. This findings support different pathogenic pathways of PH in both chronic lung diseases and would state the potential use of PAH-approved drugs as a bridge to LTx.

P514 | BEDSIDE
Pulmonary artery compliance assessed by wave intensity analysis and its impact on the right ventricle in patients with or without pulmonary hypertension. First in humans
K. Wustmann1, J.E. Davies2, F. Borgia3, M. Prapa4, W. Li5, P. Kilner6, K. Dimopoulos7, M. Gatzoulis7. 1 Bern University Hospital, Berri, Switzerland; 2 Imperial College London, International Centre for Circulatory Health, London, United Kingdom; 3Royal Brompton Hospital, London, United Kingdom

Purpose: Wave intensity analysis (WIA) is a method to assess the speed and energy of forward- and backward-travelling flow and pressure waveforms. It has been used in the systemic and coronary circulation, but never previously in the pulmonary arteries (PA). We aimed to apply WIA in the pulmonary circulation in order to assess compliance of the central PA in patients (pts) with or without pulmonary hypertension (PAH).

Method: 23 pts underwent a diagnostic heart cath and cardiac magnetic resonance scan (21 pts). After assessment of “conventional” hemodynamic parameters, high-resolution PV was studied the influence of WIA derived MPA compliance parameters on right ventricular (RV) function by CMR.

Results: 17 pts with PAH (meanPAP 48±14mmHg, PVR 10.5±6.8) and 6 controls (meanPAP 18±3.5mmHg, PVR 1.5±0.4WU, p<0.0001 for all) were included. Wave speed in the MPA was increased in PAH compared to controls (9.5±1.8 vs. 2.2±1.0 m/s, p<0.0008), unrelated to heart rate (p=0.4). Reservoir pressure integral reflecting Windkessel function in the MPA was high in PAH compared to controls (1.03±0.64 vs. 0.6±0.17X106 Pa/s p=0.0008). Close relationships were found between WIA derived compliance parameters to meanPAP, PVR, indexed RVmass and RVEF (Table).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>MeanPAP, mmHg</th>
<th>PVR, Wood units</th>
<th>RVEDI, m²/m²</th>
<th>RVmi, g/m²</th>
<th>RVEF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.0001±0.07</td>
<td>0.0001±0.07</td>
<td>0.0005±0.06</td>
<td>0.0002±0.06</td>
<td>0.0006±0.58</td>
</tr>
</tbody>
</table>

Conclusion: Assessment of pressure and flow velocity-derived waves by WIA in the pulmonary circulation is feasible. Higher wave speed and pulmonary reservoir pressure (Windkessel function) reflect increased arterial stiffness in patients with PAH. This likely contributes to RV remodeling. Both velocities may serve as additional outcome measures in the management of PAH.

P515 | BEDSIDE
A high intrapulmonary shunt ratio exacerbates exercise tolerance in patients with pulmonary hypertension
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Purpose: Intrapulmonary collateral vessels do not contribute to oxygenation in the lung; however, they often develop in patients with pulmonary hypertension (PH). While these vessels reduce pulmonary arterial pressure, they also bring impaired oxygenation. Little is known about the association between intrapulmonary shunt and exercise tolerance in PH patients, thus we investigated whether an increased intrapulmonary shunt is preferable to exercise tolerance in PH patients.

Methods: We analyzed subjects from a single center who underwent right heart catheterization (RHC) and a 6-minute walk test (6MWT) within 2 days as the first PH diagnosis from Jan 2007 to Dec 2013. Patients with an unrepaired intracardiac shunt, pulmonary capillary wedge pressure ≥15 mmHg, or PH associated with the lung disease were excluded. Intrapulmonary shunt ratio (Qs/Qt) was calculated according to the equation in the figure below, with blood samples obtained during the RHC. Patients were divided into two groups based on the results.

Conclusions: A high intrapulmonary shunt ratio exacerbates exercise tolerance in patients with pulmonary hypertension.
Table. The significant correlation between wave speed and MP A distensibility vs. controls (p=0.0008). Reservoir pressure in the MP A was increased in PAH (meanPAP 18±5mmHg, PVR 1.5±0.3WU, all p<0.0001) were included. Overall, forward and backward wave speed was increased in the MPA in PAH vs. controls (p=0.0008). Reservoir pressure in the MPA was increased in PAH vs. controls (p=0.0008). MPA distension and distensibility was impaired in PAH (Table). The significant correlation between wave speed and MPA distensibility (r=0.83; p<0.001) supports a close relationship between the vessel stiffness parameters obtained using these two methods. A strong relationship was also found between reservoir pressure and MPA distensibility assessed by CMR (r=0.58; p<0.0006).

Conclusions: WIA in the pulmonary circulation is feasible. Hemodynamically derived increases in arterial wave speed and pulmonary reservoir pressure (Windkessel function), reflecting increased vessel stiffness in PAH, are strongly related to MPA distensibility assessed by CMR. These parameters may pose useful in the diagnosis and treatment of PAH.

P517 | BEDSIDE Right ventricular function in adult survivors of childhood cancer


1University of Oslo, Rikshospitalet University Hospital, Department of Cardiology, Oslo, Norway; 2Norwegian University of Science and Technology, Dept. of Circulation and Medical Imaging, Trondheim; 3Oslo University Hospital, Dept. of Pediatric Medicine, Oslo; 4Oslo University Hospital, National Resource Center for Late Effects after Cancer Treatment, Oslo, Norway

Purpose: Right ventricular (RV) function is strongly associated with prognosis in several chronic cardiac conditions, but data on RV function in childhood cancer survivors (CCS) are very limited.

Methods: Echocardiograms were obtained by a high-end digital scanner (Vivid 7 or E9, GE). RV function was evaluated measuring tricuspid lateral annular systolic velocity (s') using pulsed tissue Doppler. Logistic regression analyses with RV function (s'<10 cm/s) as dependent variable, and gender, age at exam, cancer diagnosis, previous treatment exposure (anthracyclines, cyclophosphamide, iv methotrexate, mediastinal radiotherapy, spinal radiotherapy), left ventricular (LV) function and valvular function as covariates, were performed. CCS were compared 1:1 to healthy controls. Exploratory analyses indicate an association between RV and LV function, but not between RV dysfunction and previous anti-cancer treatment. Prospective studies are needed to determine the prognostic value of RV dysfunction in CCS.

Conclusions: Peak transverse strain is a strong independent predictor of mortality in our population of PH patients and could explain the improved survival of CHD-PAH patients, probably because of preservation of the RV fetal phenotype.

P519 | BEDSIDE Impaired RV systolic function in lymphoma survivors after radiotherapy


1University of Oslo, Rikshospitalet University Hospital, Department of Cardiology, Oslo, Norway; 2Norwegian Radium Hospital, Oslo, Norway

Purpose: Lymphoma survivors (LS) have increased cardiovascular disease burden, because of cardiotoxic treatment, in particular anthracyclines (AC) and radiotherapy (RT) involving the heart. Our aim in the present study was to assess RV systolic function after RT in this patient group.

Methods: All LS treated with high dose chemotherapy with autologous stem cell transplantation (HDT) in Norway in the period 1987–2008, aged ≥18yr at time of HDT were invited to a medical examination including echocardiography. This cohort includes 166 LS (66% men) examined at our university hospital. All had received AC and 78 had additional radiotherapy involving the heart. Patients were categorized into three groups according to treatment: AC (n=108, age 58yr ± 12yr, 11yr ± 5yr since primary treatment), AC-MRT (mediastinal radiotherapy, AC-MRT (mediastinal radiotherapy,
median dose 31.9 Gy, range 19-41 Gy; n = 39, age 47±3 years, 14yr ± 6yr since primary treatment) and AC-TBI (total body irradiation, 13 Gy, n = 39, age 56±7 years, 22yr ± 3yr since primary treatment). Conventional echocardiograms were obtained by Vivid 7 or E9 (GE Vingmed, Norway). RV global longitudinal strain (GLS, six segments) and RV-free wall GLS (three segments) by two-dimensional speckle tracking, and fractional area change (FAC) of the RV were all measured from the apical four chamber view. Analysis for differences between groups according to treatment were done by One-Way ANOVA.

Results: RV systolic function was significantly impaired in LS receiving AC + RT in comparison with CRT patients (p<0.001, Table 1). The treatmentgroups had comparable body mass index, p=0.96.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>MRT-AC (n=39)</th>
<th>TBI-AC (n=39)</th>
<th>AC (n=108)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAC (%)</td>
<td>45.5±0.0001</td>
<td>43.5±0.0001</td>
<td>41.5±0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td>RV GLS (%)</td>
<td>-23.1±3.3</td>
<td>-21.2±3.3</td>
<td>-23.1±3.0</td>
<td>0.001</td>
</tr>
<tr>
<td>RV Free Wall GLS (%)</td>
<td>-25.5±4.0</td>
<td>-26.3±4.3</td>
<td>-27.6±3.8</td>
<td>0.02</td>
</tr>
<tr>
<td>TAPSE (mm)</td>
<td>24±0.0</td>
<td>24±0.0</td>
<td>22±0.0</td>
<td>0.05</td>
</tr>
<tr>
<td>s (mm/s)</td>
<td>12.3±2.6</td>
<td>12.3±2.6</td>
<td>12.9±2.8</td>
<td>0.03</td>
</tr>
<tr>
<td>TRP (mmHg)</td>
<td>21±7</td>
<td>22±12</td>
<td>22±7</td>
<td>N</td>
</tr>
</tbody>
</table>

Conclusion: RV systolic function is impaired when RT involving the heart is added to AC in LS.

TECHNICAL ASPECTS OF CARDIAC RESYNCHRONISATION THERAPY

P521 | BEDSIDE

Minimally-invasive robot-aided surgical implantation of left ventricular leads for CRT: a new alternative after failure of the conventional approach?

S. Amraoui1, P. Ritter1, L. Labrousse1, J.L. Janssens2, S. Ploux1, A. Zemmoura, M. Haissaguerre, R. Bordachar1.1 University Hospital of Bordeaux - Hospital Haut Leveque, Bordeaux-Pessac, France; 2Free University of Brussels (ULB), Brussels, Belgium

Introduction: Left ventricular (LV) lead implantation through the coronary sinus is frequently challenging, and even, not possible in some cases: alternative approaches are needed. A mini-invasively robotically guided LV lead implantation (RobotLV) has major advantages, but there are little published data about the short and long-term follow up, in terms of feasibility, safety, electrical performance and impact on the clinical outcome.

Methods: 21 heart failure patients (pts) underwent a RobotLV with the Da Vinci Robotic System because of failed implant (n=15), non-response to conventional approaches (n=5) or no venous accesses (n=1). During the procedure, the entire LV free wall was exposed, allowing to choose stimulation sites and to implant 2 LV leads to optimize CRT response (use of a Y connector). We prospectively followed the patients during 1 year.

Results: The 2 LV leads were successfully implanted in all pts. We did not observe any complication during the procedure. One pt died before discharge (mesenteric ischemia). After a mean stay of 1.2±0.4 days in the intensive care unit, the 21 pts were hospitalized in the EP department during 6.7±2.9 days. The acute LV thresholds were excellent (1.0V±0.4ms) including one pt with a threshold ≥1.4 veins per case were visualized, excluding coronary sinuses which was visualized in all. Exact data about visualization of selected veins is presented in the table below. 29 variants of coronary veins were identified. Ten variants among them were 10 or more times found (each) in the examined population (total 258 cases; 81.9%). Rest of variants occurred almost incidentally. In all frequent variants at least one vein in the target area for CRT occurred (2 veins in 4 variants and 3 or more veins in 2 variants). In 3 variants which occurred in 9 cases (2.6%) lack of coronary veins in target area were confirmed. If those cases it is possible that small vein(s) under 1 mm can exist, however they can't be identified by coronary computed tomography.

An apicality index was automatically computed for each lead (values from zero to one corresponding to basal and apical positions, respectively). Identified subgroups were: basal LV lead + apical RV lead (G1, N=3), mid LV lead + apical RV lead (G2, N=2), mid LV and RV lead (G3,N=2), apical LV and RV lead (G4,N=2).

Subgroup outcome was compared to the % recovery of total activation time (TAT) measured in the LATM (differences between TAT in LBBB and after CRT).

Conclusions: The proposed methodology allows to automatically relate CRT lead positions with electrical activation. The obtained results confirm in a quantitative way the optimal positions suggested by previous clinical studies.

P522 | BENCH

Quantitative analysis of CRT leads position against activation time recovery in an experimental swine model

D. Soto-Iglesias1, N. Duchateau1, C. Butkofst, D. Andreu2, J. Fernandez-Armenta2, B. Bijnen2, M. Sitges2, O. Camara1, A. Berruezo2 on behalf of Spanish Industrial and Technological Development Center. 1University Pompeu Fabra, Physense, Barcelona, Spain; 2University of Barcelona, Hospital Clinic, Barcelona, Spain

Purpose: Recent studies have suggested that apical position of the LV lead in Cardiac Resynchronization Therapy (CRT) is associated to a worse clinical outcome. However the underlying mechanisms are not fully understood due to a lack of reliable data and tools to analyze it. We propose to study the influence of LV lead position on electrical recovery in an experimental swine model of LBBB/CRT.

Materials and methods: The study included 9 pigs (34.3kg) with no structural disease under baseline, LBBB and CRT conditions. Local activation time maps (LATM, biventricular epicardium) were acquired with an electroanatomical mapping system. A bull’s eye plot representation was used for data comparisons.

P523 | BEDSIDE

Analysis of coronary venous system by means of cardiac computer tomography

R. Mlynarski1, A. Mlynarska2, M. Sosnowski2.1 Upper-Silesian Cardiology Center, Katowice, Poland; 2Medical University of Silesia, Katowice, Poland

Variability of coronary venous system (CVS) was documented previously, however mostly on small groups of patients. There is no research on bigger population to evaluate the anatomy of CVS in cardiac computed tomography – results can potentially be important for invasive cardiology procedures were cannulation of CVS is needed as e.g. cardiac resynchronization (CRT).

Methods: In 315 subjects (aged 58.27±11.6; 117W) a cardiac computed tomography with retrospective gating by using Aquilion 64 (Toshiba) were performed according to the appropriateness criteria. Standard protocol for coronary arteries was used during scanning. Additional reconstructions dedicated for coronary veins during post processing was used to analyze the data.

Results: Average 3.6±1.4 veins per case were visualized, excluding coronary sinuses which was visualized in all. Exact data about visualization of selected veins is presented in the table below. 29 variants of coronary veins were identified. Ten variants among them were 10 or more times found (each) in the examined population (total 258 cases; 81.9%). Rest of variants occurred almost incidentally. In all frequent variants at least one vein in the target area for CRT occurred (2 veins in 4 variants and 3 or more veins in 2 variants). In 3 variants which occurred in 9 cases (2.6%) lack of coronary veins in target area were confirmed. If those cases it is possible that small vein(s) under 1 mm can exist, however they can’t be identified by coronary computed tomography.

Table 1. Visualization of coronary veins

<table>
<thead>
<tr>
<th>Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior vein</td>
<td>163/315</td>
</tr>
<tr>
<td>Postero-lateral vein</td>
<td>210/315</td>
</tr>
<tr>
<td>Lateral vein</td>
<td>267/315</td>
</tr>
<tr>
<td>Antero-lateral vein</td>
<td>140/315</td>
</tr>
<tr>
<td>Anterior vein</td>
<td>270/315</td>
</tr>
</tbody>
</table>

Conclusions: In most of subjects, coronary veins potentially useful for cardiac resynchronization were found. In about 3% of patients there is no veins which can be useful for CRT. In those patients sub-optimal placement of LV lead to the middle cardiac vein (which always is available) or anterior area veins may cause non responding of selected CRT candidates.

P524 | BEDSIDE

Effectiveness and reliability of selected site pacing for avoidance of phrenic nerve stimulation in CRT patients with quadripolar leads: results from the multicenter EFFACE-Q trial

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Purpose: To investigate the frequency of suitable left ventricular pacing configurations (LVPcs) of a quadripolar LV pacing lead used for cardiac resynchronization therapy (CRT).

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This method. However, more evidences and multicenter studies are needed to evaluate the surgical epicardial procedure when transvenous implantation could not be applied.

Conclusion: After the implantation, 2 of the patients died due to the progression of the heart failure at 8 and 15 months after the implantation.

Results: Coagulation therapy with INR between 2-3. No thromboembolic complication was observed. Because of intraoperatively started anticoagulation therapy with INR between 2-3, the lead was fixed in the left ventricle in all cases with good pacing morphology.

Methods: In 93% of patients, one or more viable LVPC was available, exceeding the predefined margin of 90% (p=0.048), and exceeding the availability of suitable traditional LVPC alone (89.6%; p=0.002). The lead was inducible more often in distal (54%) than in middle (M2: 40%; M3: 35%) or proximal (30%) LVPCs (p<0.001). Pacing thresholds were higher in proximal (3.9±2.3V) than middle (M3: 2.9±2.2; M2: 2.3±2.0V) or distal (1.7±1.4V) LVPCs (p<0.001). During the study, reprogramming of LVPCs was observed in 49% of patients, leading to a use of advanced LVPCs in 52% of patients.

Conclusions: The higher number of programming possibilities of a quadrupolar LV lead leads to an increased availability of viable pacing configurations when compared to traditional left ventricular pacing configurations alone. Thus, with a quadrupolar LV lead, more effective LV pacing can be delivered.

### P525 | BEDSIDE

**Long term efficacy and safety of transseptal endocardial left ventricular lead implantation after left ventricular lead implantations**

L. Geller, L. Molnar, S.Z. Szilagyi, E. Zima, G. Szepaki, I. Osztheimer, T. Tahin, E. Evren Ozcan, A. Apor, B. Merkely. Semmelweis University, Cardiovascular Center, Budapest, Hungary

**Introduction:** Transvenous left ventricular (LV) lead positioning might be challenging or in some cases impossible, in these patients alternative methods are needed.

**Objectives:** The aim of this study was to investigate the effectiveness and safety of transseptal endocardial left ventricular lead implantation (TELVLI) in severe heart failure patients, and evaluate the long term follow-ups of the patients.

**Methods:** TELVLI was performed in 33 patients (28 men, 63±7 years, NYHA III-IV stage). Transseptal (TS) puncture was performed via the femoral vein. Intracardiac ultrasound was used to guide the puncture in 24 pts. The site of the puncture was dilated with a 6mm (3 pts), later with an 8 mm balloon (30 pts). After the puncture of the left subclavian vein, an electrophysiological deflectable CS catheter was introduced into the CS sheath. The CS catheter was used to reach the left atrium and the left ventricle through the dilated transseptal puncture hole. At the latest LV activation site 65 cm active fixation bipolar lead was screwed into the LV wall.

**Results:** The lead was fixed in the left ventricle in all cases with good pacing threshold values (0.84±0.4 V,0.4 ms). Puncture complication, pericardial effusion was not observed. Because of intraproactively started anticoagulation therapy, pocket haematoma was observed postoperatively in three (11%) and needed evacuation in one case (3%). Follow-up is longer than one month in 32 patients (34±11 months). Significant improvement of the NYHA class was observed in all but one case (97%), on the first month control LV EF was 30±9% vs 38±6%.

**Conclusion:** The lead was fixed in the left ventricle in all cases with good pacing threshold values. Puncture complication, pericardial effusion was not observed. Because of intraproactively started anticoagulation therapy, pocket haematoma was observed postoperatively in three (11%) and needed evacuation in one case (3%). Follow-up is longer than one month in 32 patients (34±11 months). Significant improvement of the NYHA class was observed in all but one case (97%), on the first month control LV EF was 30±9% vs 38±6%.

**Conclusion:** This study demonstrates that epicardial LV leads have an excellent long-term performance and durability. Therefore, epicardial leads might be a viable alternative for selected patients eligible for CRT.

### P527 | BEDSIDE

**Larger interventricular lead distance at implantation is associated with improvement in biomarkers, ejection fraction and clinical outcome in CRT patients**


**Background:** We aimed to evaluate the impact of LV-RV lead distance (ILD) on biomarkers, ejection fraction (EF) and clinical outcome in patients implanted with cardiac resynchronization therapy (CRT). Stratified by baseline LBBB ECG morphology.

**Methods:** Heart failure (HF) patients undergoing CRT implantation with EF ≤35% and QRSd ≥120 ms were evaluated based on the ILD at implantation. Baseline performance of epicardial lead.
and 6-month EF, NT-proBNP and apelin values were assessed. All-cause mortality and HF episodes were captured during the follow-up.

**Results:** A total of 125 patients undergoing CRT implantation were studied, with a mean age of 67.6 ± 13.7 years, and mean ejection fraction (EF) of 28.7 ± 6.2%. Sixty-two percent of them had typical LBBB. During the mean follow-up of 2.2 years, 38 (29%) patients died, 44 (35%) patients had HF death. Patients with ILD ≥ 88 ms (lower quartile of ILD) had significantly lower risk of HF/death (HR: 0.42; 95% CI: 0.22-0.79; p = 0.007), and all-cause mortality (HR: 0.45; 95% CI: 0.21-0.92; p = 0.029) after adjustment for relevant clinical covariates (including lateral LV lead location) compared to those with ILD < 88 ms. Patients with ILD ≥ 88 ms and LBBB showed the greatest improvement in EF (mean EF 28.6 ± 6.2 to 37.7 ± 10.4%; p < 0.001), NT-proBNP (median 3744 to 1776 ng/ml; p < 0.001), apelin (median 586.6 ng/ml to 349.6 ng/ml; p = 0.01), and they had the highest survival (p = 0.001) and HF-free survival (p = 0.001) (Fig. 1), compared to ILD < 88 ms or non-LBBB. There was no difference in outcome by ILD in patients with non-LBBB.

**Conclusions:** LBBB patients with larger ILD at CRT implantation had greater improvement in biomarkers, EF and better clinical outcome. Larger ILD is preferred over non-LBBB.

**P528 | BEDSIDE**

**Is a second CRT implantation after CRT device extraction as effective as the first time?**

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**Background:** The growing number of CRT implantations, upgrades and box chances in Europe as well as increase of lead dysfunction leads to more device and lead extractions in combination with device-related interventions. After lead extraction the need of CRT reimplantation caused by ongoing heart failure will often follow in the course of the time. The prognoses of these patients are unclear and not investigateable.

**Methods:** We analyzed all patients with CRT reimplantation after complete device and lead extraction in our center (n=53; age 68 ± 9.9 years; 5 woman; 60 days (49-87) median time interval from extraction to reimplantation; 47 endovascular laser extraction and 6 cardiac surgery extractions; LVEF 27±7.2%, 15 AV block third degree without escape rhythm).

**Results:** Only 30 (57%) of 53 patients could implanted in the optimal posterolateral or lateral coronary vein. In 16 (30%) of all patients the past coronary vein were obstructed, in 4 (8%) patients both coronary veins were occluded and in 3 (5%) patients a complete thrombosis of the cava superior vein were found. For that reason no CRT reimplantation were reached in 7 patients.

In the median follow up of 25.4 (8.5-39) months 7 patients died and 2 patients reached a surgical tricuspid valve reconstruction. Further 3 (6%) patients developed a new bacteremia with a repeat need of complete device and lead extraction and in 5 (9%) patients a new pocket or lead revision were followed.

**Conclusion:** Thrombosis of coronary and subclavian veins are very common in patients with prior CRT device and lead extraction. For that reason the success of CRT reimplantation procedure is not comparable to first CRT implantation. The prognosis of these patients is marked with higher mortality and reinfection.

**P529 | BEDSIDE**

**Sensor-based electromagnetic navigation to facilitate implantation of left ventricular leads - a revolutionary step into a future with less radiation**

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**Introduction:** Implantation of left ventricular (LV) leads for cardiac resynchronization therapy (CRT) is associated with a substantial radiation exposure. A new non-fluoroscopic tracking system (MediGuide Technology [MGT], St. Jude Medical) allows for non-fluoroscopic visualization of sensor-equipped LV lead delivery tools. We report the results of a single center observational study using this new technology.

**Methods:** Between February and September 2013 thirty-four consecutive patients were implanted with a CRT device using this new tracking technology. Subjects were matched with conventional implanted patients regarding factors affecting radiation exposure. Demographics, detailed fluoroscopy need, procedure time, and adverse events were collected and compared between the two groups.

**Results:** A successful lead implantation was possible in all patients with a nonfluoroscopic CS intubation in 29 (85%) of the 34 patients in the study group. Use of the tracking technology for LV lead delivery significantly reduced total procedural fluoroscopy time (median [quartiles] from 8.0 (5.8; 11.5) minutes to 4.5 (2.8; 7.3) minutes (P = 0.016) and radiation dose from 603 (330; 969) cGy cm² to 338 (176; 680) cGy cm², respectively (P = 0.044). There was no difference in outcome by ILD in patients with non-LBBB.

**Conclusions:** The new electromagnetic tracking system allows for safe and successful LV lead implantation with a significantly reduced radiation exposure.
The primary endpoint was the HF clinical composite score, which scores patients as improved, unchanged, or worsened. The secondary endpoint was the cumulative survival from any cause of death, HF hospitalization, and spontaneous ventricular arrhythmias.

**Results:** Tri-V was successfully implanted in 23 patients. Clinical composite score was improved in 19 (83%) and unchanged in 4 (17%) of 23 patients with Tri-V, whereas it was improved in 31 (59%), unchanged in 17 (32%) and worsened in 5 (9%) of 53 patients with Bi-V at 1 year after implantation (p=0.033). After a median follow-up of 2.5 years, there was no significant survival rate difference between Tri-V and Bi-V (p=0.57). However, Tri-V group showed non-significant higher survival from HF hospitalization (p=0.074) and significant higher survival from ventricular arrhythmias (p=0.041).

**Conclusions:** CRT with Tri-V appears to be more beneficial on clinical status than Bi-V.

**PS32 | BEDSIDE**

Multipoint left ventricular pacing in a single coronary sinus branch improves 12-month response to cardiac resynchronization therapy relative to conventional biventricular pacing

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**Purpose:** Cardiac resynchronization therapy (CRT) with multipoint left ventricular (LV) pacing (MultiPoint™ Pacing MPP) improves acute LV function and CRT response at 12 months. We hypothesized that MPP can also improve response at 12 months.

**Methods:** Consecutive patients (pts) receiving a CRT implant (Unify Quadra MP™ or Quadra Assura MP™ CRT-D and Quartet™ LV lead) were randomized to receive pressure-volume (PV) loop optimized biventricular pacing with either conventional CRT (CONV) or MPP. Echocardiography was performed prior to implant (BASELINE) and 12 months post-implant and analyzed by a blinded observer. CRT response was prospectively defined as a reduction in end-systolic volume (BASELINE) and 12 months post-implant and analyzed by a blinded observer. ESV reduction and EF increase relative to BASELINE was 1.1 ± 0.8 in the MPP group and 0.95 ± 0.4 in the CONV group (p=0.6, Fig. 1C).

**Conclusions:** Sustaining the trend observed 3 months post-implant, PV loop guided multipoint LV pacing resulted in greater LV reverse remodeling and higher CRT response rate at 12 months compared to PV loop guided conventional CRT.

**INNOVATIONS IN CARDIAC PACING**

**P534 | BEDSIDE**

A electrocardiogram score to identify pacing sites in selective site right ventricular pacing

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**Purpose:** When performing selective site right ventricular (RV) pacing, it has been indicated that leads are often accidentally placed in sites associated with risk of cardiac perforation of the free wall or groove between the septum and free wall, despite the intended placement site being the interventricular septum. To avoid cardiac perforation, it is best to place leads at a fixed distance from the free wall defined as the true septum (TS). We believe not only that placement of leads in TS needs lead position to be observed carefully, but it is also important to observe paced QRS waveforms before screw-in as an auxiliary diagnosis. However, few reports exist on useful electrocardiogram (ECG) scores that combine simplicity with high diagnostic accuracy. The aim of the present study was to create a useful and simple ECG score that could be used to determine whether leads had been placed in TS or not.

**Methods:** Seventy-nine patients, who had undergone pacemaker implantation to treat bradyarrhythmias and in whom the RV lead was placed in the non-apex sites, were enrolled in this study. Multislice computed tomography scanning was used to separate subjects into those whose RV lead was positioned in TS (n=33) and those whose lead was not positioned in TS (n=46). Each QRS duration (ms), R wave height (mm), and negative wave depth (mm) in leads I and II were measured, and number of positive precordial leads (number of leads that were positive R wave) among the precordial leads were counted from paced ECG (0.1 mV/mm). We analyzed QRS variables from paced ECG by multivariate logistic regression analysis and created a ECG score to predict if the lead was placed in TS.

**Results:** Multivariate logistic analysis indicated that R wave height (mm) in lead I, number of positive precordial leads, and QRS duration (ms) were significantly associated with TS, with odds ratios of 1.57, 4.09, and 0.94, respectively. For R wave height in lead I, 1 point was given for 3 mm or greater and an additional 1 point was given for 7 mm or greater (total 2 points). For QRS duration, 1 point was added for ~150 ms. For the number of positive precordial leads, n points were awarded for n leads (from 1–3, with 1–3 points awarded for each). TS score was defined as the total score of these points. The TS score odds ratio was 5.2, the area under the curve of the receiver operating characteristic curve was 89% (P < 0.001), and when the cutoff was set at 4 or higher, sensitivity was 76% and specificity was 83%.

**Conclusions:** Our study suggested that TS score is a simple and useful method for TS prediction.

**P535 | BEDSIDE**

Septal right ventricular lead positioning and optimized DDD pacing versus intrinsic conduction in sinus node disease: an echocardiographic study

The Optimist trial

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**Introduction:** Preserved intrinsic conduction in paced sinus node disease (SNDD) patients seems to be associated with a better outcome when compared with a normal right ventricular (RV) DDD pacing. The prospective, multicenter, randomized OPTIMIST study was designed to compare RV lead positioning in the septum to preserved intrinsic conduction in chronically paced SNDD patients.

**Methods:** SNDD patients with a class I indication were implanted with a DDD pacemaker (ST. Jude medical), the RV lead being located in the mid-septum. The algorithm VIP™ (Ventricular Intrinsic Preference) was programmed “on” in all patients at hospital discharge. After a 6 weeks observational period, patients with a ventricular pacing percentage inferior to 10% were randomized in 2 groups: VIP “on” (preserved natural conduction – group 1) or “off” with AV delay optimization (RV pacing – group 2). Patients were followed every 6 months with echo- cardiography through 18 months. The primary endpoint was the left ventricular cardiac causes and one pt from each group was lost to follow-up. After 12 months, 12/21 (57%) pts in the CONV group and 16/21 (76%) pts in the MPP group were classified as CRT responders. ESV reduction and EF increase relative to BASELINE were significantly greater with MPP than with CONV (ESV: -28.4 ± 15.7% vs. -14.9 ± 16.3%, P = 0.01, Fig. 1A; EF: +13.9 ± 8.5% vs. +2.1 ± 10.2%, P = 0.001, Fig. 1B). NYHA functional class reduction relative to BASELINE was 1.1 ± 0.8 in the MPP group and 0.95 ± 0.4 in the CONV group (P = 0.6, Fig. 1C).

**Conclusions:** Sustaining the trend observed 3 months post-implant, PV loop guided multipoint LV pacing resulted in greater LV reverse remodeling and higher CRT response rate at 12 months compared to PV loop guided conventional CRT.
end-systolic diameter (LVESD) (Corelab analysis), with a non inferiority hypothesis.

Results: 216 patients mean age 76.07±9.45 years were included and 167 randomized. The baseline characteristics were comparable in group 1 and 2 including left ventricular ejection fraction. LVEF (62.4±12.6 vs 64.4±8.7%), LVESD (32.7±8.5 vs 32.5±11.3 mm) and 6 weeks RV pacing percentage (1.81±1.92 vs 2.15±2.07%). At the end of FU, as expected the percentage of RV pacing was significantly higher in group 2 (79.3±1.6 vs 79.1±17.4%). The LVEF was 62.3±10.1% in group 1 and 60.9±9.9% in group 2 (NS) and the LVESD was 31.9±7.23 mm in group 1 and 31.26±7.21 mm in group 2 (NS). The non-inferiority hypothesis was validated (p=2.572 e-06 for a delta = 4.785). AF burden was not different between the 2 groups.

Conclusion: When implanting the RV lead in the midseptum, DDD pacing with high percentage of RV capture was not associated with LV echocardiographic deterioration as compared to preserved intrinsic conduction pacing mode.

PS36 | BEDSIDE
Comparisons of long-term outcome between VDD and DDD pacing in patients with atrioventricular block
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Background: Permanent pacemaker (PPM) with atrioventricular synchronous pacing offers better prognosis for patients with atrioventricular block (AVB). Except for dual chamber pacing (DDD), single lead VDD mode has been discussed about the efficacy and risk of atrial undersensing. Whether VDD can be a good alternative in patients with AVB remains unknown because of the lack of long-term, large-scale analysis. The aim of the present study was to compare the long-term outcome of VDD with DDD pacing.

Methods: A total of 207 patients undergoing PPM implantations with VDD mode were enrolled from 2000 to 2013. Another 828 age- and gender-matched patients undergoing DDD mode implantations during the same period of time were selected as the control group at a 1:4 ratio. The study endpoint was mortality.

Results: A total of 1,035 patients (64.3% male) were followed up for 46.5±43.1 months. The mean ages were 75.1±11.6 years for VDD, and 75.0±10.9 years for DDD. The long-term survival rate was not significantly different between VDD and DDD groups (figure). After the adjustment for baseline characteristics, VDD and DDD groups had similar long-term prognosis with a adjusted hazard ratio of 1.915 (95% confidence interval 0.849-1.671, p value =0.311). Further analysis of cumulative rate of cardiovascular death or non-cardiovascular death between two groups also showed no difference.

Conclusions: The long-term prognosis of VDD mode was comparable to DDD mode. Therefore, single lead VDD could be considered as an alternative choice in patients with AVB.

PS37 | BEDSIDE
Myocardial minimal damage associated with pacemaker implantation: randomised comparison between active and passive fixation leads
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Background: The implantation of permanent pacemakers may be associated with a Troponin release which reflects the minimal myocardial damage owed to the procedure. It is unknown if the type of lead used (active versus passive fixation) influences the amount of Troponin release.

Methods: Patients with standard indications for single or dual chamber pacemaker implantation were eligible for study participation. They were randomly assigned to either receive an active or a passive fixation ventricular lead. In dual chamber pacemaker recipients the randomisation only referred to the ventricular lead and for the atrial lead an active fixation mechanism had to be used. Pre- and post-operatively serum levels of high sensitive TroponinT were determined.

Results: A total of 326 patients (age 74±9 years, 64% male) were included in 6 international centres. The indication for pacemaker placement was sinus node disease (n=103), atrio-ventricular block (n=131), biventricular disease (n=15), atrial fibrillation with slow ventricular response (n=73), or others (n=4). In 202 (62%) patients a dual chamber pacemaker was implanted. 166 patients were assigned to receive an active fixation ventricular lead and 160 patients were assigned to a passive fixation lead. The baseline characteristics did not differ significantly between the 2 groups in terms of age, gender, cardiovascular risk factors, clinical presentation, LVEF, LVESD, and the other echocardiographic parameters. The primary purpose of the study was to demonstrate that right ventricular pacing (RVP) is significantly reduced by using the VPS feature. The secondary objective was to confirm the safety of the VPS feature. Additionally, the possibility of the VPS feature to reduce ventricular pseudo-stimulations was assessed. The VPS feature was a prospective, multicenter, randomized, simple-blinded, and cross-over designed study.

Methods: Patients with sinus node dysfunction and/or paroxysmal atrial fibrillation with at least 1 episode per week lasting at least 5 minutes. They were eligible for enrolment. Patients were randomised post-implant into groups of VpS ON (DDD(R)-AD(Ri)-mode) or OFF (DDD(R) mode). After 6 weeks patients were crossed-over to the other group. The VPS status switched. The efficacy of the VPS feature was assessed by comparing the mean pacing percentage values of patients with the VPS feature ON respectfully OFF and vice versa. Safety of the VPS feature was evaluated by assessing all feature related adverse events. The ability of the VPS feature to reduce pseudo-stimulations was tested using a 24h ECG and analysing the ECG for capture of RVP and pseudo-stimulations.

Results: A total of 93 patients (female age 73±10 years) were enrolled. The overall mean reduction of RVP in percentage (%) with VPS ON was calculated to be 57.4±39.5, two-sided 95% confidence interval [48.8, 66.6]. (t(df=97)=12.88, p<0.001). In total complications related to the VPS feature were observed. In order to test the hypotheses, an exact binomial test resulted in a p-value of p=0.0085. In addition, the core laboratory analyzed Holter ECG recordings, and revealed an average ventricular pacing reduction of 55.8% and an average reduction of pseudo-stimulations of 84% with VPS ON.

Conclusion: The VPS algorithm proved to be safe and effective in significantly reducing RVP and pseudo-stimulations. The reduction of RVP and pseudo-stimulations is associated with a significant benefit for the patient, since it significantly reduces artificial ventricular dysynchrony and increases longevity of the pacemaker.

PS39 | BEDSIDE
Pacing of the inter-ventricular septum versus the right ventricular apex: a prospective, randomized study
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Introduction: Left ventricular (LV) function might be impaired by right ventricular (RV) apical pacing. The interventricular septum is an alternative pacing site, but randomized data are limited. Our aim was to compare LV function and asynchrony resulting from pacing the interventricular septum versus the RV apex.

Methods: Patients with atrio-ventricular (AV) block and normal ejection fraction candidate to dual-chamber pacemaker (PM) implantation were randomized to permanent ventricular stimulation either in the apex (group A) or the septum (group B). LV function and global dyssynchrony parameters were estimated by echocardiography before and 6 months after PM implantation.

Results: We collected 57 patients, of whom 29 were randomized to group A and 28 to group B. Six-month follow up data are available for 48 patients. After PM implantation, the QRS duration was significantly increased in both groups, but the increase was higher in group A (27.2 versus 22.9msec. p=0.002). Immediately after pace maker implantation, there was not a significant difference between the two groups in terms of LV ejection fraction, LV end-systolic volume, and LV end-diastolic volume. However, after 6 months of follow up, there was a significant difference (p=0.005) and E/A ratio (p=0.013). In addition, both the tissue Doppler imaging (TDI) velocity and strain analysis showed a difference in the dysynchrony index between apical and septal pacing.
Furthermore, six months after PM implantation, the global myocardial function was still better in patients undergoing septal stimulation assessed by a higher Tei index (p<0.002) and E/A ratio (p<0.001). Analysis of both atrioventricular and intraventricular dysynchrony parameters did not reveal any significant difference between the two groups.

Conclusions: Although the absence of difference in Left ventricular dysynchrony between the two pacing sites at baseline and six months later, the septal stimulation seems to be associated to a better global LV function. Thus, we recommend this site of stimulation as an alternative to the classic apical stimulation.

PS450 | BEDSIDE

Bachmann’s bundle pacing improves left ventricle filling and reduces the need for ventricular pacing

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Background: Patients treated for sick sinus syndrome may have interatrial conduction disorder. Moreover, up to 20% of them have atrioventricular conduction disorder which worsens over time and is responsible for the need of ventricular pacing. Both pathologies can lead to atrial and atrioventricular dysynchrony and diminish mitral diastolic flow. Implantation of atrial lead in right atrium appendage (RAA) furthermore contribute to hemodynamic impairment even in patients without conduction disorders.

Purpose: The aim of this study was to assess influence of atrial pacing site on left ventricle diastolic filling and atrioventricular conduction and the percentage of ventricular pacing in population with SSS implanted with DDD pacemaker.

Method: The study consisted of 86 patients (54 F, 32 M) aged 72.3 ± 16.4 years. Patients were divided in two groups: group I (n=41) with RAA pacing, group II (n=45) with Bachmann’s area pacing. Differences in interatrial and atrioventricular conduction in sinus rhythm and AAI 60 pacing were assessed. Also P wave width at sinus rhythm and during atrial pacing as well as percentage of ventricular stimulation were compared. AED was set at 200 ± 180 ms (pacing/sensing). Two-dimensional and Doppler echocardiography was performed using a standard echocardiographic system. Total LV filling time was determined as the time interval from the onset of the mitral diastolic flow – E wave to the offset to the offset of A wave. Mitral velocity flow integral (VTI MR) was assessed.

Results: There were no differences in baseline P wave duration in sinus rhythm between the groups (98.6 ± 15 ms vs 102.2 ± 21 ms, p=n.s.). Atrial pacing 60 bpm revealed longer P wave duration with atrial lead location in RAA in comparison to Bachmann’s bundle region (143.2 ± 27.5 vs 106.1 ± 16.3 ms, p<0.01). The percentage of ventricular pacing was higher in group II (22.0 vs 4.5%, p<0.01). Total LV filling time was shorter in RAA lead location (460 ± 48 vs 550 ± 55 ms, p<0.05) which corresponded with smaller VTI MR (16.4 ± 3.2 vs 20.6 ± 4.1 cm, p<0.05).

Conclusions: 1. RAA pacing decreases mitral diastolic flow worsening left ventri-

cular diastolic dysfunction. 2. The Bachmann’s bundle region pacing of right atrium results in better left ventricle filling pattern. 3. Right atrium appendage pacing in SSS pts promotes atrioventricular conduction disorder which results in higher percentage of ventricular pacing in DDD mode.

PS541 | PARADISE

Paradoxic undersensing of atrial electrograms during atrial fibrillation in patients with implanted dual chamber pacemakers: a clinical and in vitro study


Purpose: Paradoxic atrial undersensing (PAUS), which is an undersensing at a high atrial sensitivity and with the return of normal sensing at a lower sensitivity during atrial fibrillation (AF), may be caused by repeated activation of the quiet atrium during AF, may be caused by repeated activation of the quiet atrium during AF.

Methods: The study group consisted of 86 patients (54 F, 32 M) aged 72.3 ± 16.4 years. Patients were divided in two groups: group I (n=41) with RAA pacing, group II (n=45) with Bachmann’s area pacing. Differences in interatrial and atrioventricular conduction in sinus rhythm and AAI 60 pacing were assessed. Also P wave width at sinus rhythm and during atrial pacing as well as percentage of ventricular stimulation were compared. AED was set at 200 ± 180 ms (pacing/sensing).

Results: There were no differences in baseline P wave duration in sinus rhythm between the groups (98.6 ± 15 ms vs 102.2 ± 21 ms, p=n.s.). Atrial pacing 60 bpm revealed longer P wave duration with atrial lead location in RAA in comparison to Bachmann’s bundle region (143.2 ± 27.5 vs 106.1 ± 16.3 ms, p<0.01). The percentage of ventricular pacing was higher in group II (22.0 vs 4.5%, p<0.01). Total LV filling time was shorter in RAA lead location (460 ± 48 vs 550 ± 55 ms, p<0.05) which corresponded with smaller VTI MR (16.4 ± 3.2 vs 20.6 ± 4.1 cm, p<0.05).

Conclusions: 1. RAA pacing decreases mitral diastolic flow worsening left ventri-

cular diastolic dysfunction. 2. The Bachmann’s bundle region pacing of right atrium results in better left ventricle filling pattern. 3. Right atrium appendage pacing in SSS pts promotes atrioventricular conduction disorder which results in higher percentage of ventricular pacing in DDD mode.

FS542 | BEDSIDE

Right ventricular lead placement in a pacemaker population: comparison of apical and septal position. The right pase study

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Aim: Chronic right ventricular (RV) pacing induces mechanical left ventricular (LV) dysynchrony and may decrease systolic function in subjects with normal LV ejection fraction. Many patients may develop heart failure at long-term follow-up. It was hypothesized that pacing at a septal RV site could induce less variation in timing of RV pacing and therefore lead to a more regular RV filling pattern. The aim of this study was to assess the influence of atrial pacing site on LV filling pattern and atrioventricular conduction.

Methods: The RIGHT PACE study is a multi-center, prospective, single-blind trial comparing pacing from the RV apex and the RV septal area. Patients with idiopathic dilated cardiomyopathy and no indication for implantable defibrillator and/or resynchronization therapy were enrolled in 14 centers. The primary objective was to acutely evaluate the pacing-induced LV dysynchrony, calculated as the delay between septal and lateral wall contraction (SLD), as recorded by means of the multi-Doppler echocardiography.

Results: A total of 438 patients were enrolled (male 61%, age 75±10 years). 268 patients received an RV lead in the apex and 170 in the septal area (high-septum 10, mid-septum 110, low-septum 35). The two groups were similar in terms of ejection fraction (58±9% versus 56±9%), prevalence of coronary artery disease (25% versus 29%), indication for pacing for atrioventricular block (59% versus 63%), QRS duration (89±1 ms versus 92±1 ms). During spontaneous LV activation, SLD was comparable between groups (47±28 ms versus 52±28 ms) and the proportions of patients with spontaneous LV dysynchrony (i.e. SLD >41 ms) were 46% and 44%, respectively. During RV pacing, SLD increased to 57±28 ms in Apex group and 61±30 ms in Septal group (p=0.333). The proportions of patients with pacing-induced LV dysynchrony were 62% and 60% (p=0.833). Nonethe-

less, the QRS increased by 45±29 ms versus 36±27 ms in Apex and Septal group, respectively (p=0.017).

Conclusions: Although pacing at the RV septal area resulted in less marked QRS lengthening than pacing at the RV apex, it did not reduce the pacing-induced LV dysynchrony. However, the comparison of long-term results will elucidate whether septal pacing is associated with better patient outcome.

PS543 | BEDSIDE

Long term follow-up of atrioventricular conduction with the safeR mode in pacemaker implanted patients

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Introduction: Nearly half of the pacemaker population is implanted following a diagnosis of atrio-ventricular disorder (AVD). These patients are usually implanted with a dual chamber pacemaker programmed with spontaneous conduction saving algorithms that have been shown to reduce unnecessary ventricular pacing and thus better follow AVD progression. The SafeR mode allows AAI mode functioning with a short atrio-ventricular delay (AVD) when the T-wave is correctly sensed. Also it allows detailed AV conduction status recordings. The ETOVAC study aimed to prospectively study the evolution of AVD patients programmed in Safe R mode.

Methods: Out of the 91 patients included (73±12 y; 67% men), 82 patients were followed for 65±40 months (9 premature loss of follow-up after documented paroxysmal AVB III (n=13) or syncpe with concomitant long His-Ventricular conduction disorders (additional disorders: LBBB n=29, bifascicular block n=23, none n=17). SafeR recordings were evaluated every 6 months up to 3 years. Patients were stratified depending on the severity of their AV conduction disorders, defined by the duration of switches to DDD mode recorded in the device memory. A logistic multivariate model was applied to identify predictive factors for AVB severity.

Results: After a mean follow-up of 3 years:...
40% of patients developed permanent AVB (defined as 1 month duration of switch in DDD), 87% the switch occurred within 6 months post implant. 23% of patients developed paroxysmal AVB episodes, but ventricular spontaneous conduction was maintained throughout the follow-up in this sub-group of patients. 37% of patients did not experience any AVB.

The multivariate model showed that 2 factors were significant predictors of AVB severity: evidence of paroxysmal AVB III before implantation and recurrent syncope at implant predicted permanent AVB (p=0.04 and p=0.02, respectively).

**Conclusions:** The EVOCAV study showed that 37% of PM patients implanted for atrio-ventricular disorders remained free from recurrence up to 3 years. Documented AVB and multiple syncopeces before implantation appeared as major predictors for recurrence. Utilization of the SafeIR mode and memories might bring more knowledge around the evolution of this pathology and leverage the implant indication.

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**P544 | BEDSIDE**

Real necessity of magnetic resonance imaging examinations after permanent pacemaker implantation

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**Background:** The usage of magnetic resonance imaging (MRI) is restricted for patients with a permanent pacemaker. While several manufacturers have launched MRI-conditional pacemakers, no data is available for the real necessity of MRI after pacemaker implantation. The aim of this study was to investigate the prevalence of the MRI-required events after pacemaker implantation.

**Methods and results:** Permanent pacemaker implantation was performed in 254 patients between January 2000 and September 2012. All patients received regular follow-up at the outpatient clinic of the Social Insurance of our hospital. We excluded one patient for moving, and 3 for non-cardiac death from the original population. Ultimately, we analyzed 250 patients (98.4%) in this study. The patients were divided into two groups (an event group and a non-event group) depending on the MRI-required event.

The MRI-required events were cumulatively observed in 42 (16.8%) patients during the mean observational period of 38.1 months (5.3%)/year. Intracranial disease was found in 18 (43%) patients, heart disease in 5 (12%) patients, upper canal disease in 6 (12%), lower canal disease in 12 (29%), and pelvic area disease in 1 (2%). There were no differences in patient's characteristics between the two groups. Multivariable logistic analysis showed that no specific factor was associated with the MRI-required event.

**Conclusions:** The MRI-required event cumulatively increases at the rate of 5.3% per year after permanent pacemaker implantation. No specific predictive factor was found for the future MRI-examination necessity. Our results suggest that MRI-conditional pacemaker should be considered for all patients, especially with a long life expectancy.

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**P545 | BENCH**

Alterations in the expression of genes related to contractile function and hypertrophy of the left ventricle in chronically paced patients from the right ventricular apex

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**Purpose:** The purpose of this study is to assess in the peripheral blood alterations of the expression of genes related to contractile function and hypertrophy of the left ventricle, after right ventricular apical pacing in patients with preserved left ventricular systolic function.

**Methods:** In this study, we enrolled patients who underwent pacemaker implantation due to bradyarrhythmic indications and divided them into two categories. Group A consisted of individuals paced due to atrioventricular conduction disturbances and ventricular pacing exceeded 90%, while group B who suffered sinus node dysfunction, had preserved intrinsic atrioventricular conduction. At the time of implantation, 3 and 12 months later, we evaluated in the peripher-

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**P547 | BENCH**

Positive haemodynamic response to cardiac resynchronisation therapy in right bundle-branch block requires coexisting left ventricular activation delay

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**Purpose:** To evaluate the suitability of cardiac resynchronisation therapy (CRT) for treatment of right bundle-branch block (RBBB) compared to left bundle-branch block (LBBB).

**Methods:** The CirAdapt model of the human heart and circulation was used to simulate cardiac function of a heart failure patient with synchronous ventricular activation. Ventricular contractility was decreased so that left ventricular (LV) ejection fraction was 30% and end-diastolic pressure 24 mmHg. Starting from this reference simulation, different degrees of LBBB and RBBB were simulated by introducing septal-to-LV lateral wall activation delays (ranging from 0-180 ms) and septal-to-RV lateral wall activation delays (ranging from 0-156 ms), respectively. Each combination of RV and LV activation delay in these ranges was simulated. CRT was applied to each of these models of baseline electrical dyssynchrony by simulating conventional biventricular pacing. Haemodynamic response to CRT was defined as the increase in stroke volume relative to baseline value.

**Results:** CRT did not improve or even caused deterioration of haemodynamic function in the simulations of RBBB with little or no coexisting LV electrical activation delay (see figure). Clinically relevant response to CRT only occurred when a sufficiently large LV electrical activation delay was also present.

**Conclusions:** Simulations indicate that “pure” RBBB without LV electrical activation delay is not a substrate amenable to conventional CRT, however, the efficacy of CRT in patients with atypical RBBB (with a coexisting LV electrical substrate) should be investigated in future clinical studies.

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**P548 | BEDSIDE**

Difference between native and right-ventricular-paced QRS duration predicts QRS shortening by cardiac resynchronization therapy: a novel marker of true complete left bundle branch block

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**Purpose:** True complete left bundle branch block (cLBBB) predicts greater response to cardiac resynchronization therapy (CRT). Right-ventricular (RV) mid-septum pacing approximates a true cLBBB QRS complex morphology. We inves-
tigated whether the difference between native and right-ventricular-paced QRS duration \((QRS_d)\) predicts QRSd shortening by CRT.

**Methods:** We prospectively collected ECGs and EGMs in 110 consecutive patients (aged 66.9 years; 72% males; 59% non-ischemic cardiomyopathy; LVEF 26±5%) with native non-RBBB QRS morphology undergoing CRT implant. Recordings of spontaneous rhythm, RV and CRT pacing were carefully edited, signal-averaged and manually measured by electronic calipers.

**Results:** Native QRS width was 181±21 ms. Left ventricular \((LV)\) pacing lead was implanted at the position with Q-LV \((QRS_d)\) ratio of 0.73±0.11. QRSd was prolonged by 27±25 ms during RV pacing \((delta-QRS-RVP)\) and shortened by 15±26 ms during CRT pacing \((delta-QRS-CRT)\). Delta-QRS-CRT correlated with delta-QRS-RVP \(r=0.71\), Figure, with native QRSd \(r=0.65\), and with Q-LV ratio \(r=-0.43\); all \(p<0.0001\). In multivariate analysis, delta-QRS-CRT was most strongly associated with delta-QRS-RVP \(r=-0.33, p=0.00001\), followed by native QRSd \(r^2=0.27, p=0.00001\), and Q-LV ratio \(r^2=0.15, p=0.02\).

**Conclusions:** The QRSd prolongation by RV midseptum pacing is a surrogate of recordings of dyssynchrony. The difference between native and RV-paced QRSd is the strongest predictor of CRT-induced QRSd change independent of native QRSd. Whether this is also independent of pre-implant surface ECG markers of true CLBBB remains to be investigated.

**P549 | BEDSIDE**

**Prediction of ICD-therapies by 12-lead ECG in primary prophylactic CRT-D: observations in 434 patients during 10 years**

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**Purpose:** Indications for a primary prophylactic ICD and for CRT are generally based on severe LV-dysfunction. A considerable number of pts with ICD or CRT-D will never profit from ICD-therapy but experience complications. A parameter independent from LVEF to predict which patient will retrieve adequate ICD-therapy is needed. The modified Selvester-ECG-score \((MSES)\) correlates with the LV scar burden. In a retrospective analysis of SCD-HeFT it has shown a value in describing pts at high vs low risk for ICD-therapy. Another retrospective study revealed that benefit of CRT was more likely in pts with lower MSES. Combining these findings with the fact of less necessary ICD-therapy in pts with good response to CRT makes the MSES a promising parameter to predict ICD-therapies in CRT-D pts.

**Methods:** We studied 434 pts who underwent CRT-D implantation at our institution between 2000-2010. Pts with secondary prophylactic indication for ICD \((n=61)\), upgrade from existing devices \((n=95)\) and regular follow-up in other institutions \((n=132)\) were excluded. Of the 146 pts left following characteristics among others were investigated: modified Selvester-ECG-score \((MSES)\), QRS-duration, bundle branch block/LV/hypertrophy (defined by the method of MSES), LVEF, ischemic vs dilatative cardiomyopathy, occurrence of time from implantation to first ICD-therapy or to last follow up.

**Results:** Median follow-up time was 605.5 days \((range 191-1420\) d.). 24% suffered adequate ICD-therapy. Pts with adequate ICD-therapy had significant lower event-free rate \((HR=2.0, 95\% CI=1.02-7.1, p=0.001)\). Furthermore, sudden cardiac death \((SCD)\) or ventricular arrhythmic events occurred more frequently in patients with an IQRSCRT \((p<0.05)\) than in those without \((p=0.001)\). In a wide QRS complex including bundle branch block or paced QRS, 2 notches in the R or S wave. The primary endpoint was a composite of the death and hospitalization due to heart failure or arrhythmias.

**Results:** An IQRS was found in 59 patients \((52\%)\) before the CRT \((IQSRCRT)\). Those with an IQRS\([preCRT]\) had a longer QRS-duration than those without \((178 vs 158\) ms; \(p<0.01\)). However, an IQRS\([preCRT]\) was not associated with the 18 month follow-up clinical outcome after CRT. An IQRS was also found in 36 patients \((32\%)\) during biventricular pacing after CRT \((IQSRCRT+CTR)\). The diagnostically lower in patients with an IQRS\([postCRT]\) vs \(11\%\) \((31\%)\) than in those without \((46\%\); 60%; log rank test: \(p=0.05\), See the figure). A Cox regression analysis revealed that IQRS\([postCRT]\) was an independent predictor of an unfavorable outcome \((HR=3.1; 95\% CI=1.3-7.6, p=0.05)\) as well as the baseline NYHA class \([HR=3.8; 95\% CI=2.0-7.1, p<0.001]\). Furthermore, the role of ECG parameters in the resynchronization therapy of heart failure patients

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Cardiac resynchronization therapy \((CRT)\) improves the mortality of heart failure, however not all patients do respond adequately. We aimed to investigate the possibility to predict this response and the 2-year survival of patients by means of ECG analysis.

We examined the 12-lead ECG records of 137 heart failure patients \((43\%\) non-responders, \(49\%\) responders) prospectively with a digital caliper before CRT and \(3\) months later \((109\) ± 4 ms, \(p=0.01\)). However, an fQRS\([preCRT]\) was not associated \((HR=1.15-7.69)\). The mortality was higher when the QRS was wider than 112 ms \((HR=1.03-4.33)\). Longer than 286 ms JT at 1 month was associated with an increased mortality \((HR=0.02, 2.68, 95\% CI of HR=1.15-7.69)\). The mortality was higher when the QRS was wider than 112 ms 6 months after CRT implantation \((HR=0.02, HR=3.82, 95\% CI of HR=1.17-11.49)\).
In conclusion, CRT normalized QRS size and QT time after 6 months, but influenced less Jt time. Based on our approach, basic ECG parameters were able to predict the mortality of heart failure patients with CRT as well as their response to the treatment.

P552 | BEDSIDE
Importance of dobutamine dose during stress echocardiography to assess left ventricular contractile reserve for cardiac resynchronization therapy

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Background: The presence of myocardial contractile reserve (CR) determined by dobutamine stress echocardiography (DSE) predicts response to cardiac resynchronisation therapy (CRT). Using lower doses of dobutamine during DSE would have been inadequate to elicit a full contractile response in patient with heart failure, who have downregulation of β1-adrenoreceptor. Nevertheless, incremental doses of dobutamine may lead to worsening of myocardial contractility (biphasic response due to ischaemia). We assumed that CR assessed by high-dose DSE compared to low-dose DSE is better predictor of response to CRT.

Methods: 51 consecutive symptomatic patients (62±11 years) with heart failure (EF 26.4±7.0%), which coronary anatomy were not suitable for revascularization, underwent DSE before CRT implantation. The difference in ejection fraction at rest and during low-dose (20 μg/kg/min) and high-dose (40 μg/kg/min) DSE declared global myocardial contractile reserve. Responders to CRT were defined as a decrease in left ventricular end-systolic volume ≥15% and/or increase in EF ≥5% after 6 months of CRT.

Results: Responders (27 patients, 53%) showed higher global myocardial contractile reserve compared to non-responders during low-dose DSE (8.3±9.5% vs. Δ 2.8% ± 6.8%, p=0.0299) and during high-dose DSE (9.6% ± 8.9% vs. Δ 2.9% ± 7.7%, p=0.0046), respectively. ROC analysis confirmed statistically non-significant difference between using low and high-dose DSE to predict response to resynchronisation therapy (AUC 0.69±0.08 vs. 0.75±0.07, p=0.4041).

Conclusion: Global myocardial contractile reserve determined by high-dose DSE showed no additional benefit to predict CRT response compared to low-dose DSE.

P553 | BEDSIDE
New contraction heterogeneity detected by cross correlation tissue doppler imaging after cardiac resynchronization therapy is a marker for ventricular arrhythmias

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Purpose: Though cardiac resynchronization therapy (CRT) often results in beneficial effects to patients with severe heart failure, its effect on ventricular arrhythmias (VA) is controversial. Our objective was to test the hypothesis that VA is associated with changes in left ventricular (LV) mechanical heterogeneity by cross correlation (CC) of tissue Doppler (TDI) longitudinal acceleration before and after CRT implantation.

Method: We studied 165 CRT patients with QRS ≥120 ms, NYHA II-IV, EF ≤35% with TDI at baseline and 6 months follow-up. CC analysis was performed on the basal LV segments of opposing walls using myocardial acceleration derived from TDI from 3 apical views. A cutoff of 35 ms was predefined as CC positive. Out-with TDI at baseline and 6 months follow-up. CC analysis was performed on the

Results: Nine patients (9.6%) met the primary endpoint at 6 months and 22 patients (23.6%) at 2 years. Fifty-seven (61.2%) patients were considered responders to CRT. Baseline LV global longitudinal strain (Gls) was deteriorated in both early and 2 years mortality (-10.4±5.3% vs. -6.6±4.2%, p=0.013; 11.0±5.2% vs. -7.0±4.3%, p=0.0003). In multivariate Cox regression analysis after adjustment of relevant clinical covariates LV Gls lower than the median (-10%) remained an independent predictor of both short- and long-term mortality (HR: 13.2; CI: 1.72 – 101.89, p=0.013 and HR: 4.7; CI: 1.63 - 13.8, P=0.004 respectively). The Kaplan-Meyer curve of survival with LV Gls median diverged early during follow up and continued to diverge over time (log-rank, p=0.001).

Conclusion: Our findings indicate, that baseline LV dysfunction is associated with poor short- and long-term outcome after CRT implantation.

P555 | BEDSIDE
The presence of a left bundle branch block contraction pattern evaluated by 2D strain is closely associated with long-term survival after cardiac resynchronization therapy

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Purpose: The value of echocardiographic dyssynchrony in prediction of response to Cardiac Resynchronization Therapy (CRT) is unclear with current guidelines...
favouring left bundle branch block (LBBB) >150ms by ECG alone. However, specifically identifying mechanical LBBB contraction patterns of opposite wall motion may provide additional clinical information. We hypothesized that the presence of a LBBB-related contraction pattern by strain imaging is associated with favourable long-term outcome in CRT-patients.

Methods: We studied 159 patients from two centers (NYHA II-IV, EF<35, and QRS>120ms) with LBBB prior to CRT. Longitudinal 2D-strain analysis was performed in the apical 4 chamber view. A LBBB-related contraction pattern was defined by the presence of 3 criteria: 1) early pre-stretch in the lateral wall, 2) early termination of septal contraction, within 70% of ejection phase, 3) late peak contraction in the lateral wall. Outcome was pre-defined as freedom from death, LVAD or heart transplantation over 4 years.

Results: Of 159 patients, 101 had a classic LBBB contraction pattern defined by QRS duration information and 58 patients had no pattern. The event rate was 10.9% (11/101) in the presence of a pattern prior to CRT vs. 34.4% (20/58) if the pattern was absent: Hazard Ratio (HR) 0.3, 95% Confidence Interval (CI) 0.14-0.60 (P=0.001). Patients with patterns had a more favourable event-free survival regardless of QRS-duration. For QRS >150 ms; HR 0.27, CI 0.09-0.81 (P=0.004). For QRS >150 ms; HR 0.28, CI 0.1-0.81 (P=0.03).

Conclusion: The presence of a LBBB- contraction pattern by 2D strain before CRT is highly associated with favourable long-term survival in patients with LBBB by ECG, independent of QRS-duration, and has additive prognostic value to the ECG criteria alone.

P556 | BEDSIDE
Left ventricular contractile reserve and septal flash presence in prediction of response to CRT: the multicentre ViaCRT study - 1-year follow-up


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Purpose: The multicentre Viability in Cardiac Resynchronization Therapy (ViacCRT) trial was designed to investigate impact of myocardial viability on CRT efficacy. Aim of the study was to determine role of “septal flash” presence and myocardial contractile reserve determined in Low Dose Dobutamine Stress Echo (LDSE) in prediction of response to CRT.

Methods: We assessed 133 subjects (102 males, aged 63±10 years) with HFREF of ischemic (51%) and non-ischemic (49%) etiology, who met clinical criteria for CRT. Baseline echo and LDSE was performed prior to CRT implantation. Contractile reserve was expressed as number of segments with improved contractility on LDSE. Baseline and one-year follow-up data were analyzed. Response to CRT was defined as decrease of ≥1 NYHA class (clinical response) or ≥15% decrease of LVEDV (echocardiographic response).

Results: In logistic regression analysis only number of viable segments in LDSE was a predictor of echocardiographic response (OR 1.2/segment, 95% CI 0.92-1.2, p=0.05). ROC curve indicated 7 viable segments to be a cutoff point. Viability defined as ≥7+ viable segments was a predictor of echocardiographic response with OR 3.55 (95% CI 1.11-11.0, p=0.03). Subjects with septal flash showed significant improvement in LVEF and LVEDV, but in logistic regression analysis septal flash was not significant predictor of echocardiographic response. Neither contractile reserve nor septal flash were significant predictors of clinical response to CRT. Kaplan-Meier analysis revealed significantly better survival in patients with contractile reserve (figure); presence of septal flash did not affect survival.

Conclusion: LDSE is a useful parameter that helps to predict objective response to CRT and affects survival among HF patients treated with CRT.
Older patients had ischaemic cardiomyopathy, bypass grafting, past myocardial infarction and arterial hypertension more often than younger (p<0.05). The older group had worse renal function, lower haemoglobin and platelet count (p<0.05).

Patients of younger group were more likely to have larger hearts (left ventricular end-diastolic diameter 6.8±1.97 cm vs 6.2±0.8 cm, p=0.000; left ventricular end-systolic diameter 5.7±1.1 cm vs 5.0±1.0 cm, p=0.000) with worse left ventricular function (left ventricular ejection fraction 27.7±8.7% vs 30.6±9.9%, p=0.002) than older.

There was no difference between groups in hospitalisation duration after implantation (10.4±3 days vs 5.7±3.0 days, p=0.515). Complication rate did not differ between groups (in 15 younger patients (6.0%) vs 4 (2.8%), p=0.13). Older patients were re-hospitalized more during the first year after implantation (41/242 (28.3%) vs 40/145 (16.6%), p=0.006). Re-hospitalization rate during long-term follow-up (12 months) was 15.1% in younger group and 10.3% in younger patients (p=0.876).

Conclusions: CRT-P proved to be similarly effective in older people with HF in terms of all-cause mortality or admission due to HF worsening. Compared to younger patients with HF, older patients did not have higher incidence of adverse events and complications after CRT-P system implantation procedure.

P560 | BEDSIDE
The incidence and clinical significance of de novo cardiac resynchronization therapy recipients
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Purpose: The aim of the study was to assess the incidence and clinical significance of depression that developed after initiation of cardiac resynchronization therapy (CRT).

Methods: The prospective, single-center, interventional, non-randomized study encompassed 260 consecutive heart failure (HF) patients implanted with CRT-D. All patients completed the Beck Depression Inventory (BDI-II) and underwent a psychiatric examination at baseline. The assessment of psychiatric status was repeated at 3, 6, and 12 months after implantation. 131 (50.4%) patients free of depression symptoms at baseline were included further analysis. Data on long-term follow-up (12 months) were screened to identify patients who developed a composite endpoint of death or hospitalization for HF.

Results: The depression was diagnosed in 24 (18.3%) subjects after 3 months of CRT, while mean BDI-II scores increased significantly in the whole group within this period (7.87±3.46 vs. 5.74±2.44, P<0.001). Patients who developed depression (Depression Group) had a significantly higher risk for a composite endpoint than those free of this disorder (Control Group): 33.3% vs 10.4% pre-CRT, 16.9% vs. 9.1% at 12 months post-CRT (P<0.001). A total of 36 of 100 patients (36%) in the Depression Group had worse renal function, lower haemoglobin and platelet count (p<0.0001), and PR interval from 202.9 ms to 133.45 ms (p<0.001). The EF goes from 27.7±10.44% pre-implantation to 35.77±9.72% post implantation (p<0.0001). 29 deaths had occurred (35.36%), all in patients with CRT-P. 25 (86.2%) were from cardiac deaths and 13 (52%) were sudden. There were no episodes of sudden death in the CRTD arm, many patients in this arm had appropriate therapies for ventricular arrhythmias.

Conclusions: There was no difference in patients with LBBB and RBBB+LAFB. position of the left ventricular lead and distance between left and right leads show significant difference in the acute response to the therapy. CRT proved to be useful in treatment of refractory HF of CD. Considering the high mortality for sudden cardiac death, even in the group of good responders with CRT-P, we should always consider the indication of CRT-D for those pts.

P562 | BEDSIDE
Cardiac resynchronization therapy is associated with better long-term outcome in females, even in non-ischemic cardiomyopathy
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Background: Previous studies indicated that females have better echocardiographic improvement and short-term clinical outcome with an implanted cardiac resynchronization therapy (CRT) compared to males. However, data on long-term outcome with CRT by gender are scarce and it has been suggested that the incremental benefit is mainly driven by the differences in etiology of cardiomyopathy by gender.

Methods: We evaluated patients undergoing CRT implantation at a high-volume single center in Hungary. Data on all-cause mortality was assessed using clinic follow-up data and the Hungarian National Healthcare Fund Death Registry. Kaplan-Meier survival curves and multivariate Cox proportional hazards regression analysis were used to analyze mortality in CRT patients by gender and etiology of cardiomyopathy.

Results: From June 2000 to April 2011, 261 females (23%), and 857 males received a CRT. A total of 317 of 857 males (37%) died compared to 317 of 857 males (37%) (p<0.001). Females had a significant 45% lower risk of all-cause mortality (HR=0.55, 95% CI: 0.41-0.72, p<0.001) compared to males after adjustment for age, ischemic etiology, and diabetes at baseline. This association was consistent in non-ischemic etiology, females had 56% lower risk of all-cause mortality (HR=0.44, 95% CI: 0.31-0.63, p<0.001). A total of 36 of 187 (17%) females died with non-ischemic cardiomyopathy compared to 179 of 478 (37%) males (p<0.001) (Figure). Our results were similar after adjustment for QRS duration.

Conclusions: Among patients undergoing CRT implantation, females have significantly better long-term clinical outcome compared to males. This finding pertains to females with non-ischemic etiology of cardiomyopathy and across different QRS durations.

P563 | BEDSIDE
Chagas disease and resynchronization therapy, results of 5 years of follow up in 130 patients
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Resynchronization Therapy (CRT) has resulted an effective treatment for heart failure (HF) in pts, with LVD and ventricular dyssynchrony. In Chagas disease (CD) however only a few series cases has been published. We present a cohort of 130 patients (pts) of our experience with CRT in CD. From January 1992 to December 2013, 156 pts with CD and HF were submitted to CRT. Clinical records of 130 patients were analyzed retrospectively. males (57.3%) and females (42.6%) with age of mean 58.25 years. 27 pts (33%) were in NYHA class III, 5 pts (6%) in NYHA II and none in NYHA I. All pts had intraventricular conduction disturbances: 50 pts (60.9%) with Right Bundle Branch Block (RBBB) + Left Anterior Fascicular Block (LAFB) and 32 pts (39%) with Left Bundle Branch Block (LBBB). Mean width of QRS complex was 186.1±31.31 ms. The echocardiogram showed important systolic dysfunction in all pts with mean Ejection Fraction (EF) of 27.71±10.44%. All 82 pts were submitted to CRT, 69 pts (84.14%) received a CRT pacemaker (CRT-P) and 13 pts (15%) a CRT defibrillator (CRT-D). The statistical analysis of data was performed using the program SPSS Statistics v. 20.0. In mean follow-up of 24.5±39.7 months we observed clinical benefits in 80% of pts. 19 pts (23%) were in NYHA class I, 47 pts (57%) in NYHA class II, and 16 (20%) remained in NYHA class III or IV (p<0.0001), we found a significant reduction of the mean width of QRS complex after CRT (110.65±9.72 ms, p<0.0001), and PR interval from 202.9 ms to 133.45 ms (p<0.0001), and number of hospitalizations from 2.84 to 0.89 post intervention (p<0.001). A also significant reduction in the average doses of diuretics (from 60mg before to 35mg after surgery, p<0.001) and an increase in the average doses of Beta Blockers (from 22.2 mg to 35 mg after surgery, p<0.0001). The EF went from 27.71±10.44% pre-implantation to 35.77±9.72% post (p<0.0001). 29 deaths had occurred (35.36%), in all patients with CRT-P. 25 (86.2%) were from cardiac deaths and 13 (52%) were sudden. There were no episodes of sudden death in the CRTD arm, many patients in this arm had appropriate therapies for ventricular arrhythmias.

Conclusions: Determinants and impact of new persistent atrial fibrillation on long-term outcome in patients receiving cardiac resynchronization therapy
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Purpose: Cardiac resynchronization therapy (CRT) has favorable effects on prognosis in heart failure patients. We aimed to investigate the determinants and im-
Cardiac resynchronisation therapy across different patient profiles: who benefits?

P565 | BEDSIDE
Hospitalization rates and associated cost analysis of quadripolar versus Bipolar CRT-D: comparative effectiveness analysis from a single-center prospective Italian registry

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This analysis compares the post-implant hospitalization rates and costs of CRT-D with quadripolar (QUAD) versus non-quadripolar (BIP) left ventricular (LV) leads.

Methods: Consecutive patients receiving de novo CRT-D implants with either a QUAD (Quadrifascicular [n=116]) or a BIP (n=77) LV lead were enrolled at implant and followed until June 2013 at a single institution in Rome, Italy. LV lead re-visions/replacement and heart failure (HF)-related hospitalizations (hosps) were identified using ICD-9-CM diagnoses and procedure codes. National reimbursement rates were determined. Propensity scores were estimated using a logistic regression model based upon 11 pre-implant baseline characteristics and was used to derive a 1:1 matched cohort of QUAD and BIP patients. Hosp rates and associated payer costs for the two groups were compared using non-parametric bootstrapping (x10,000) and one sided hypothesis test (α=0.05).

Results: Baseline characteristics of the matched groups (n=77 QUAD and n=77 BIP) were similar. In-patient hosp rates of the QUAD group (0.13/pt-year) were lower than those of the BIP group (0.25/pt-year). The average reduction in hospitalization rates were determined. Propensity scores were estimated using a logistic regression model based upon 11 pre-implant baseline characteristics and was used to derive a 1:1 matched cohort of QUAD and BIP patients. Hosp rates and associated payer costs for the two groups were compared using non-parametric bootstrapping (x10,000) and one sided hypothesis test (α=0.05).

Conclusions: In a comparative effectiveness assessment of well-matched groups of CRT-D patients with bipolar and quadripolar LV leads, this analysis suggests that QUAD patients experience a lower rate of hospitalizations for LV lead procedures and HF. It also suggests that QUAD patients have lower healthcare resource utilization and lower cost. This has important implications for LV pacing lead choice.

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De-novo versus upgrade cardiac resynchronization therapy: results from a prospective observational study

S. Linzbach1, M. Mutallimov2, S. Deelawar2, M. Kalyani2, L. Ekosso Ejangue2, M. Mirzazadeh2, A. Steidl1, C. Israel2, S. Hohnloser1.

1 JW Goethe University, Department of Cardiology, Frankfurt am Main, Germany; 2Evangelical Hospital Bielefeld, Bielefeld, Germany

Background: Patients (pts) with de-novo implantation of a cardiac resynchronization therapy (CRT) device are reported to respond to this therapy clinically in approximately 60-70% of cases. There are indications to upgrade pts with a single- or dual-chamber device to CRT (i.e. high percentage of right ventricular pacing in heart failure pts). However, there is only sparse data regarding the outcomes of upgrade CRT in comparison to de-novo CRT

Methods: Prospective observational study. De-novo versus upgrade CRT: results from a prospective observational study. Comparison of hospitalization rates and costs of CRT-D with quadripolar versus non-quadropolar (BIP) left ventricular (LV) leads.

Results: Baseline characteristics of the matched groups were similar. In-patient hosp rates of the QUAD group (0.13/pt-year) were lower than those of the BIP group (0.25/pt-year). The average reduction in hospitalization rates were determined. Propensity scores were estimated using a logistic regression model based upon 11 pre-implant baseline characteristics and was used to derive a 1:1 matched cohort of QUAD and BIP patients. Hosp rates and associated payer costs for the two groups were compared using non-parametric bootstrapping (x10,000) and one sided hypothesis test (α=0.05).

Conclusions: In a comparative effectiveness assessment of well-matched groups of CRT-D patients with bipolar and quadripolar LV leads, this analysis suggests that QUAD patients experience a lower rate of hospitalizations for LV lead procedures and HF. It also suggests that QUAD patients have lower healthcare resource utilization and lower cost. This has important implications for LV pacing lead choice.

Baseline demographics: Total (n=529) Day-case (n=180) Planned overnight (n=349) P value

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Day-case</th>
<th>Planned overnight</th>
<th>p-value</th>
</tr>
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<tbody>
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<td>Age (months)</td>
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<td>72.65±10.14</td>
<td>72.65±10.14</td>
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</tr>
<tr>
<td>Male (n, %)</td>
<td>168 (73.4%)</td>
<td>134 (74.4%)</td>
<td>34 (69.4%)</td>
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</tr>
<tr>
<td>NYHA Class IV/V (n, %)</td>
<td>204 (89.1%)</td>
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<td>45 (91.8%)</td>
<td>0.48</td>
</tr>
<tr>
<td>GRS ≤150 msce (n, %)</td>
<td>168 (73.4%)</td>
<td>125 (69.4%)</td>
<td>43 (87.8%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Successful LV lead placement (n, %)</td>
<td>222 (96.9%)</td>
<td>173 (96%)</td>
<td>49 (100%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Total complications (n, %)</td>
<td>23 (10.0%)</td>
<td>17 (9.4%)</td>
<td>6 (12.3%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Immediate: (n, %)</td>
<td>7 (3.5%)</td>
<td>5 (2.7%)</td>
<td>2 (4.1%)</td>
<td>0.64</td>
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<td>LV lead displacement (n)</td>
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<td>LV Lead displacement (n)</td>
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<td>RA/RV Lead displacement (n)</td>
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Conclusions: Pts who were upgraded to CRT-D showed a similar response rate (approximately 60%) compared to de-novo pts. However, during follow up upgrade pts had a higher mortality probably reflecting a higher incidence of a prior history of VT/VF leading to secondary prevention indication for a defibrillator.

P565 | BEDSIDE
Daycase cardiac resynchronisation therapy implantation is safe and cost effective: experience from a UK tertiary centre

G.M. Atherton, C.J. McAlone, D.P. Heinig, B.M. Anderson, J.J. Barker, J. Gaywood, R.J. Browne, F. Osman. University Hospitals of Coventry and Warwickshire NHS Trust, Coventry, United Kingdom

Purpose: Cardiac resynchronisation therapy (CRT) improves outcome of selected patients with heart failure. Many centres perform elective CRT with planned overnight stay. We commenced day-case CRT in Oct09 and report our experience.

Method: Retrospective analysis of consecutive, elective CRT implants between

Baseline demographics: Total (n=529) Day-case (n=180) Planned overnight (n=349) P value

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Conclusions: In a comparative effectiveness assessment of well-matched groups of CRT-D patients with bipolar and quadripolar LV leads, this analysis suggests that QUAD patients experience a lower rate of hospitalizations for LV lead procedures and HF. It also suggests that QUAD patients have lower healthcare resource utilization and lower cost. This has important implications for LV pacing lead choice.
Cardiac resynchronisation therapy across different patient profiles / Haemodynamic aspects of cardiac resynchronisation therapy

Jan09-Apr13. Data collected on patient demographics, indications, procedural details and complications: immediate (±24hrs), short-term (±24hrs-4mths) and long-term (≥4mths). Outcomes were compared between day-case and planned overnight stay cohorts and a cost analysis was performed.

Results: 229 CRT procedures performed (180 day-cases). Baseline parameters and complications were not different between the 2 cohorts (table). There were 8 (4.4%) unplanned overnight stays in the day-case cohort (immediate complication or late finish). Overnight stay costs €350. We implanted 172 devices without overnight stay resulting in a €60,200 cost saving.

Conclusions: Day-case CRT is safe and cost-effective with significant benefits for patients and healthcare providers.

HAEMODYNAMIC ASPECTS OF CARDIAC RESYNCHRONISATION THERAPY

P568 | BEDSIDE

Hemodynamic optimization of transseptal LV endocardial pacing site during a definitive implantation of a CRT device: the long-term follow up

S. Amraoui, P. Bordachar, P. Ritter, S. Ploux, A. Zemmoura, M. Hocini, M. Haissaguerre, P. Jais. University Hospital of Bordeaux - Hospital Haut Leveque, Bordeaux-Pessac, France

Introduction: Transseptal endocardial (Endo) left ventricular (LV) lead implantation is a must for some patients as an alternative to conventional CRT. Recently, a subclavian approach became available. The long-term follow-up of transseptal Endo-LV lead implantation after hemodynamic optimization in CRT patients has not been described yet: we thus analyzed the clinical outcome of CRT patients after Endo-LV lead implantation guided by acute hemodynamic response (dP/dt max).

Methods: Under general anesthesia, heart failure patients meeting criteria for CRT and with failed CS implants or suboptimal CS anatomy, underwent permanent implantation of a transseptal Endo-LV lead through the subclavian vein: A-synch protocol. A guidewire containing a pressure sensor was inserted into the LV cavity along with the transseptal lead delivery system to record LV dP/dt max. A minimum of 2 Endo-LV positions was tested. The final Endo-LV lead position was fixed in the highest dP/dt max LV site (compared to baseline in AOO). All patients had a clinical follow up to evaluate CRT response at 1 year (>20% LV EF, class NYHA improvement ≥1, and no hospitalization for heart failure).

Results: 16 heart-failure patients (71±10 years, 2 women, LVEF 26±6%, NYHA 3±0, ORS duration>176±27ms) underwent successfully an Endo-LV lead implantation because of failed CS implant (N=5), suboptimal CS anatomy (N=10) or non-response to conventional CRT (N=1). For each patient, 3±1 Endo-LV sites were tested, with a mean ±dP/dt max improvement (over baseline) of 27±16% for the best Endo-LV site. The Endo-LV lead threshold was 1V±0.2±0.4mV. After 1 year follow up, 13/16 patients were responders (81%) with a mean LVEF of 40±11% (p=0.0002) and a mean class NYHA of 2±0.7 (p=8.10-07). Endo-LV threshold was 1V±0.2±0.4mV (p=0.1 compared to D1). Only 1 non-responder patient was hospitalized for acute cardiac insufficiency. There were no side effects during the follow up.

Conclusions: This first study demonstrates the potential advantages of Endo-LV lead implantation when guided by the best acute hemodynamic response in the different sites tested.

P569 | BEDSIDE

Does atrial high rate episode mean atrial fibrillation?

E. Jedrzejczyk-Patej, M. Mazurek, R. Lenarczyk, A. Liberska, J. Boidol, T. Podolecki, J. Kowalczyk, A. Sokal, O. Kowalski, Z. Kalarus. Medical University of Silesia, SCHD, Dpt of Cardiology, Congenital Heart Disease & Electrothoracic, Zabrze, Poland

 Aim: The aim of the study was to assess how many of the device-detected atrial high rate episodes (AhREs) were indeed atrial fibrillation (AF) and what were the reasons for inadequate detection of atrial arrhythmia.

Methods: The study population consisted of 304 consecutive patients (76.3% males; mean age of 62 years) who were implanted with cardiac resynchronization devices (CRT-D) and subsequently monitored on a daily basis via remote monitoring for the median follow-up (FU) of 30.5 months. Every recorded and transmitted AhRE episode was assessed on the basis of intracardiac electrogram (EGM) and none was classified (AF vs no AF) by two alternative cardiologists.

Results: AhRE episodes were detected in 57.9% (n=176) of patients during the whole FU. In 89.2% of them (n=157) these episodes were in fact AF, while in 10.8% (n=19) no AF has been confirmed in a detailed EGM analysis. The reasons for CRT-D inadequate AhRE detection were atrial far-fields signals in 89.5% and noise in atrial signal in 10.5%. The mean atrial burden (percent of day spent in AhR) was significantly more frequent in patients with real AF episodes in comparison to subjects with no AF (54.9%, range 0.03-100% vs 5.86%, 0.001-27% respectively; P<0.001). What is more, low CRT pacing episodes (defined as <5% CRT% within 24h) were also more often present in AF subjects than in patients with no real AF (82.8% vs 55%; P=0.003).

Conclusion: Nearly 2/3 of CRT-D patients have AHRE episodes detected by a device in the median follow-up (FU) of 30.5 months. Almost 90% of AHREs were in fact atrial fibrillation. Inadequate AHREs were caused by atrial far-fields sensed or noise. Both, high mean atrial burden and low CRT pacing do increase the likelihood of a real AF being a reason of AHREs.

P570 | BEDSIDE

Proarrhythmic effect of cardiac resynchronization therapy and transmural dispersion in patients with nonischemic heart failure

A. Suzuki1, T. Shiga1, K. Yoshida1, K. Ejima1, T. Suzuki1, T. Manaka1, M. Shoda1, K. Nakai2, H. Kasanuki1, N. Higawara1, T. Tokyo Women’s Medical University, Tokyo, Japan 2National Cardiovascular Center, Osaka, Japan

Purpose: The effectiveness of cardiac resynchronization therapy (CRT) in preventing sudden cardiac death is controversial in high-risk heart failure (HF) patients despite its hemodynamic benefit. Transmural dispersion of repolarization (TDR) with epicardial activation of left ventricular (LV) pacing may induce ventricular tachyarrhythmia. This study aimed to evaluate the effect of CRT on ventricular arrhythmia requiring implantable cardioverter-defibrillator (ICD) therapy and indexes of TDR on an electrocardiogram (ECG) in nonischemic HF patients receiving CRT with ICD (CRT-D).

Methods: This prospective study included 88 consecutive nonischemic HF patients (age: 59±14 years, 63 men) with a newly implanted CRT-D and an indication for primary prevention of sudden cardiac death, between 2007 and 2012. A 12-lead ECG and 18-channel repolarization interval-difference mapping ECG (187-ch RIDM-ECG) were recorded before, within 7 days and 6 months after the implantation. We measured Tpe interval and Tpe dispersion using a 12-lead ECG. The inter-lead difference between corrected Tpe intervals was measured using a 187-ch RIDM-ECG. The occurrences of ventricular tachyarrhythmia that required ICD therapy, including both shock and antitachycardia pacing, were examined. A responder was defined as having a >15% decrease in LV end-diastolic volume 6 months after CRT compared to baseline.

Results: During the 24-month follow-up period, 17 patients (19%) received appropriate ICD therapy. Among them, 35% had ventricular tachyarrhythmia within 1 month after device implantation. Patients with appropriate ICD therapy had a significantly higher Tpe dispersion on 12-lead ECG (80±31 vs 57±37ms, p<0.01) and inter-lead difference between Tpe intervals on 187-ch RIDM-ECG (54±26 vs 57±20ms, p<0.01) than those without therapy 7 days after implantation. However, during the 24-month follow-up, there was no significant difference in Tpe dispersion on 12-lead ECG (40±19 vs 40±23ms) or inter-lead difference between Tpe intervals on 187-ch RIDM-ECG (69±26 vs 58±23ms) between patients with and without appropriate ICD therapy. There was no difference in the incidence of ICD therapy or these indexes of TDR on ECG between responders and nonresponders.

Conclusion: Appropriate ICD therapy occurred in 19% of nonischemic HF patients 1 year after CRT-D implantation. Increased TDR may cause an increased incidence of ventricular arrhythmia in the early period after device implantation, but it may decrease during long-term CRT in non-ischemic HF patients.

P571 | BEDSIDE

Prognostic value of interventricular lead electrical delay in patients under cardiac resynchronization therapy


Purpose: Cardiac resynchronization therapy (CRT) is an established therapy for patients with moderate-to-severe left ventricular HF, low EF and wide QRS duration. Few studies have related the electrical delay between the RV and LV leads at implantation with the CRT response. The aim of the present study was to determine the prognostic value of RV-LV electrical delay in patients with CRT devices.

Methods: We performed a retrospective analysis of a prospective register of patients referred to CRT for standard indication, from 2007 to 2012. Clinical and echocardiography evaluation was performed prior to the implant and a minimum of 12 months of follow up. An increase of LVEF 15% or one NYHA functional class was used to define CRT responders. Implantation of transvenous CRT systems was performed according to standard techniques. The veins from the lateral wall were used as the first choice for LV lead placement. The inter-LV lead electrical delay was measured during spontaneous rhythm between the sensed markers recorded from the RV and LV leads using a device programmer.

Results: A total of 156 patients were evaluated (mean age 63±10, 75% males, 67.1% non ischaemic cardiomyopathy, mean QRS duration 171±27 ms, 10% ICD, 8% LV EF 23.7±6.3%, and mean RV EF 27.1±1.8%). During the follow up 30 patients died or were transplanted. The patients were analyzed according the RV-LV distance in two groups: Group 1 (n=84) <100 ms, and Group 2 (n=72) >100 ms. The characteristics of the patients are summarized in the Ta-
ble 1. Patients in the group 2 had a lower LVEF (24.59% ± 5.6 vs 27.02% ± 6.8, p value 0.016), wide QRS duration (177.1 ms ± 23.5 vs 162.5 ms ± 24.2, p value <0.001) and higher responder rate (76.4% vs. 57.1%, p value 0.017). Patients with higher RV-LV interlead distance had a significant lower rate of cardiovascular deaths ± cardiac transplants.

Conclusion: A higher RV-LV interlead electrical delay help us to identify patients with better prognosis after implantation of CRT.

P572 | BEDSIDE
Cardiac resynchronization therapy acutely improves heart-arterial coupling by reducing the arterial load. Assessment by pressure-volume loops
P. Pieragnoli1, G.B. Perego2, G. Ricciardi, S. Sacchi1, A. Michelucci1, S. Valsicchi1, L. Padovani1, 1University of Florence, Florence, Italy; 2Italian Institute for Austerity III/CCCS, Milan, Italy; 3Boston Scientific Italia, Rome, Italy

Introduction: Cardiac resynchronization therapy (CRT) was demonstrated to im-
prove LV-arterial coupling, by decreasing effective arterial elastance (Ea) at mid-
and long-term follow-up. No detailed invasive studies showing possible acute pe-
ripheral effects of CRT are not available.

Methods: We studied 37 patients scheduled for implantation of a CRT de-
vice based on conventional criteria. At implantation, LV pressure and volume data were determined via conductance catheter. Twelve patients with a stan-
dard indication for electrophysiologic study and preserved LV function were in-
cluded as control group. LV function was quantified by stroke volume (SV), end-
diastolic (EDV), end-systolic volume (ESV), end-systolic (ESP) and end-
diastolic pressure (EDP), and minimal and maximal rate of LV pressure change (dp/dtmax, dp/dtmin). Stroke work (SW) was calculated as the area of the pressure-volume loop, LV end-systolic elastance (Ees) as ESP/ESV, and Ea as ESP/SV. Ventricular-arterial coupling was quantified as Ees/Ea. Dyssyncrhony was quantified as the percentage of time that segmental LV conductance signals are opposite in phase with the global LV volume signal.

Results: In comparison with the control group, CRT candidates showed re-
duced systolic (SV, SW, dp/dtmax) and diastolic function (EDP, dp/dtmin). Ees was impaired (0.79 ± 0.33 versus 1.89 ± 0.93 mmHg/ml, p=0.002), with reduced Ees/Ea (0.36 ± 0.17 versus 1.38 ± 1.69, p=0.043). CRT immediately improved sys-
tolic function, increasing SW from 3.9 ± 1.8 to 6.9 ± 3.3 L'mmHg (p=0.001) and Ees to 1.0 ± 0.62 mmHg/ml (p=0.001). Ea decreased from 2.59 ± 1.35 to 1.68 ± 0.91 mmHg/ml (p<0.001), leading to an increase in Ees/Ea to 0.70 ± 0.38 (p<0.001). The increase in SW negatively correlated with the change in Ea (r=0.651, p=0.0001), while no correlations were detected with Ees (r=0.107, p=0.535) or with indices of systolic or diastolic dys synchrony.

Conclusion: Our data indicate that the reduction in arterial load occurs imme-
diately after CRT initiation. This peripheral effect of CRT results to be the major
factor in CRT patients with better prognosis after implantation of CRT.

P574 | BENCH
Cardiac resynchronization therapy in left bundle branch block improves right ventricular function
P. Storsten1, E.W. Remme2, E. Boët3, M. Eriksen4, E. Kongsgaard5, O.A. Smiseth6, H. Skulstad7, on behalf of Integrated cardiovascular function.
1 Institute for Surgical Research and Center for Cardiological Innovation, Oslo University Hospital, Oslo, Norway; 2K.G. Jebsen Cardiac Research Centre and Inst. for Surgical Research, Oslo University Hospital, Oslo, Norway; 3Institute for Surgical Research, Oslo University Hospital, Oslo, Norway; 4Dept. of Cardiology, Rikshospitalet, Oslo University Hospital, Oslo, Norway; 5Dept. of Cardiology and Inst. for Surgical Research, Rikshospitalet, Oslo University Hospital, Oslo, Norway

Purpose: Right ventricular (RV) function has been recognized as a predictor of clinical response to cardiac resynchronization therapy (CRT) during left bundle branch block (LBBB). In an experimental setting, we aimed to study the impact of CRT on RV function in LBBB.

Methods: In 6 anaesthetised dogs with LBBB induced by radio frequency abla-
ation, we applied CRT with one electrode on the right side of the interventricular septum and one epicardially on the LV lateral wall. RV pressure was measured by a micromanometer in the RV cavity and segmental length (SL) by sonomicrom-
etry in the RV free wall. The area of the RV pressure-SL loop was used as an index of regional work in the RV free wall. Pre-ejection RV shortening, measured at 50% increase of RV pressure, was calculated in percentage of peak systolic shortening.

Results: Induction of LBBB was associated with a reduction in RV free wall work from 41.3 ± 16.16 mmHg*mm (P<0.05). This was in part due to distortion of the pressure-SL loop with marked pre-ejection shortening (33 ± 14%) of to-
tal shortening. CRT increased segmental work to 41.3 ± 15 mmHg*mm, P<0.05 and RV dp/dt max increased from 361.7 ± 78 to 446.7 ± 76 mmHg/s (P<0.05). Neither maximum RV pressure (28 ± 3 vs. 27 ± 3 mmHg, NS) nor total shortening (8.3 ± 3 vs. 8.3% NS) was changed by CRT. However, the RV pre-ejection shortening de-
creased substantially to 13 ± 12% (P<0.05 vs. LBBB) of total shortening (figure).

Conclusions: During LBBB there is ineffective contraction in the RV free wall as approximately 1/3 of the contraction occurs during low pressure prior to ejection. The efficiency was improved by CRT, which markedly increased regional work in the RV free wall. The findings suggest that improvement in RV function may be important for success of CRT in LBBB.

P575 | BENCH
Left ventricular electrical delay predicts acute hemodynamic response to CRT patients
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Purpose: One of the causes of non-response to Cardiac Resynchronization Therapy (CRT) is sub-optimal position of the left ventricular (LV) lead. The electrical delay between the body surface Q wave and the local activation of candidate CRT on LV site during intrinsic rhythm (Q-LV) has been reported to be a prognostic parameter for the response to CRT. We evaluated the correlation between Q-LV and an index of LV contractility (LVdp/dt max) inotropicatively in order to optimize the LV pacing site.

Methods: Forty-one consecutive patients, 29 male, age 71±11 years, LVEF 30±7%, 23 with ischemic cardiomyopathy, QRS duration 181±25 ms, underwent CRT device implantation. Patients were instrumented with body surface ECG and a pressure sensor within their LV. The Q-LV interval and LVdp/dtmax were col-

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lected from multiple LV sites within multiple tributaries of the coronary sinus at baseline and during biventricular pacing.

Results: Overall, 2.9 ± 0.8 difference veins and 6.5 ± 1.2 pacing sites were tested. In 40/41 (97.6%) patients, the highest LVdP/dtmax coincided with the maximum Q-LV interval. Q-LV interval and the log rank test for survival analysis. We found that CRT did not influence this survival. Aspirin and statin therapy lowers the plasma level of fractalkine, which might be in relation with the improvement of endothelial dysfunction.
Results: Median age was 75.7 years (interquartile range 70.3 – 81.6), 49.4% were men. After PM implant, the proportion of SND patients experiencing >1 fall over 12 months was reduced from 54.0 to 20.7% (Odds ratio = 0.22; 95% confidence interval 0.11 to 0.45, p < 0.0001). The proportion of patients experiencing >1 fall with injury or requiring medical attention was also significantly reduced (OR = 0.36 (95%CI 0.15-0.83) and 0.37 (0.16-0.82), respectively). The annual total number of falls was significantly reduced by 62.6% (from 182 to 68, p < 0.0001) with reductions in the number of falls with injuries and requiring medical attention of similar magnitude (>6.5%, p < 0.001 and -72.9%, p < 0.0001, respectively). Before PM implant, 6 falls caused 7 fractures compared to no falls causing a fracture after PM implant.

Conclusion: In patients with SND, the implantation of a PM was associated with a statistically significant and clinically relevant decrease in the number and severity of falls.

P581 | BEDSIDE Procalcitonin in cardiovascular implantable electronic device infections

D. Sedehi, N. Siddiqi, N. Shrestha, S. Agarwall, K. Taraki, O. Wazni, V. Menon. Cleveland Clinic Foundation, Cardiovascular Medicine, Cleveland, United States of America

Purpose: Diagnosis of Cardiovascular Implantable Electronic Devices (CIED) infections can be challenging especially in the absence of definitive cultures. Currently, clinical signs along with culture results have been used as the standard diagnostic criteria. A novel biomarker, procalcitonin (PCT), has been utilized in sepsis to help guide antibiotic therapies, both before and even after antibiotic therapy has been instituted. The utility of PCT as an adjunct in the diagnosis and management of CIED infections has not been previously evaluated.

Methods: From April 2013 through November 2013, all patients admitted to our tertiary care center with suspected CIED infections had PCT levels measured upon admission. Pocket infections were defined as clinical presentation of erosion or wound dehiscence along with negative blood and lead cultures and a negative transesophageal echocardiogram (TEE). Systemic infections were defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three. A positive PCT level was defined as patients with positive blood cultures, positive cultures from the extracted lead, TEE positivity, or any combination of these three.

Results: Twenty-seven subjects with suspected CIED infection had a PCT assay on presentation. The average age was 71.6 years and 23 were male. Twenty-three subjects had at least one day of antibiotics prior to PCT level being drawn, with eleven subjects having over 10 days. The culprit organisms included: Coagulase negative Staph; 8; Methicillin Resistant Staph aureus; 6; Methicillin Sensitive Staph aureus; 6; Staph epidermitis; 2; Pseudomonas; 2; Peptostreptococcus: 1; Overall, systemic infection was identified in 24 subjects, whereas the infection was confined to the pocket in three. Of the pocket infection group, all had normal PCT levels. In the systemic infection group, six had abnormal PCT, and 18 had normal PCT. Eight patients with pocket erosion, negative blood cultures, but positive lead-tip cultures had a normal PCT. In contrast to published data with sepsis, there was no significant difference in subjects with pocket and systemic CIED infections were evaluated.

Conclusion: There was no significant difference in R wave amplitude and pacing threshold between Linox TD leads and Linox SD leads at both implantation and last follow-up. However, impedance at both implantation and last follow-up in Linox TD leads were significantly higher than those in Linox SD leads (986±197 ohm vs. 660±182 ohm at implantation, 784±544 ohm vs. 482±103 ohm at last follow-up). During mean follow-up periods of 44.1±16 months, we had 5 Linox TD leads failure (11.1%). In 4 of 5 Linox TD leads, impedance was gradually increasing beyond 1500 ohm and in the other Linox TD lead, impedance was suddenly increasing, which caused inappropriate ICD shock. During mean follow-up periods of 40.1±18 months, we had no Linox SD lead with high impedance beyond 1500 ohm (p<0.03, chi-square). In 5 failed Linox TD leads, mean periods from implantation to start of impedance increasing was 36.2±15.0 months. We were aware of high impedance by remote monitoring system in 3 Linox TD leads. We have not recognized lead dislodgement, decreased R wave amplitude, increased pacing threshold, oversensing and inappropriate ICD shock in 4 failed Linox TD leads, in which impedance was gradually increasing. We exchanged 4 of 5 failed Linox TD leads because of high impedance beyond normal range. We would not extract all 4 leads, but we recognized that distal conductor (cathode) was injured.

Conclusions: This is the first report that 11.1% of Linox TD leads failed in mid-term period. Although the obvious cause of impedance increasing was unknown, distal conductor (cathode) injury was suspected and we have to exchange early to prevent failure lead related adverse events.

P584 | BEDSIDE Remote monitoring follow-up of RIATA defibrillation leads under advisory: is it useful to identify defective leads?

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Introduction: Insulation defects with externalized conductors have been reported most frequent one but the diagnosis is also the most challenging one. The diagnosis is still a clinical decision, based on findings at the generator pocket site: basic inflammatory markers (e.g. WBC) are not elevated in this setting. However, the accurate diagnosis of pocket infections is of paramount importance on one hand to avoid delayed removal of infected systems and on the other hand to avoid unnecessary interventions of non-infected systems. Aim of the study was to identify biomarkers to ease the diagnosis of CIED pocket infections.

Methods: The study enrolled consecutively patients with a pocket infection at five European centres and excluded confounding condition such as antibiotic pre- treatment, malignancy, recent trauma or surgery. The diagnosis of a pocket infection was confirmed by surgical pocket exploration and growth of microorganism. Control patients (n=50) with no signs of infection at the time of pulse generator exchange or lead revision were recruited from the same centres. Pre-operative levels of 14 inflammatory biomarkers were compared between both groups.

Results: A total of 25 patients (70.1±13 years, 76% male, 60% pacemaker recipients) with isolated pocket infection occurring 22±30 months after the index operation were included. The control group of 50 patients did not differ significantly in their baseline characteristics. None of the participants with a pocket infection presented with a leukocytosis. Patients with an isolated pocket infection had statistically significantly higher serum levels of high-sensitivity CRP (p=0.019) and Procalcitonin (PCT (p=0.010) than control patients. Median PCT was 0.06ng/ml (IQR 0.03-0.07ng/ml) in the study group compared to 0.02ng/ml (IQR 0.02-0.04ng/ml) in the control group. The threshold between Linox TD leads and Linox SD leads at both implantation and last follow-up were 1500 ohm and in the other Linox TD lead, impedance was suddenly increasing, which caused inappropriate ICD shock. During mean follow-up periods of 40.1±18 months, we had no Linox SD lead with high impedance beyond 1500 ohm (p<0.03, chi-square). In 5 failed Linox TD leads, mean periods from implantation to start of impedance increasing was 36.2±15.0 months. We were aware of high impedance by remote monitoring system in 3 Linox TD leads. We have not recognized lead dislodgement, decreased R wave amplitude, increased pacing threshold, oversensing and inappropriate ICD shock in 4 failed Linox TD leads, in which impedance was gradually increasing. We exchanged 4 of 5 failed Linox TD leads because of high impedance beyond normal range. We would not extract all 4 leads, but we recognized that distal conductor (cathode) was injured.

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Remote monitoring follow-up of RIATA defibrillation leads under advisory: is it useful to identify defective leads?

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Introduction: Insulation defects with externalized conductors have been reported...
Conclusion: TLE in patients with large right heart vegetations is relatively efficacious and safety procedure. Procedural risk factors and technical problems were comparable in analyzed groups, exceptionally loops of the leads presence, probably connected with large RVH development and increased risk of procedure. The most difficulty is security before pulmonary embolism during procedure. The special nitrolin baskets are tested in this Center.

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Table

<table>
<thead>
<tr>
<th>Patients/procedures</th>
<th>Patients with large RVH (cm²)</th>
<th>Patients with smaller RVH (cm²)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>53</td>
<td>228</td>
<td></td>
</tr>
<tr>
<td>Age of pts (years)</td>
<td>65.8±12.0</td>
<td>65.5±15.0</td>
<td>0.87</td>
</tr>
<tr>
<td>Sex-male %</td>
<td>59.6</td>
<td>68.0</td>
<td>0.25</td>
</tr>
<tr>
<td>Number of leads extracted (mean) (SD)</td>
<td>11.2±1.3</td>
<td>21.1±0.9</td>
<td>0.60</td>
</tr>
<tr>
<td>Lead dwell time – in months (mean) (SD)</td>
<td>88.0±7.8</td>
<td>83.9±5.67</td>
<td>0.66</td>
</tr>
<tr>
<td>Unnecessary loops of the leads (%)</td>
<td>17.3</td>
<td>7.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Number of procedures before extraction (mean) (SD)</td>
<td>2.3±1.6</td>
<td>2.3±1.4</td>
<td>1.00</td>
</tr>
<tr>
<td>Procedure time – in minutes (mean) (SD)</td>
<td>120.6±61.7</td>
<td>109.3±45.1</td>
<td>0.13</td>
</tr>
<tr>
<td>Full procedural success (%)</td>
<td>82.3</td>
<td>91.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Clinical success (%)</td>
<td>86.5</td>
<td>98.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Technical complications</td>
<td>19.6</td>
<td>16.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Major complications (%)</td>
<td>5.8</td>
<td>0.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Pulmonary embolism (%)</td>
<td>1.9</td>
<td>0.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Minor complications (%)</td>
<td>1.8</td>
<td>2.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Procedure related death (%)</td>
<td>3.9</td>
<td>1.3</td>
<td>0.21</td>
</tr>
</tbody>
</table>

PS587 | BEDSIDE

Are there any specific factors affecting vegetation development in patients with implantable pacing systems?

A. Polewczyn1, A. Tomaszewski2, W. Brzozowski2, M. Janion3, R. Podlaski4, A. Kutarski4, 1 Swietokrzyskie Cardiology Center II - Cardiology Department, Kielce, Poland; 2 Medical University of Lublin, Department of Cardiology, Lublin, Poland; 3 Medical University of Lublin, Department of Cardiology, Lublin, Poland; 4 Swietokrzyskie Cardiology Center II Cardiology Dept. The Jan Kochanowski University, Dept of Health Sciences, Kielce, Poland; 4 The Jan Kochanowski University, Institute of Biology, Dept of Nature Protection, Kielce, Poland

Background: Right heart vegetations (RVH) are the serious signs of lead dependent infective endocarditis (LDIE). Factors affecting vegetation development are relatively little known.

Methods: Analysis of factors potentially related to risk of vegetation development in group 414 patients with LDIE (280 with confirmed RVH presence) undergone transvenous lead extraction (TLE) procedures in years 2006-2013 in the single Reference Center was conducted. Results: The results were demonstrated in the table.

Group 414 LDIE patients

| Age (years ± SD) | 65.5±14.4 | 67.5±14.8 | 0.2 |
| Gender (%)       |           |           |     |
| Male             | 66.4       | 73.1      | 0.17 |
| Patient-dependent risk factors (%) |           |           |     |
| Type 2 diabetes mellitus | 24.9       | 17.8      | 0.11 |
| Chronic renal failure (creatinine > 2 g/dl) | 7.3       | 3.1       | 0.11 |
| Dialysis         | 0.0        | 0.6       | 0.12 |
| Mechanical cardiac valve | 5.0       | 6.7       | 0.35 |
| Biological cardiac valve | 1.4       | 1.5       | 0.96 |
| Antiprostacyclin therapy | 41.4       | 34.3      | 0.17 |
| Oral anticoagulants | 24.3       | 27.6      | 0.16 |
| Procedure-related risk factors (%) |           |           |     |
| Number of leads prior to TLE (mean ± SD) | 2.3±1.4       | 1.2±0.8     | 0.02 |
| Number of abandoned leads (mean ± SD) | 0.3±0.7       | 0.3±0.7     | 0.89 |
| Number of procedures prior to TLE (mean ± SD) | 2.3±1.4       | 2.3±1.2     | 0.89 |
| Time interval from the last procedure prior to TLE (months ± SD) | 31.3±27.7       | 23.3±23.1    | 0.004 |
| Unnecessary loops of the leads (%) | 26.0         | 21.7      | 0.15 |
| Dwell time (mean ± SD) | 84.7±61.3     | 77.2±58.7   | 0.24 |
| Intracardiac abrasion of the leads (%) | 40.7         | 23.1      | 0.0005 |

Conclusions: The most significant factor affecting vegetation development was intracardiac abrasion of the leads. This phenomenon is the most often observed in the long time interval from the previous procedure. The important observation is the high percentage of unnecessary loops of the leads in all LDIE patients group. This abnormality also advances the intracardiac abrasion of the leads development. The role of patient-related factors seems to be less essential.
P588 | BEDSIDE
Risk factors of infectious related death in cardiac device infection
Université Lille 2, EA2689, Lille, France

Background: Complete implantable material extraction is now recognized paramount in the management of cardiac device infections (CDIs) but mortality risk associated with this complication spans beyond the extraction procedure of the infected device. Many major questions remain about optimal management of device related-infections. We have studied the risks factors of mortality related to the infectious process in a prospective cohort of patients hospitalized for CDIs with standardized management.

Design: 564 consecutive patients were referred for CIDI between February 1994 and July 2008. Material removal was systematically proposed. The choice of percutaneous versus surgical extraction was based on vegetation’s size. Antibiotics were administered intravenously for 2 weeks after lead removal, then orally for 4 weeks. CDI was confirmed based on positive bacteriological test from lead or infection resolution after material removal. Follow-up was 55.13±1 months. The purposed risks factors for pre-discharge mortality were analyzed using univariate and multivariate models.

Results: 39 pre-discharge deaths occurred (6.9%) including 5 vena-cava injury per-procedural deaths. Septic shock or severe sepsis was the first etiology of pre-discharge mortality (15 septic shocks or severe sepsics, 6 septic shock). A systemic embolism was incriminated in 8 cases. Age, fever, pulmonary symptoms, hemodynamic instability, CRP elevation, positive blood culture, Staphylococcus aureus in blood culture, number of vegetations, vegetations maximal length and total length of vegetations were associated with pre-discharge mortality in univariate analysis. But results of leads cultures, adapted antibiotic treatment before extraction and mode of extraction (surgical versus percutaneous) are not. In multivariate analysis, only age (<0.001; HR: 1.953 [1.04-1.14]), fever (<0.008; HR: 3.626 [2.93-3.98]) and hemodynamic instability (<0.001; HR: 7.37 [2.14-16.48]) are associated with pre-discharge mortality.

Conclusion: The severity of the infectious process is of paramount importance on mortality risk in CDIs. The management of CDIs is not limited to complete material removal. New anti-infectious strategies are strongly required and must be evaluated to improve the prognosis of this complication.

P589 | BEDSIDE
Temporal trends in patient characteristics and outcomes after ICD implantation for primary prevention in France: overview of the 2002-2012 decade
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Background: During the last decade (2002-2012), important evidence for the use of implantable cardioverter defibrillator (ICD) in the setting of primary prevention has emerged. However, the extent to which patient characteristics and outcomes have evolved during the same period is unknown.

Methods: DAI-PP Registry is an observational multicentric French registry of 5500 consecutive ICD recipients implanted in the setting of primary prevention between 2002 and 2012. Patients characteristics and outcomes (appropriate therapy mortality related complications) were analyzed through three time periods.

Results: From 2002 to 2012, the annual number of ICD implantations doubled. Patients’ characteristics and outcomes are presented in the following table:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>876</td>
<td>3155</td>
<td>1508</td>
<td></td>
</tr>
<tr>
<td>Age (Yrs)</td>
<td>61±12</td>
<td>62±11</td>
<td>63±11</td>
<td>0.002</td>
</tr>
<tr>
<td>Male proportion (%)</td>
<td>89</td>
<td>84</td>
<td>84</td>
<td>0.004</td>
</tr>
<tr>
<td>% of ICD implanted in private clinics vs. university centres</td>
<td>6.6</td>
<td>22.6</td>
<td>21.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median tLVF (interquartile)</td>
<td>25 (20; 30)</td>
<td>35 (21; 30)</td>
<td>27 (25; 30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Width QRS (&gt;120ms)</td>
<td>337 (67)</td>
<td>1595 (70)</td>
<td>758 (69)</td>
<td>0.30</td>
</tr>
<tr>
<td>Number of comorbidities median (interquartile)</td>
<td>1 (0; 1)</td>
<td>1.0 (0; 1)</td>
<td>0.0 (0; 1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Proportion of ischemic CM (vs. dilated CM)</td>
<td>598 (69)</td>
<td>1877 (66)</td>
<td>829 (55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type of ICD</td>
<td>Single chamber ICD</td>
<td>185 (22)</td>
<td>793 (25)</td>
<td>293 (20)</td>
</tr>
<tr>
<td>Dual chamber ICD</td>
<td>301 (35)</td>
<td>681 (22)</td>
<td>301 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICD and cardiac resynchronization therapy</td>
<td>375 (44)</td>
<td>1671 (53)</td>
<td>906 (40)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: ICD insertion and cardiac resynchronization therapy are increasingly used in clinical practice over the last decade. Although the number of patients with ICD implantation has increased, no significant changes were observed regarding age (<0.002), underlying heart disease (<0.001), and type of implanted devices (<0.001). The annual incidences of appropriate (<0.001) therapies significantly decreased, whereas annual mortality rates did not significantly change over time.

P591 | BENCH
Serial changes of inflammatory markers after permanent pacemaker implantation

Purpose: Transvenous insertion of endocardial leads for permanent pacing is often accompanied by minor myocardial damage. It is presented by increased levels of several inflammatory markers. The aim of our study was to assess the changes of troponin (cTnI) and C-reactive protein (CRP) after permanent pacemaker implantation.

Methods: Serum levels of cTnI and CRP were measured by (ELISA), in peripheral blood, pre-(baseline), 6h and 24h after permanent pacemaker implantation in 101 patients (mean age: 78±7 years). Patients were categorized according to the lead fixation in two groups: active and passive.

Results: At 6 h after pacemaker implantation CRP levels were increased compared to baseline values (p<0.01) and at 24 h were even more increased compared to the 6th and the baseline measurement (p<0.01). In contrast, cTnI levels were increased at 6h compared to baseline values (p<0.02), but returned to the baseline values during the same period (24h; p<0.01). Active fixation group presented significantly higher values of CRP and cTnI at 6h after pacemaker implantation, compared to passive fixation group, while at 24h CRP and cTnI levels did not differ significantly between the two groups (see table, values presented as median, min, max).

Table 1. Serial changes of CRP and cTnI levels after permanent pacemaker implantation with passive and active fixation

<table>
<thead>
<tr>
<th>Time</th>
<th>CRP (mg/dl)</th>
<th>cTnI (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.55 (15.0-34.40)</td>
<td>0.04 (0.02-0.09)</td>
</tr>
<tr>
<td>6h</td>
<td>7.00 (2.50-101.90)</td>
<td>0.04 (0.04-0.03)</td>
</tr>
<tr>
<td>24h</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Conclusion: CRP and cTnI levels increased in the first 6hours after permanent pacemaker implantation and may be used in the evaluation of the myocardial injury during implantation. Active fixation leads presented greater myocardial injury, compared to passive fixation leads.

P592 | BEDSIDE
Intraoperative Byrd sheath fractures in patients undergoing transvenous lead extraction
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1 Medical University of Warsaw, Warsaw, Warsaw, Poland; 2 Medical University of Lublin, Department of Cardiology, Lublin, Poland

Beside clinical complications of transvenous lead extraction (TLE) there are several possible technical issues of this procedure. One, observed, however rarely described and investigated, phenomena is intraoperative fracture of Byrd dilator telescoping polypropylene sheaths (figure).

Aim: To investigate occurrence, presentation, clinical importance and risk factors for sheath fracture.

Results: In material of 1304 patients sheath fractures were observed 37 times in 32 patients (<2.5%). Fractures were localized in following segments of venous system: 1) subclavian/innominate vein - 12 (32.5%), 2) upper - 12 (32.5%) and 3) lower part of vena cava - 9 (24%), 4) right atrium - 3 (8%), 5) right ventricle - 1 (3%). When sheath length was divided into four equal segments beginning at inlet to bypass, fractures were located in 14 (41%), 2 (5%), 18 (51%), 1 (3%), III - 3 (8%) and none in IV. Patients with sheath fracture were younger (median, 50 vs. 68 years, p<0.05), had longer dwelling time of oldest extracted lead (median, 100.9 vs. 70 months, p<0.01), longer procedure time (median, 142.5 vs. 100 min, p<0.01). Occurrence of sheath fracture was associated with more often lack of radiological success - 6 (18,75%) vs. 69 (5,42%), p<0.01; and doubled
the incidence of major and minor clinical complications however this observation was
not statistically significant: 17 (1,34%) vs. 1 3 (1,3%) and 21 (1,65%) vs. 1
(3,13%).

Conclusions: Byrd sheath fracture phenomena observed during TLE is a rare
technical issue however when occurs it decreases procedure success rate and
more influence clinical complications. Fracture usually occurs in initial part
of venous system when sheath breaks at its intra- vessel half-length.

P593 | BEDSIDE
Long-term prognosis in patients with Brugada syndrome based on
Class II indication for implantable cardioverter defibrillator in the
HRS/EHRA/APHRS expert consensus statement
M. Takagi1, Y. Seiguchi2, Y. Yokoyama3, N. Aihara1, M. Hiraoka1, K. Aonuma1,
on behalf of J-IVFS study, 1 Osaka City University Graduate School of Medicine,
Osaka, Japan; 2 University of Tsukuba, Tsukuba, Japan; 3 Tokyo Medical
and Dental University, Tokyo, Japan; 4 Senni central hospital, Suita, Japan

Background: Recently, the Expert Consensus Recommendations for therapeutic
interventions on Brugada syndrome (BrS) were published as HRS/EHRA/APHRS
Expert Consensus Statement. The validity of the Class II indication for Im-
plantable Cardioverter Defibrillator (ICD) is still unknown.

Purpose: To evaluate the validity of the Class II indication for ICD implantation in
the Consensus Statement with a large Japanese cohort of BrS (The Japan
Idiopathic Ventricular Fibrillation Study [J-IVFS]).

Methods: A total of 155 consecutive BrS patients with ICD implanted by the class-
II indication and no previous cardiac arrest (mean age 52±15 years, 142 males)
were enrolled. Clinical outcomes during the follow-up period were compared be-
 tween patients with Class IIa (n=51) and Class IIb (n=104) indication.

Results: The incidence of cardiac events (sudden cardiac death [SCD] or VF)
during also included follow-up period of 55-30 months was significantly higher in pa-
 tients with Class IIa (n=8, 3.2%/y) than as those with Class IIb indication (n=3,
0.6%/y) p=0.009, as determined by the Kaplan-Meier method. In patients with
Class IIa indication, the incidences of cardiac events in patients with induced VF,
family history of SCD or without these clinical factors were 2.9, 5.5, 7.8%/y, re-
 spectively. In patients with Class IIb indication, the incidences of cardiac events
in patients with syncope, spontaneous type-1 ECG or family history of SCD were
2.0, 1.3, 0%/y, respectively.

Conclusions: We confirmed the validity of the Class II indication for ICD implan-
tation in the Expert Consensus Recommendations. In patients with Class IIb in-
dication, previous syncope might be important factor to distinguish intermedi-
ate-low risk patients with BrS.

P594 | BEDSIDE
Female gender - does it consist the risk factor of transvenous lead
extraction?
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University of Lublin, Lublin, 1District Hospital, 2Medical University of
Lublin, Dept of Cardiac Surgery, Lublin, 3District Hospital, Kielce, Poland

There is considerable controversy regarding influence of pt. gender on safety of
transvenous lead extraction (TLE) and TLE in woman was recognized as more
riskier. Mechanism remains unknown. Objective: Analysis of safety and feasibility of
TLE in man. May be different anatomy and endurance of connecting tissue play
important role.

Methods: Using mechanical systems we have extracted ingrown PM/ICD leads
from 1536 pts (5-94y; 64.6±16.1y) within the last 7 years. We compared TLE
effectiveness and complications in both groups. Results are shown in the table.

Impression: Prior sternotomy, shorter mean lead body dwelling time and less
frequent non-indicative infections may explain lower occurrence of TLE complica-
tions in man. May be different anatomy and endurance of connecting tissue play
more important role, but implant duration seems to be more important.

Patient/system/procedure information

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Females</th>
<th>Males</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s age (SD)</td>
<td>64.0±15.7</td>
<td>65.5±16.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Infective indications (LDIE)</td>
<td>237 (31.7%)</td>
<td>137 (23.1%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Infective indications (pocket infection)</td>
<td>153 (16.3%)</td>
<td>57 (9.6%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Non-infective indications</td>
<td>484 (57.1%)</td>
<td>399 (67.2%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Prior sternotomy</td>
<td>148 (15.8%)</td>
<td>71 (11.9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Long-term coagulation</td>
<td>299 (31.9%)</td>
<td>221 (37.0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Diabetes (I or II)</td>
<td>222 (23.7%)</td>
<td>122 (20.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Renal failure (crea or haemodialysis)</td>
<td>89 (9.5%)</td>
<td>35 (5.9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>27.1±4.2</td>
<td>27.8±11.2</td>
<td>NS</td>
</tr>
<tr>
<td>VH therapy (ICD) lead extraction</td>
<td>303 (32.5%)</td>
<td>84 (14.1%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Mean extracted lead body dwelling time</td>
<td>78.4±57.8</td>
<td>90.1±68.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Major complications</td>
<td>7 (7.0%)</td>
<td>15 (2.5%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Minor complications</td>
<td>6 (0.8%)</td>
<td>18 (3.0%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Full radiological success</td>
<td>888 (94.9%)</td>
<td>561 (94.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical success</td>
<td>926 (98.9%)</td>
<td>576 (97.0%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death during post-procedural period</td>
<td>7 (0.7%)</td>
<td>5 (0.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Procedure related death</td>
<td>2 (0.2%)</td>
<td>3 (0.5%)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Conclusions: There are slight more TLE complications in woman but final TLE
effectiveness is similar to male patients.

P595 | BEDSIDE
Atrial fibrillation in cardiac resynchronization recipients with and
without prior arrhythmic history. How much of arrhythmia is too much?
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O. Kowalski, B. Sredniawa, A. Sokol, Z. Kalarus on behalf of TRUST CRT
Randomized Trial investigators, Silesian Medical University, Silesian Center for
Heart Disease, Zabrze, Poland

Purpose: The aim of the study was to assess long-term incidence of atrial fibr-
illation recorded in cardiac resynchronization (CRT) patients with and without
previous arrhythmic history, factors predisposing to arrhythmia, as well as to evaluate
the prognostic power of cumulative arrhythmia burden, duration of the longest
episode and the number of episodes.

Methods: Device-collected data from 380 episodes during 24 months in 96 par-
ticipants of randomized CRT-trial were analyzed (15% in NYHA class IV, sinus
rhythm, median LVEF=24% and QRS=169ms). Blindly adjudicated major adverse
events (MACE) and any-cause death were censoring variables.

Results: Two-year incidence of AF was 70%, including 66% of patients without
previous arrhythmic history. No baseline characteristics distinguished those who
developed arrhythmia de novo. Percent of time spent in AF (adjusted hazard ratio
HR 1.05±0.95% confidence interval CI 1.01-1.10), but not number of episodes pre-
dicted mortality and MACE incidence (HR 1.03±1.01-1.07P=0.03). Duration of the
RAA morphology and relationships with the surrounding cardiac structures, foc-
using on the regions for atrial leads placement.

Design: An anatomical review of a consecutive series of human hearts spec-
imens coming from routine autopsies is reported. A total of 100 human hearts
have been examined in order to achieve anatomical study of RAA, CT and TS;
cases with extensive right atrial surgery have been excluded. Attention was paid
to the anatomical variability of TS in its “entrance” into the RAA.

Results: The TS has shown 3 main types of anatomic variability related to the
presence of a main trunk TS (type 1, present in 76% of cases), double TS (type 2
present in 13% of cases) and a fine arborization without a clear TS representation
(type 3 present in 10% of cases). A triple morphology of TS was found in one
case. The RAA region proximal to TS routing (“antral RAA region”) faces the
aortic root, without a clear pericardial space in between; the distal deeper region
of the RAA, behind TS (“saccular RAA region”) faces even though not closely, the
pulmonary artery infundibulum, due to its “unbound” nature that better complies
the atrial systolic cycles. This could represent a safer region for leads placement,
especially when screw-in leads are used.

Conclusions: The TS morphology is mainly represented as one trunk and, less
frequently, two main trunks, connecting anteriorly the CT to RAA. Two separate
regions can be identified within the RAA, separated by the TS routing: the “sac-
cular RAA region”, a safer coronal space, a safer region for atrial leads implantation
and anchorage, and the “antral” proximal RAA, which is close to the ascending
aorta. This may have clinical implications for screw-in atrial leads Technologies.

P597 | BEDSIDE
Abnormalities in AutoCapture pacemaker algorithm in atrial fibrillation
patients compromise battery longevity
La Vieja, S. Calle, M.A. Quinones, P. Sanchez-Borque, J. Farre, Foundation
Jimenez Diaz, Madrid, Spain

Introduction: AutoCapture works different in VVIR and DDDR units. In VVIR, Au-
toCapture is only performed if ventricular pacing is present, it does not overdrive
intrinsic rhythm. In DDDR, it is programmed shortening the AV interval to
assure capture. During the Automatic mode switch, DDDR units work like

Device therapy: general aspects
103
Downloaded from https://academic.oup.com/eurheartj/article-abstract/35/suppl_1/1/541954 by guest on 09 January 2019
Methods: We examined AutoCapture recorded data in the programmer reports of scheduled PM check-ups during 2012.

Results: 160 consecutive patients (58% men) aged 78±9 years were evaluated. PM stimulation mode was VVI in 44 patients (27.5%) in chronic AF. History of AF was present in 97 patients (60%). 73 patients (45.6%) showed an Abnormal AutoCapture pattern (a high variability of the AutoCapture threshold values along time and/or the presence of repeated out-of-range values). Figure (Panel A: patient (113) changing from Normal AutoCapture pattern to Abnormal pattern in relation with a recurrence of AF. Panel B: patient (151) showing in the programmer reports an alert of high energy mode stimulation (5V) because the automatic stimulation threshold was considered unknown (out of range) but the stimulation threshold performed manually was 1 V). The univariate analysis showed differences between DDD mode and VVI mode OR 0.36 (0.18-0.74). After multivariate analysis, Abnormal AutoCapture pattern was associated to the presence of atrial fibrillation (OR 3.96 [1.59 - 9.82; p<0.05]) and a ventricular pacing <25% of the time (OR 4.80 [2.09 - 11.05; p<0.05]).

Conclusion: DDD units were not likely to underperform owing to the dedicated fusion avoidance algorithm for AutoCapture while VVI units may underperform when a competing rhythm causing fusion is present. Therefore, AF patients, especially those with ventricular pacing <25%, may not benefit from AutoCapture activation.

P598 | BENCH Pacemaker use in familial amyloid cardiomyopathy patients: prophylactic implantation and the evolution of cardiac conduction abnormalities


Introduction: Familial Amyloid Cardiomyopathy (FAP) can affect the cardiac conduction system, but the indications for permanent pacemaker (PP), and, particularly, for prophylactic implantation before liver transplantation (LT) are still controversial. The beneficial impact of LT on cardiac involvement is also unclear. Our aim was to evaluate the appropriateness of pacemaker implantation in these patients (pts) and the evolution of cardiac changes after LT.

Methods and results: We enrolled 664 pts with FAP Met30 mutation [median age 58 years] patients (pts) and the evolution of cardiac conduction abnormalities before LT were evaluated.

Conclusion: Prophylactic PP before LT didn’t have a clear prognosis benefit (16,4 vs 23% and intraventricular conduction in 14%.

P601 | BENCH The IgCAM CAR regulates calcium homeostasis in the developing heart and nervous system

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The IgCAM adenosine receptor is a transmembrane protein of the Ig superfamily which serves as receptor for adenosine and crosstalk B viruses. CAR is strongly expressed in the developing brain and heart but becomes downregulated at early postnatal stages. In adult hearts CAR is primarily expressed at the myocardial intercalated disc in contrast to the widely diffuse localization of CAR on the surface of cardiomyocytes. CAR knockout mice die at embryonic days 11.5 to 13 due to malformations of the heart indicating a developmental function of CAR. To unravel the adhesion and signaling function of CAR we studied embryonic cardiomyocytes from CAR deficient mice. In the absence of CAR cardiomyocytes show a significant higher beating rate that correlated with a higher frequency of Ca2+ transients compared to wild type cells. Furthermore, CAR transients of CAR knockout myocytes revealed a significant faster decline in calcium levels. Inhibition of SERCA2 by thapsigargin or CPA did not result in a similar decrease in the frequency of Ca2+ transients by releasing Ca2+ from intracellular stores. Fiber knob induced Ca2+ increase was blocked by Wortmannin suggesting that CAR signaling triggers Ca2+ release via PI3K. Overall, we conclude that the cell adhesion protein CAR regulates intracellular Ca2+ levels and modulates calcium homeostasis.
the transmission of the cardiac excitation and contraction between neighbouring cardiomyocytes.

P602 | BENCH
T-box 5 controls age-dependent cardiogenic activity in human cardiac progenitor cells through insulin-like growth factor-1 receptor signaling

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Background: The rate of human myocyte turnover declines with age. However, whether the differentiation potential of resident progenitor pool may also be affected remains elusive, as is the question how it is regulated.

Methods: Human cardiac progenitor cells (CPCs) were isolated from myocardic specimens of 90 patients and classified into 2 groups (neonate and infant) along with age. Global gene expression analysis, quantitative RT-PCR, and cardiogenic activity by co-culture experiment with neonatal rat ventricular myocyte were examined. RNA interference was performed to verify the genetic function.

Results: Co-culture experiment showed that neonatal CPCs had higher cardiogenic activity. Knockdown of IGF1R in neonatal CPCs resulted in a reduced cardiogenic potential compared with control CPCs. Gene expression analysis between neonatal and infant CPCs showed several candidate genes for cardiogenesis which include TBX5, HB-EGF and ZFHX4 were significantly up-regulated. Among them, Tbx5 expression levels were decreased by knockdown of IGF1R in neonatal CPCs. Moreover, knockdown of TBX5 significantly decreased the cardiogenic activity similar to that found in CPCs treated by IGF1R inhibition.

Conclusions: Our results suggest a functional significance of IGF1R-mediated physiological alteration of human CPC differentiation potential. The limited myocyte turnover in postnatal heart may be associated with age-dependent decline of IGF1R signaling.

P603 | BENCH
Loss of versican in vascular smooth muscle cells causes arterial hypotension and cardiac hypertrophy

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Purpose: Versican is a large secreted chondroitin sulfate proteoglycan, which is important for cardiac development, and is also implicated in adult cardiovascular disease. Due to the N-terminal G1 domain of versican interacts with hyaluronan growth factor binding proteins was observed, which might be involved in the retention of arterial elasticity. To determine whether there is an induction of regenerative processes via paracrine mechanisms in pathological and pathophysiological conditions in order to identify stimulation of secreted proteins due to pathophysiological stimuli. This analysis should verify, whether there is an induction of regenerative processes via paracrine mechanisms or a potential impairment of progenitor cell function due to pathophysiological conditions.

Methods and results: Stem cell therapy is a promising new therapy option for patients with heart failure. While many clinical studies involving stem cell transplantation after myocardial infarction show encouraging results, little is known about the mechanisms that lead to an improvement in cardiac function. This study was aimed to analyse the secretory activity of resident cardiac progenitor cells under physiological and pathophysiological conditions in order to identify stimulation of secreted proteins due to pathophysiological stimuli. This analysis should verify, whether there is an induction of regenerative processes via paracrine mechanisms or a potential impairment of progenitor cell function due to pathophysiological conditions.

Conclusion: We have demonstrated that IPSC-DC can integrate into host ventricle and create a biological pacemaker.
that hints to a functional impairment of these cells due to long-term exposure to pathophysiological stimuli.

**Conclusions:** This study showed that there is a time-dependent influence of pathophysiological aldosterone level on the secretory activity of Sca-1+ cardiac progenitor cells. Aldosterone led to a significant change in the secretome of these cells compared to untreated cells. Among the time points that were analysed in this study, treatment of Sca-1+ stem cells with aldosterone for 24 h led to a distinct change in secretome. Most changes were related to proteins that were associated with cell mobilization, cell migration and angiogenic processes. This study could give some insights in the secretory activity of cardiac progenitor cells under diseased and healthy conditions and their possible role in regenerative processes in damaged heart tissue via paracrine mechanisms.

**P606 | BENCH**

Spiral wave behaviors and antiarrhythmic drug efficacy in human induced pluripotent stem cell-derived myocardial sheet are different from those in original heart: A simulation study

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**Introduction:** Recently, myocardial sheet consisting of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) has been attempted to be utilized in clarifying the mechanisms of inherited arrhythmias and evaluating the efficacy of antiarrhythmic drugs. However, whether the electrophysiological property of the hiPSC-CM sheet is consistent with that of the original human heart is still unclear.

**Methods:** To clarify this issue, we constructed in silico models of hiPSC-CM sheet (by modifying ion channels and cell size) and original human ventricular myocardium (hVM) based on previously reported experimental data. Then we analyzed the behaviors of spiral wave reentry in the in silico sheet models, and the effect of IKr blockade was also evaluated.

**Results:** (1) The in silico model of hiPSC-CM had spontaneous activations 0.5-1Hz and the diastolic potential was positively shifted by ~15 mV. (2) Conduction velocity (CV) in the hiPSC-CM sheet was ~5 cm/s, which was only ~1/10 of CV in the hVM. (3) Mean cycle length (mCL) of excitations during the spiral wave reentry in the hiPSC-CM sheet was ~0.9Hz, whereas that in the hVM was ~5Hz identical to mCL of real human VF (see Figure). (4) Both the CV and mCL in the hiPSC-CM sheet model were very consistent with previous experimental data observed in cultured hiPSC-CM sheets. (5) The mCL of spiral wave reentry in hVM was markedly prolonged by IKr blockade, whereas this was not the case in hiPSC-CM sheet.

**Conclusions:** The spiral wave behaviors and the antiarrhythmic drug efficacy in the simulated myocardial sheets of hiPSC-CM and hVM were different. Our findings suggest that such in silico analytical approach might fill the gap between hiPSC-CM and original hVM when we apply the hiPSC-CM sheet model to clinical practice.

**P607 | BENCH**

Intracoronary infusion of allogeneic cardiosphere-derived cells during acute ischemic phase of myocardial infarction reduces infarct size and attenuates remodeling in a porcine model of ICMi

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**Introduction:** Acute MI was induced in 12 farm pigs by occlusion of the LAD with an over-the-wire balloon for 60 minutes. After 60 minutes of ischemia (and prior to reperfusion), pigs were randomized to receive either allogeneic CDCs (5x106, n=6) or PBS (control group, n=6) in the infracted area using a catheter that crossed the occlusion site. Five minutes after cell infusion, reperfusion was allowed. Animals were followed for 30 days. Transthoracic echocardiography was performed at baseline and after 30 days of follow up to assess LV end-diastolic and end-systolic diameter (EDD and ESD), LV end-diastolic and end-systolic volume (EDV and ESV), and LV ejection fraction (EF). At day 30 post-MI animals were sacrificed and area at risk (AR) and infarct size were estimated histologically, with gentian violet and TTC stain.

**Results:** At one month post-MI, morphometric analysis revealed no difference in area at risk (AR) between the two groups. There was a strong trend towards smaller infarct size in CDC-treated animals compared to control animals (91±5.8 vs. 104±7.6 m2, p=0.069). Infarct size in the CDC-treated group was significantly smaller than in the PBS control group (91±5.8 vs. 104±7.6 m2, p=0.041). In addition, control animals showed a significant increase in LVESV (11.1±1.4 mm, p=0.001) while in CDC-treated animals the increase in LVESV was numerically smaller and did not reach statistical significance (5.9±1.9 mm, p=0.06). Global systolic function, as assessed by LVEF, was similar in both study groups.

**Conclusions:** Infusion of allogeneic CDCs during the acute ischemic phase of MI was safe, decreased infarct size and attenuated remodeling in a porcine model of ischemic cardiomyopathy.

**P608 | BENCH**

Retention of endothelial progenitor cells in bone marrow in a murine model of endogenous tissue plasminogen activator (tPA) deficiency in response to critical limb ischemia

H.K. Yip, Y.L. Chen, P.H. Sung, S. Chua. Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Cardiology, Kaohsiung, Taiwan

**Purpose:** This study tested the hypothesis that tissue plasminogen activator (tPA) is crucial for regulating endothelial progenitor cell (EPC) mobilization from bone marrow to circulation in murine critical limb ischemia (CLI) by ligating left femoral artery.

**Methods and results:** Wide-type (C57BL/6) (n=40) mice were equally divided into group 1A (sham control), group 2A (CLI), group 3A [control tPA (4.0 mg/kg, intravenously at 3h after CLI)], group 4A (CLI-tPA). Similarly, tPA knock-out (tPA−/−) mice (n=40) were equally divided into group 1B (sham control) group 2B (CLI), group 3B [control tPA (4.0 mg/kg)], group 4B (CLI-tPA). The circulating levels of EPCs (CD34+, CD133+, CXCR4+) were lower in groups 1B and 2B than in groups 1A and 2A, respectively (all p<0.01), and were reversed after tPA treatment (3B vs. 3A or 4B vs. 4A, p<0.05) at 6h and 18h post-CLI. Levels of these biomarkers decreased again 14 days after CLI in tPA−/− mice compared to those in wild-type between the respective groups (all p<0.01). Laser Doppler flowmetry showed a higher ratio of ischemic-to-normal blood flow in 2A than in 2B and in 4A than in 4B by day 14 after CLI (all p<0.05). Angiogenesis at protein (CXCR4, SDF-1α, VEGF) and cellular (CXCR4+, SDF-1α+, and CD31+ cells) levels were highest in animals with CLI+tPA, significantly higher in mice with CLI only than in sham controls for both wild-type and tPA−/− mice (p<0.01).

**Conclusion:** tPA played an essential role in augmenting circulating EPCs, angiogenesis, and blood flow in the ischemic limb in a murine model.
Purpose: Cardiac Stem Cells (CSCs) have recently been reported to have cardioregenerative potential. The optimal timing of CSCs administration is still unclear. The safety of early intramyocardial administration and the possible influence of the timing of allogeneic porcine CSCs (pCSCs) delivery after experimental acute myocardial infarction (AMI).

Methods: Female swine surviving a 90 minutes occlusion of the mid-LAD received vehicle injection on day 7 (n=5, CON), 25x10⁶ pCSCs either two hours (n=5, D0) or 7 days (n=5, D7) after reperfusion. Magnetic resonance was performed at 1 and 10 weeks, determining Ejection Fraction (EF), End Diastolic Volume (EDV), End Systolic Volume (ESV) and infarct size (%). Healthy weight-matched swine (n=5) were also imaged at 10 weeks. Pathological examination, including the study of vascularization at the infarct border, was carried out at wk 10.

Results: No major adverse cardiac events were seen in any case. Cardiac function parameters and infarct sizes were similar between study groups with a trend for increased EF and EDV at 10 weeks in the D7 group. The treated groups had significantly reduced ESV values and less tissue remodelling (mean ± SD: D0, D7; ESV: 5.41±2.79 mL vs. 6.09±3.09 mL; EDV: 11.6±4.6 mL vs. 16.3±5.9 mL).

Discussion: Our initial results suggest that hCPCs can be reseeded onto rat de-cellularized scaffolds to develop three-dimensional cardiac grafts. The hiPS cells implantation in patients with cardiac dysfunction. Heart transplantation remains the definitive treatment for end-stage heart failure, but the supply of donor organs is limited. We used non-immunogenic extracellular matrix as a scaffold to seed the human cardiac progenitor cells (hCPCs) and human umbilical vein endothelial cells (HUVEC) or vascular endothelial cells derived from human induced pluripotent stem (hiPS) cells on the platform with acellular architecture.

Methods and results: We generated a modified Langendorff apparatus and located the entire systems in the clean conditions. The apparatus was then applied on an 8-week-old male Sprague-Dawley rat’s heart to decellularize the entire heart, minimizing the heart was decellularized with 0.02% SDS, 3% Triton X-100, and 4% deoxycholic acid followed by serial perfusion. The acellular constructs contain architecture of original tissues, including the vessels, components of valves, and intact chamber geometry. A subtype of collagen, laminin, and fibronectin were confirmed by immunofluorescence and dye perfusion through the aorta demonstrated the preserved coronary arteries and capillary vasculatures. To generate whole heart grafts, we perfused hCPCs or hiPS cells-derived vascular endothelial cells with CO₂ incubation followed by perfusion reseeding system. We found that the scaffolds reseeded under these conditions for 14 days could achieve significant hCPCs engraftment and distribution along with coronary perfusion area. The vascular endothelial cells derived from hIPS cells could promote to substantial recellularization with enhanced microcirculation. The recellularized cardiac constructs kept growing as thickening tissues with constant and physiological loading conditions.

Conclusions: Our initial results suggest that hCPCs can be reseeded onto rat de-cellularized scaffolds to develop three-dimensional cardiac grafts. The hiPS cells derivatives could reinforce the vascular endothelium to enhance the cell engraftment and survival. Further challenge could apply by cardiac and smooth muscle cells directly differentiated from hiPS cells to provide mechanically contractile heart organ.
ults showed overwhelming association with CAD (OR=1.2, 95% CI = 1.1–1.3; OR=1.4, 95% CI = 1.1–1.7, and OR=1.2, 95% CI = 1.1–1.3; p<0.001 for the three models respectively). Sixteen studies with 3,682 patients and 2,724 controls were included for T786-C polymorphism. Using appropriate effects for analysis, all comparisons for this polymorphism using dominant, recessive and allelic genetic models showed significant association with CAD (OR=1.5, 95% CI = 1.3–1.8, p<0.001; OR=1.3, 95% CI = 1.0–1.7, p=0.036 and OR=1.3, 95% CI = 1.2–1.5, p<0.001 respectively). Similar results were seen with comparisons for eNOS 27bp VNTR polymorphism in which 24 studies with 8,179 patients and 6,048 controls were included. Comparisons employing all three genetic models and using appropriate effects for analysis showed significant associations (OR=1.3, 95% CI = 1.1–1.5, p=0.009; OR=1.3, 95% CI = 1.1–1.6, p=0.008 and OR=1.3, 95% CI = 1.1–1.5, p<0.001 for three genetic models respectively). Comparisons in the present study, which is to our knowledge, the most comprehensive meta-analysis on the subject till date, indicates that all three common polymorphisms of eNOS gene are clearly associated with CAD. Early detection of individuals at risk and delaying endothelial dysfunction among them by means of drugs, diet and physical activity can thus be recommended.

**P616 | BENCH**

**Transcription coactivator Eya4 is a critical regulator in cardiac physiology**

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**Introduction:** Eyes absent 4 (Eya4) is a transcription cofactor involved in a number of cellular and developmental processes. We have previously shown that a truncating mutation in Eya4, E193, causes hearing impairment followed by terminal heart failure suggesting Eya4 is a regulator in cardiac physiology.

**Methods and results:** Transgene- or adenovirus mediated overexpression of Eya4 or E193 altered the expression of p27kip1, a critical mediator of cardiac hypertrophy in adult cardiomyocytes. Luciferase reporter and EMSA assays revealed that Eya4 directly binds to and suppresses p27kip1 promoter activity, while E193 exerts an opposing effect, respectively. Activity and phosphorylation of downstream molecules were significantly altered in Eya4 and E193 transgenic (TG) mice in a contradictory manner. Cardiac phenotypes evolved in both TG models already under basal conditions. Eya4 TG hearts developed hypertrophy as judged by increases in heart weight and cross-sectional cell surfaces and reactivation of fetal genes as well as fibrosis. E193 TG animals showed onset of DCM along with wall thinning, ventricular dilatation, fibrosis and slightly compromised cardiac function. These two distinct cardiac phenotypes were even more aggravated upon pressure overload or Angiotensin II infusion.

Finally, we just recently identified a new mutation in Eya4, E215, which also causes hearing impairment and heart failure.

**Conclusion:** Our data indicate that Eya4, in a physical complex with S6x1, plays a critical role in regulating normal cardiac function via p27/CDK2–HDAC2 and allude that mutations within the Exa4/Six1 transcriptional complex interfere with this newly established signalling pathway, finally leading to age-related onset of cardiomyopathy.

**Clinical perspective:** Gaining a better understanding of this disease mechanism could help identify new treatment options for heart failure patients.

**P617 | BENCH**

**Integrin-linked kinase promotes proliferation of mammalian cardiomyocytes**

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**Background:** The mammalian heart can not regenerate effectively after cardiac injuries due to the restricted proliferative potential of cardiomyocytes. Here we investigated whether integrin-linked kinase (ILK) may promote the proliferation of mammalian cardiomyocytes.

**Methods and results:** Primary cultured neonatal rat cardiomyocytes were infected with adenoviral vectors and the infection efficiency was assessed by determining the percentage of GFP-positive cells using confocal microscopy. ILK expression was confirmed by Western blotting. Overexpression of ILK was associated with increased DNA synthesis, karyokinesis and cytokinesis, as well as an increase in cardiomyocyte number. Activation of PKB/Akt kinase was required for ILK-induced cardiomyocyte proliferation, whereas the ERK1/2 signaling pathway was not associated with ILK-induced cardiomyocyte proliferation. Moreover, ILK can activate PKB/AKT by direct phosphorylation at serine 473, inhibit GSK-3β activity by indirect phosphorylation at serine 9 and increase the protein level of cyclin D1.

Additionally, overexpression of ILK did not affect the proliferation of c-kit+ cardiac stem cells in our culture condition.

**Conclusions:** Our findings indicate that ILK promotes proliferation of mammalian cardiomyocytes through the PKB/Akt signaling pathway in vitro. Thus, ILK and the signaling pathway it regulates may represent a target for novel strategies to promote myocardial regeneration in mammalians.

**P618 | BENCH**

**The role of microRNA-29b during angiotensin II-induced epithelial-mesenchymal transition in renal tubular epithelial cells**

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**Purpose:** The Angiotensin II (Ang II) contents and its receptor density in the
kidney of young spontaneously hypertensive rats (SHRs) were significantly higher than in age-matched Wistar-Kyoto rats (WKYS). Ang II has been proved to induce Epithelial-Mesenchymal Transition (EMT). The present study aimed at testing the role of microRNA-29b (miR-29b) during Ang II-induced EMT.

Methods: Differential expression of miR-29b in renal cortex between 15-weeks SHRs and age-matched WKYS was determined by real-time quantitative polymerase chain reaction (RT-qPCR). The effect of miR-29b on EMT-associated genes such as transforming growth factor (TGF-β), α-smooth muscle actin (α-SMA), Collagen I (Col I) was examined after transfecting miR-29b mimics (24 h before treatment with 10-7M Ang II) and miR-29b inhibitor into cultured renal tubular epithelial cells line–NRK-52E cells. The level of expression of these genes was confirmed by RT-qPCR, western blot and immunofluorescence staining.

Results: Downregulation of miR-29b in renal cortex of SHRs was demonstrated by RT-qPCR compared with that of WKYS. Transfection of miR-29b inhibitor significantly increased the expression of TGF-β, α-SMA and Col I, while transfection of miR-29b mimics inhibited Ang II-induced upregulation of expression of these genes.

Materials and methods: Satellite cells were obtained from soleus muscle of four-five weeks old C57BL/6 males and transduced with concentrated lentiviral suspension (MOI=30), encoded non-aggregate prone and aggregate prone desmin mutations and GFP as reporter gene. Cells were grown during one week, after that differentiation was induced and continued two weeks more. Changes in rhod-2 fluorescence were detected using laser confocal microscopy. Electrical stimulation was applied for up to 30 s as follows: 1 Hz, rest, 10 Hz, rest, and 100 Hz, rest. Intensity of fluorescent signal was measured in baseline (without any stimulation (F0)) and during stimulation (F). Ratio F/F0 was calculated and represented peaks amplitudes of mitochondrial calcium transients.

Results: After electrical stimulation the peak amplitude of mitochondrial calcium uptake was similar in non-transduced and DesWT cells. However, in Des345P myotubes and DesA357P myobies, the mitochondrial calcium uptake was markedly decreased by 50% and 80% respectively, in comparison with DesWT cells. Interestingly, mitochondrial calcium uptake in the DesD399Y myotubes was similar to that seen in DesWT cells and was equalled 3.45±0.53. Des370P cells didn’t decrease peak amplitude as much as DesA357P and DesL345P and showed transitional peak, F/F0 was 2.85±0.31.

Conclusions: Mitochondrial capacity to uptake calcium depended on conformational form of desmin protein and aggregate prone mutations markedly decreased mitochondrial calcium uptake in comparison with non-aggregate prone mutation. Therefore we assumed that desmin aggregates disturbed proper spatial mitochondrial calcium distribution within the muscle cell, i.e. their location in calcium release microdomains.

P620 | BENCH
Long non-coding RNAs and cardiac hypertrophy
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Purpose: Long non-coding RNAs (IncRNAs) constitute a group of non-coding RNAs longer than 200 nucleotides. IncRNAs are able to regulate almost every stage of gene expression, from epigenetic modification to post-transcriptional regulation. Recent landmark studies revealed that IncRNAs are involved in cardiac development. However, the role of IncRNAs in cardiac diseases is unknown. Here, we investigated the regulation of IncRNAs in the hypertrophied heart.

Methods: Wild-type and adenosine A2a receptor overexpressing mice (A2a-Tg) were subjected to transverse aortic constriction (TAC) as a model of cardiac hypertrophy or doxorubicin treatment as a model of cardiotoxicity. Hearts were harvested and expression of IncRNAs was investigated using Affymetrix Mouse Gene 1.0 ST microarrays. A specific analytical pipeline was developed to extract from these microarrays the data related to IncRNAs.

Results: Analysis of microarray data identified 2 IncRNAs up-regulated and 3 down-regulated in the hearts of A2a-Tg mice subjected to TAC. Quantitative PCR showed that expression of the IncRNA 2900055J20Rik was highly downregulated in A2a-Tg mice compared to wild-type littermates (-3.5-fold, P < 0.001). To confirm the association between the overexpression of this IncRNA and cardiac hypertrophy, we used a public microarray dataset from mice subjected to TAC. In this public dataset, expression of 2900055J20Rik was found to be up-regulated in TAC mice compared to sham-operated animals (6-fold after 28 days, P < 0.01). Interestingly, administration of the BET bromodomain inhibitor JQ1, a suppressor of cardiac hypertrophy, resulted in a decrease of 2900055J20Rik expression 3, 11 and 28 days after treatment onset (P < 0.01). Finally, to investigate the effect of adenosine on the expression of 2900055J20Rik in another model of cardiac stress, wild-type and A2a-Tg mice were treated with doxorubicin. As it was observed in TAC mice, expression of 2900055J20Rik was down-regulated upon overexpression of the adenosine A2a receptor in doxorubicin-treated animals (2-fold, P = 0.03).

Conclusions: First, we have shown that data on IncRNAs can be obtained from traditional gene expression microarrays. Second, IncRNAs are regulated in the hypertrophied heart and can be modulated by cardioprotective molecules (adenosine and JQ1). Third, we have identified the IncRNA 2900055J20Rik which may be involved in regulation of cardiac hypertrophy. These observations motivate further investigation of the therapeutic value of IncRNAs in the diseased heart.

P621 | BENCH
Application of targeted next generation sequencing (NGS) in clinical genetic diagnostics of cardiomyopathies
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Purpose: Next generation sequencing (NGS) techniques can be successfully applied to find mutations underlying genetic cardiomyopathies. The representation and coverage of several exons is incomplete in Whole Exome Sequencing (WES),
leading to clinically relevant mutations being missed. Therefore WES will, at least for now, coexist in clinical genetic diagnoses with other NGS-based strategies, such as targeted resequencing. Therefore we aimed to evaluate the yield of targeted sequencing of 55 genes in cardiomyopathy patients referred to our department.

**Methods:** We constructed an enrichment kit targeting 55 genes and implemented this into routine diagnostics. We studied the initial 150 patients evaluated in our laboratory: 43 fulfilled the generally accepted clinical criteria for hypertrophic cardiomyopathy (HCM), while 69 fulfilled the Mestrioni criteria for dilated cardiomyopathy (DCM). Twenty-two, 11 and 2 patients respectively, did not fulfill the formal criteria. Additional haplotype and cosegregation analyses were performed to further support pathogenicity of identified potentially causal mutations.

**Results:** 35 pathogenic or likely pathogenic mutations were identified in the DCM cohort (51%; 35/69). Mutations in the TTN gene were found in 13% of DCM patients (9/69). The yield in clinical criteria positive DCM and ACM patients was 40% (17/43) and 33% (1/3) respectively. The mutational yield in patients who did not completely fulfill the criteria for DCM, HCM and ACM was 36% (8/22), 27% (3/11) and 0% (0/2) respectively. In > 10% of cases two or more (potentially) pathogenic mutations were identified.

**Conclusions:** Targeted NGS results in a substantial increase in the diagnostic yield to generate larger sized grafts and complicated structures. Previously with a mouse ES cell system, we reported that simultaneous stimulation of vascular endothelial growth factor (VEGF) and cyclic adenosine monophosphate (cAMP) signaling in mesoderm cells drastically enhanced EC differentiation (Arterioscler Thromb Vasc Biol 2006;16:835). We have further established an efficient and scalable monolayer high density culture-based cardiomyocyte differentiation protocol from hiPSCs (with modifications on a differentiation method for human ESCs (CiRA), Kyoto, Japan; University of Louisville School of Medicine, Pediatric Heart Research, Louisville, United States of America; Kyoto University Graduate School of Medicine, Department of Cardiovascular Surgery, Kyoto, Japan)

**Background and purpose:** Efficient induction methods of endothelial cells (ECs) from human induced pluripotent stem cell (hiPSC) are essential for vascular regenerative medicine and disease modeling. Recently, ECs are also required to hiPSC-based tissue engineering for organogenesis such as the heart and liver to generate larger-sized grafts and complicated structures. Previously with a mouse ES cell system, we reported that simultaneous stimulation of vascular endothelial growth factor (VEGF) and cyclic adenosine monophosphate (cAMP) signaling in mesoderm cells drastically enhanced EC differentiation (Arterioscler Thromb Vasc Biol 2006;16:835). We have further established an efficient and scalable monolayer high density culture-based cardiomyocyte differentiation protocol from hiPSCs (with modifications on a differentiation method for human ESCs (Lafaille, Nat Biotechnol, 2007) (PLoS One 2011). Combining these methods, here we tried to control hiPSC differentiation to ECs with stage-specific supplementation of VEGF and cAMP.

**Methods and results:** Various concentrations of VEGF and 8-bromo-cAMP were supplemented at time points around the possible mesoderm emergence, then efficiency of EC induction was evaluated with flow cytometry on differentiation day 9 (D9). Vascular endothelial-cadherin-positive EC population was significantly increased with addition of VEGF (100ng/ml, from differentiation D4-9) and transient stimulation with 8bromo-cAMP (1mM, from D4-6) compared to those with VEGF alone; or those without both VEGF and cAMP (56.2±12.5% vs 11.8±7.2% vs 2.3±1.2% of total cells. P=0.000017, n=4). Calculated EC count was also notably increased. On D9, 0.8 ECs were collected through cell sorting from 1 hiPSC. We further modulated the method to once purify VEGF receptor-2 (VEGFR2)-positive cells from hiPSCs by VEGFR2-specific antibody and transgene cAMP. Purified VEGF receptor-2-positive cells gave rise to ECs with more than 99% efficiency at D9. Moreover, yield of ECs at D9 was increased in 4 times than the former method. Purified ECs were able to be recultured and expanded 2.5 times during additional 5 days. Finally, we could obtain 8.5 ECs from 1 iPSCs at D14. This method increased the yield of ECs to 20-folds than previous reports. We confirmed the similar efficiencies of EC differentiation in multiple hiPSC lines with this method. Induced ECs were able to be cryopreserved.

**Conclusions:** We established an efficient and scalable EC differentiation method from hiPSCs based on monolayer and serum-free culture. This method would be applicable to regenerative strategies and modeling for vascular diseases.

**FUNCTIONALLY COMPETENT STEM CELLS – II**

**P624 | BENCH**

**Functionally competent cardiac stem cells can be isolated from patients using endomyocardial biopsies**


Intraoperative infusion of Cardiac Stem Cells (CSCs) isolated from right atrial appendage, resected during CABG is effective in improving left ventricular systolic function and reducing EMB in detectable cardiac cells injected. We sought to develop in vivo, a minimally invasive and reproducible methodology for the isolation and expansion of CSCs from endomyocardial biopsies (EMB) in humans.

In our center, 37 patients with clinically suspected myocarditis (n=22) and/or cardiomyopathy of non ischemic origin including those with infiltrative or connective tissue disease (n=15) underwent either selective LV-EMB (n=28), selective RV-EMB (n=9), or biventricular EMB (n=5) after coronary angiography. Cardiovascular magnetic resonance was performed in all patients. Moreover, EMB were drawn according to intra cardiac ecocardiographic imaging and under 3D-electroanatomic guidance (3-EAM).

Samples not used for diagnostic purposes were enzymatically dissociated, and the unfractio nated cell population was expanded for 22±4 days. In all patients considered, CSC were successfully isolated. After expansion cells were sorted for c-kit: c-kit-positive CSCs were obtained in all patients considered and characterized. At P6, 70% (69±5.3%) of CSCs still expressed c-kit in culture and were negative for markers of hematopoietic and mesenchymal lineage. Only a small fraction of CSCs and non-cardiomyocytes, endothelial or smooth muscle cells contributed to the lineage population. Doubling time was measured and calculated 27.5±2.2 hours. Additionally, at P6, CSC were exposed to a pulse of bromodeoxyuridine and analyzed 12 hours later: 8.1±1.3% CSC were positive for BrdU. Telomere length was measured in CSCs by flow-FISH: telomeres varied from 8.3 to 7.8 kbp, far from telomere lengths associated with replicative senescence and growth arrest.

In the present study, we established the conditions for the isolation and expansion of c-kit-positive CSCs from EMB. 3-EAM guidance allows to accurately identify low voltage areas corresponding to areas of active inflammation or scar tissue, thus improving safety and harvesting performance even in the setting of non-ischemic cardiomyopathies.
expression levels of pluripotency genes could be used as a live screening tool for iPSC generation. We added Nanog- as well as Gdf3-specific NFs on developing iPSC in situ after transduction of murine TTFs. After addition of Nanog-specific NFs subsequent experiments confirmed that colonies with bright fluorescence signal showed enhanced expression of pluripotency markers and elevated differentiation potential into cells of all three germlayers compared to faintly fluorescing counterparts.

Conclusions: Our results show that addition of gene-specific NFs is a powerful tool to evaluate expression of pluripotency markers directly in live pluripotent cell colonies from different species. The NF system appears feasible to identify truly reprogrammed iPS cells based on the intensity of Nanog-specific fluorescence signals. Therefore, the use of NFs during iPSC generation could be a potent and easy to use tool during a high volume and automated iPSC generation process. Further, the addition of gene-specific NFs may be a useful approach to reliably detect any specific mRNA expression in distinct cell populations.

P626 | BENCH

Endothelial progenitor cell conditioned medium as a new possible alternative to cell therapy in tissue regeneration

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Purpose: Endothelial progenitor cells (EPCs) contribute to ischemic tissue repair by secretion of paracrine factors. Our aim was to analyze the effect of hypoxic stress on the pathophysiological status of ischemic tissue, on EPC viability and paracrine secretion and to assess the effect of EPC conditioned medium (EPC-CM) on in vitro and in vivo angiogenesis.

Methods: EPCs were obtained from peripheral blood of healthy donors. To obtain CM, EPCs were cultured in growth-factor free medium for 7 days. To assess the viability of EPCs, 298 proteins were identified by proteomics, comprising factors potentially involved in angiogenesis and 17 proteins significantly upregulated and 12 downregulated as compared to normoxia. Hypoxic upregulation of 6 factors involved in angiogenic pathways (VEGFR2, VEGFA, HIF-1α, HIF-2α, PIGF, PIGF2) was observed. In addition, the expression of the anti-angiogenic factor angiopoietin-2 was increased, leading to the assumption that hypoxic EPCs may contribute to ischemic tissue repair by both pro- and anti-angiogenic pathways.

Results: CM of hypoxic EPCs induced angiogenesis in vitro and in vivo. In vitro, the addition of CM to endothelial cells resulted in increased proliferation and capillary-like tube formation. In vivo, unilateral hindlimb ischemia was induced in adult male Sprague-Dawley rats (n=36), 3 intramuscular injections were performed. Blood flow was monitored at 3 time points, up to 21 d. Explants were also evaluated by histology and immunohistochemistry.

Conclusions: EPC-CM obtained after hypoxic stress may represent an alternative for regenerative therapy of ischemic tissue. Novel therapeutic strategies based on EPC paracrine factors may replace cell transplantation, as “cell-free” therapy could overcome the risk of adverse immunological reactions and the problem of heterologous rejection.

P629 | BENCH

Macrophage-targeted liposomes with hemin improve infarct healing and cardiac function after myocardial infarction

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Aims: Uncontrolled activation of pro-inflammatory macrophages after myocardial infarction (MI) accelerates adverse left ventricular (LV) remodeling and dysfunction, whereas their alternative activation facilitates myocardial regeneration. We sought to determine the effects of hemin formulated in macrophage-targeted liposomes on LV remodeling and function after MI.

Methods and results: We formulated hemin in hyaluronan liposomes (HA-L). Hemin encapsulation efficiency was ~100% at therapeutic dose levels. In vitro, hemin/HAL abolished TNF-α secretion from macrophages, whereas the same doses of free hemin and drug-free liposomes had no effect. Notably, free hemin
polarized peritoneal and splenic macrophages toward M2 anti-inflammatory cells. We next induced MI in mice and allocated them to IV treatment with hemin-HA-L (10mg/kg), empty liposomes, free hemin (10 mg/kg) or saline, 3 days after MI. Efficacy and specificity of infant macrophage targeting was confirmed with HA-L loaded with rhodamine (Fig. 1). LV remodeling and function were assessed by echocardiography before and 30 days after treatment. Significantly, hemin-HA-L increased scar thickness, and attenuated LV remodeling and dysfunction (Fig. 2).

Conclusions: Macrophage-targeted liposomes with hemin switch macrophages into an anti-inflammatory phenotype, and improve cardiac remodeling and dysfunction after MI. Our approach presents a novel strategy to modulate inflammation and improve infarct repair in high-risk patients.

P630 | BENCH
GDF11 enhances proliferation of human cardiac stem cells
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Background: The monumental discovery of c-kit-positive cardiac stem cells (CSCs) challenged the traditional view of the heart as a post-mitotic organ; the human myocardium was shown to continuously renew maintaining cardiac function. Recently, GDF11, a member of TGF-β superfamily, appeared to act as a potent factor to rejuvenate the senescent heart. Although the observed regression of the pathological hypertrophy was attributed to a potential anti-hypertrophic function of the molecule, the underlying mechanism is yet to be elucidated.

Purpose: In the current study, we aimed to examine the potential growth alteration of CSCs stimulated by GDF11, in order to investigate the possibility that CSCs are involved in this rejuvenating process.

Methods: c-kit-positive human CSCs were obtained from discarded surgical specimens and cultured. Moleculard and cellular biological experiments were performed in vitro. GDF11 stimulation was carried out under a starved condition.

Results: The presence of the membrane receptors for GDF11, TGFBR1 and ACVR1B, was demonstrated using BrdU staining (see Fig. 1). Importantly, this effect was attenuated by adding the selective common inhibitor of TGFBR1 and ACVR1B, suggesting that GDF11 functions as a specific ligand of the receptors.

Conclusions: GDF11 might play a role in the rejuvenation of the human heart through the enhancement of CSC proliferation.

P632 | BENCH
Human amniotic fluid-derived stem cells give rise to a homogenous population of fully differentiated cardiomyocytes
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Purpose: Human amniotic fluid-derived stem cells (hAFSC) bring together the differentiation capabilities of embryonic stem cells (ESC) and the therapeutic safety of adult stem cells. Moreover, they avoid the ethical issues specific of the ESC research. Recent studies reported the hAFSC differentiation toward cardiac lineage, with the limitations of high population heterogeneity and low efficiency. Aim of our study was to efficiently differentiate hAFSC into functional cardiomyocytes in vitro.

Methods: hAFSC obtained from second trimester amniocentesis of normal pregnancy were cultured in presence of inducing factors (Ascorbic Acid, 5-Azacytidine, BMP4, ActivinA, VEGF) up to 20 days. The differentiation process was monitored analyzing stem and myocardial specific markers by Western Blotting (WB), immunofluorescent (IF) and cytometric analysis. Cells were also examined with ImageStream that performs simultaneously a protein quantitative detection and cellular localization.

Results: Results obtained by cytometric and ImageStream analyses (Table I) were confirmed by IF, FACS and α adrenoreceptors were also modulated by the differentiation process and some small beating foci (about 8-10% of the plate) were observed.

Table I

<table>
<thead>
<tr>
<th>hAFSC</th>
<th>Differentiated hAFSC</th>
</tr>
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<tbody>
<tr>
<td>Cell positivity (%)</td>
<td>Cell positivity (%)</td>
</tr>
<tr>
<td>CD90</td>
<td>89.3 ± 0.5</td>
</tr>
<tr>
<td>CD105</td>
<td>141.6 ± 45.2</td>
</tr>
<tr>
<td>GATA4</td>
<td>82.5 ± 7.4</td>
</tr>
<tr>
<td>Nkx2.5</td>
<td>84.5 ± 6.5</td>
</tr>
<tr>
<td>Myosin heavy chain</td>
<td>3.7 ± 5.4</td>
</tr>
<tr>
<td>α-Myosin heavy chain</td>
<td>98.7 ± 1.0</td>
</tr>
<tr>
<td>β-Cardiac actin</td>
<td>0.3 ± 1.2</td>
</tr>
<tr>
<td>Cardiac Troponin T</td>
<td>51.0 ± 0.1</td>
</tr>
<tr>
<td>Connexin 43</td>
<td>34.5 ± 8.1</td>
</tr>
<tr>
<td>% Nkx2.5 and Gata4 nuclear positive</td>
<td>9.1 ± 0.9</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. *p<0.05 relative to hAFSC.

Conclusion: This study suggested that hAFSC efficiently differentiate into a homogenous population of cardiomyocytes with cardiac-specific molecular and functional properties.

P631 | BENCH
Multilineage-differentiating stress enduring (Muse) cells regenerate cardiomyocytes and microvessels and improve cardiac function and remodeling after myocardial infarction in rabbits
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Purpose: It has been reported that mesenchymal stem cell fraction in bone marrow aspirates contain pluripotent stem cells, multilineage-differentiating stress enduring (Muse) cells, which can self-renew and can differentiate into the cells with the characteristics of all germ layers from a single cell. We investigated whether intravenously administered Muse cells can be mobilized to the ischemic myocardium, decreases myocardial infarct size and improves cardiac function in rabbit myocardial infarction (MI) model.

Methods: Bone marrow (~1 ml) was harvested from the cavity of the femurs by an aspirator in male Japanese white rabbits. Bone marrow mesenchymal stem cells (BM-MSCs) were cultured and expanded, and then Muse cells were isolated by FACS as cells double positive for SSEA-3/CD105. In a 30-minute coronary occlusion and reperfusion rabbit model, saline (control group, n=10), 3x100000 of autologous hBM cells labeled with GFP (Muse group, n=10), were intravenously infused at 24 hours after MI. The MI size, cardiac function and the general pathology of the heart were evaluated at 2 weeks post-MI. Contocal microscopy was performed to evaluate the regeneration of the myocardium.

Results: The MI size as a percentage of the risk area assessed by TTC staining and Evans blue dye was smaller in the Muse group (18.2±2.1%) than in the control group (30.4±4.9%). The histological assessment of MI size as a percentage of LV by Masson trichrome staining was significantly smaller in the Muse group (13.9±4.9%) than in the control group (27.0±6.4%). Smaller infarct size, smaller left ventricular (LV) dimensions, increased LV ejection fraction and increased dP/dt were seen in the Muse group as compared to the control group at 14 days after MI. The number of CD31-positive microvessels was significantly greater in the Muse group than in the control group. Transplanted Muse cells were preferentially attracted to the infarction border area in the ischemic area. The GFP positive Muse cells were positive for ANP, a specific marker for neonatal cardiomyocyte and troponin I, a specific marker for cardiomyocyte, and positive for CD31, suggesting the regeneration of cardiomyocytes and microvessels from Muse cells.

Conclusions: Muse cells are known to comprise one to several percentage of whole BM-MSCs. Our results suggest that the effectiveness of MSC transplanta
tion currently performed in MI can be substantially improved by selection and full utilization of Muse cells.
Purpose: Obesity is an increasing global health problem. Obese individuals often have a clustering of cardiovascular risk factors such as hypertension, diabetes and dyslipidaemia. A symptomatic patient with significant obesity poses pre-test probability of coronary artery disease (CAD) and are frequently referred for stress testing. These patients can provide significant technical challenges for imaging. Though harmonic and contrast-enhanced stress echocardiography (SE) has been shown to provide excellent feasibility with good diagnostic accuracy, its feasibility and accuracy in significantly obese patients is unknown.

Methods: In this prospective multi-centre study, morbid obesity was defined as body mass index (BMI) >35kg/m². Patient demographics and SE test results were collected. Data on 100 consecutive patients with BMI >35kg/m² undergoing SE was also collected as a control group. SE feasibility was defined as the ability to complete the test and achieve interpretable images for all three coronary territories. Agreement with angiography findings in patients subsequently referred for cardiac catheterization was also evaluated.

Results: Over 13 month period across 3 hospitals, 2930 patients underwent SE, by 12 different operators, of whom 210 (7.2%) had morbid obesity. Mean age was 59yrs, 44% were male and 26% had known CAD. Mean BMI was 39.6kg/m². Of these, 86% were obese patients vs. 95/100 control patients (p=0.78) and with diagnostic image quality obtained in 201/210 (96%) vs. 98/100 (98%) (p=0.71). Of 32 (15%) obese patients with inducible ischaemia, 23 proceeded to angiography and 20 (87%) had corresponding significant CAD vs. 13/13 (100%) in the control group (p=0.17).

Conclusions: Contemporary SE, that incorporates harmonic and contrast-enhanced imaging, demonstrated excellent feasibility and positive predictive value in patients with significant obesity. These results are clinically pertinent given the increasing proportion of such patients sent for non-invasive testing. SE, a widely available, safe and accurate technique, can provide clinically pertinent results, suggestive of coronary ischemia in morbidly obese patients.

P635 | BEDSIDE Association between coronary flow reserve and contractile reserve in type 2 diabetic patients with normal coronary angiography: the role of coronary microvascular dysfunction


Purpose: Diabetes Mellitus (DM) has detrimental effects on the heart even in the absence of epicardial coronary artery stenosis. Aim of our study was to investigate the relationship between coronary flow reserve (CFR), a marker microvascular function in patients with diabetic arteriopathy, and astolic function reserve index (DFRI) and ii) maximum luminal stenosis. Receptor Operating Characteristic (ROC) curve analysis revealed that a recorded isometric threshold value of ≥75 predicted multi-vessel CAD with sensitivity of 90%, specificity of 97%, positive predictive value of 87.5% & negative predictive value of 97.8%.

Conclusion: Ischemic threshold measured during high-dose DSE test significantly correlates with the number of significantly stenosed coronary arteries. However, it does not correlate with the degree of vessel stenosis. Because the studied variables have important prognostic implications, these findings provide further support regarding the utility of DSE in the clinical evaluation of diabetic patients with CAD.

P637 | BEDSIDE Relationship between diabetic retinopathy and subclinical myocardial dysfunction in patients with diabetic mellitus

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Background: Patient with type 2 diabetes mellitus (T2DM) is associated with 2-5 fold higher risk of developing heart failure than those without. One of the proposed pathology leading to this is microvascular dysfunction. In concordance with this hypothesis, diabetic retinopathy, a specific manifestation of microvascular dysfunction, has been shown to be associated with heart failure in patients with T2DM. Nonetheless, the relationship between diabetic retinopathy with myocardial dysfunction is unclear.

Methods: 283 patients (mean age 63±9, 47% male) with type 2 diabetic mellitus (T2DM) without history of cardiovascular diseases was recruited. All patients performed transthoracic echocardiography at rest state and 138 of them received exercise echocardiography. Resting echocardiography parameters including i) conventional echocardiography and ii) speckle tracking derived global longitudinal strain (GLS) were measured. Stress echocardiography parameters including i) diastolic function reserve index (DFRI) and ii) GLS were measured. All patients underwent a full-fledged photography service and each image was analyzed and graded according to the American Heart Association grading classification.

Conclusion: In our study, CAD was significantly associated with contractile reserve, suggesting microvascular dysfunction as one of the pathophysiological mechanisms underlying the reduced increase of longitudinal systolic function during stress in DM patients. The reduction of Dip-derived longitudinal function when it is still normal at rest could represent an early marker of myocardial dysfunction in DM.
Potential to reach this aim, which would be of important clinical impact for early artery plaques in MRI using two different contrast agents against inflammatory summary: effective binding. In addition, the number of bound MPIOs in areas with an imaging to detect this disease entity was put on the anatomy of the vascularis. hether better understanding of the basic biology of cardiovascular disease during the last decades has shifted the interest to molecular markers as potential imaging targets, especially since the degree of stenosis is not the only and most important characteristic to determine the clinical destiny of atherosclerotic plaques. In previous experiments, we could show an elevated expression of vascular cell adhesion molecule 1 (VCAM-1) and glycoprotein VI (GPVI) on the luminal surface of vulnerable, rupture-prone plaques in ApoE−/− mice. Here we aim to translate these data into a human model of atherosclerosis.

Methods: Antibodies against vascular cell adhesion molecule 1 (VCAM-1) and glycoprotein VI (GPVI) were conjugated to microparticles of iron oxide (MPIO), a hypo intense MRI contrast agent. Human carotid endarterectomy specimens from patients with recent symptomatic stroke were perfused ex vivo with these antibodies and imaged before and after contrast agent perfusion, using a small animal 9.4 T MRI system. For the simulation of physiological flow conditions of a stenosed vessel, the specimens were incubated with the contrast agents using a MRI tissue flow chamber. As controls, we used MPIOs conjugated to non-specific IgG antibodies. After imaging, immunohistochemistry was performed for each specimen to prove specific binding of the contrast agent, and the plaque characteristics as well as plaque stage were correlated with the MRI findings of the two contrast agents.

Results: Perfusion of the endarterectomy specimens with the anti-VCAM-1-MPIO contrast agent led to a significant signal reduction in MRI (p=0.014), suggesting effective binding. In addition, the number of bound MPIOs in areas with an increased VCAM-1 staining in histology was significantly higher (p=0.014) than in areas with low VCAM-1 staining. For anti-GPVI-MPIOs, a tendency towards a significant signal reduction was observed (p=0.076). No signal change was seen with the unspecific control MPIOs.

Summary: Aim of this study is the characterization of symptomatic human carotid artery plaques in MRI using two different contrast agents against inflammatory markers of atherosclerosis. Our data for VCAM-1 and GPVI demonstrate the poten delayed healing after infarction remains hardly translationable due to unspecific properties of commonly used imaging agents (e.g., superparamagnetic iron oxide). Experimental settings in mice at 9.4 Tesla have shown that imaging macrophages by labeling them with perfluorocarbon containing nanoparticles (PFC) together with 19F-MRI allowed both also highly specific (“positive”) detection of local inflammation. The purpose of this study was to investigate whether the principles of 19F-MRI for imaging inflammation established in mice are applicable to large animals in a clinical scanner at 3T for possible human translation.

Molecular imaging of inflammatory cells like monocytes/macrophages in myocardial healing after infarction remains hardly translationable due to unspecific properties of commonly used imaging agents (e.g., superparamagnetic iron oxide). Experimental settings in mice at 9.4 Tesla have shown that imaging macrophages by labeling them with perfluorocarbon containing nanoparticles (PFC) together with 19F-MRI allowed both also highly specific (“positive”) detection of local inflammation. The purpose of this study was to investigate whether the principles of 19F-MRI for imaging inflammation established in mice are applicable to large animals in a clinical scanner at 3T for possible human translation. Myocardial ischemia (50 min) was induced in 12 pigs (−65 kg BW) by balloon angioplasty, followed by reperfusion (IR). One day after IR, two different PFC (Perfluoro-15-crown-5-ether, PFCE and perfluorocetyl bromide, PFOB) were applied by intravenous injection (5ml/kg BW) for in vivo labeling of monocytes. At day 4 after myocardial infarction, pigs received gadolinium DTPA (0.1 mmol/kg BW) for late gadolinium enhancement (LGE) and were euthanized 15 minutes later. Thereafter, hearts were removed and perfusion fixed prior to ex vivo imaging of the extent of necrosis (LGE) and local macrophage load (19F-MRI) at 3 Tesla using a flexible fluorine surface coil. Depending on the PFC used, a 3D TSE (PFCE) or a 3D UTE (PFOB) sequence was applied for imaging. Finally, hearts were processed for histology to determine infarct size, border zone and macrophage infiltration. Although the PFC dose applied was lower by factor 4 than in previous studies in mice, we were able to obtain 19F-images of the pig heart with high resolution (4 × 0.5 × 0.5 cm³) and a signal to noise ratio (SNR) of 19.8 within less than 18 minutes. Both PFC compounds exhibited comparable SNR. 19F-MRI revealed that the fluorine signal was distributed patchy across myocardial infarction as delineated by LGE. However, histology revealed an excellent correlation of 19F-Signal with macrophage appearance and frequency. Interestingly, we also found fluorine signal in coronary artery accompanied by inflammation in the vessel wall at the site of balloon angioplasty. The present investigation provides first evidence that the inflammatory response associated with myocardial infarction can be sensitively imaged using 19F MRI at 3T and discriminates different zones of infarct infiltration with macrophages. Thus, 19FMRI holds promise for a future human application.
Methods: Myocardial tissue of 10 male young Lewis rats with EAM (35 days after immunization with 0.25 mg porcine myocardial myosin) was analysed using 1H-MAS-MRS (Bruker 600 MHz). The metabolic profile was compared to fresh (n=7) and frozen (n=8) healthy controls and to the results from histology and immunohistochemistry (CD68). For fresh control samples the spectra were taken less than 10 min after death. Frozen control samples and myocarditis samples were shock-frozen in liquid nitrogen and stored for 4-6 months at −80°C before measurements. After thawing on air, myocardial tissue from a basal-cavity slice of the left ventricle (30-40 mg) excluding epicardial tissue was placed in a 4 mm zirconium rotor, packed homogeneously using a spacer and spun at 4 kHz at 293 K. A water suppression pulse sequence (water presaturation with low-power pulse at 47 dB) was applied to obtain the proton spectrum (ns=128, t=7 min). Spectra were phased (Bruker Topspin) and baseline correction using polynomial fit was applied before derivation of the peak.

Results: The metabolic ratio of taurine to creatine obtained by spectral analysis proved to be a significant biomarker for diagnosis of myocarditis compared to healthy controls (taurine/creatinine ratio in myocarditis: 4.47 (±0.83), fresh control: 2.59 (±0.09), frozen control: 2.59 (±0.28); P < 0.001). Myocarditis was confirmed histologically in all myocarditis samples with an inflammatory cellular infiltrate and CD68 positive staining.

Conclusions: Myocardial taurine/creatinine ratio as detected by proton MRS is able to differentiate between healthy myocardium and myocardium from rats with EAM. This variation may be due to creatine degradation as detected by heart failure and/or an increase in taurine due to its antioxidant activity in inflammatory reactions.

P642 | BESIDE
Prevalence and predictors of dobutamine-related coronary spasm among patients with false positive dobutamine stress echocardiography
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Background and objective: Dobutamine stress echocardiography (DSE) is being consistently used as an exercise-independent stress modality aimed at the detection of coronary artery disease (CAD) and the evaluation of myocardial ischemia. It may though occasionally induce coronary vasospasm. In this study, we aimed to investigate the prevalence and predictors of dobutamine-related coronary spasm in patients without known CAD and false positive DSE (positive DSE but no significant coronary lesions on angiogram)

Methods: 3952 patients referred to our echocardiography laboratory for DSE between January 2010 and May 2012 were prospectively investigated. Those with positive DSE underwent coronary angiograms with systematic methylergometrine intracoronary injection in case of absence of significant coronary stenosis or positive methylergometrine test but no significant stenoses were documented.

Results: 29 patients with DSE-related vasospasm (19.4% of positive DSE without known CAD) were compared with 56 patients with no lesions and no spasm (true negative false positive DSE). They were more frequently smokers (72.4% vs 37.5%; P<0.003); they had more frequently dyslipidemia (79.3% vs 43%; P<0.001); they also had a larger ischemic area at peak DSE (3.4 vs 2.7 segments; p<0.05).

On multivariate analysis, dyslipidemia (HR=6.2; 95% CI= [1.7-21.1]; p=0.004) was found to be an independent predictor of dobutamine-related coronary spasm rather than "true" false positive DSE.

Conclusion: DSE-related coronary spasm is present in a significant proportion of patients with erroneously labeled "false" positive DSE and should systematically be ruled out. Dyslipidemia and active smoking were independent predictors of spasm rather than "true" false positive DSE.

P643 | BESIDE
The predictive value of sub-eardial adipose tissue in metabolic syndrome
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Purpose: The pandemic of diabetes and obesity, particularly visceral obesity is associated with an increased risk for cardiovascular (CV) disease. The detection and clinical value of visceral fat has recently become very topical. Sub-eardial adipose tissue has been reported to be of higher risk for CV disease compared to subcutaneous adipose tissue and study on such an urban population. Methods: A randomly selected cohort of 1428 subjects was studied. Demographic data was collected using the WHO STEPS instrument. Blood samples for biochemistry, together with anthropometry measurements, were collected. Blood pressure and smoking information was performed on all subjects according to published criteria. The metabolic syndrome was classified using the International Diabetes Federation (IDF) criteria.

Results: The prevalence of MS was 47.7% using the IDF criteria, with the most common component being elevated triglyceride levels, documented in 67% of subjects. There were statistically significant echocardiographic differences between subjects with and without MS for chamber dimensions (p<0.001), left ventricular wall thickness (p<0.001) and mass (p<0.001), diastolic indices (E wave (p<0.001) and trans-mitral ratio (p=0.017)) and sub-eardial adipose tissue thickness (p<0.001). Bivariate analysis showed a strong positive correlation between SEA T thickness, visceral adiposity (Rs=0.415) and the MS (Rs= 0.392). The optimal cut-off of 3.7mm in SEA T thickness determined the presence of MS with 64% sensitivity and 80% specificity.

Discussion: The frequency of MS is very high in this population, which is in excess of reported estimates in migrant Asian Indians in other countries. The measurement of SEA T thickness has the potential benefit of predicting the presence of MS during routine examination, with the view to early detection and intervention.
Exercise pulmonary hypertension in secondary mitral regurgitation

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Background: Secondary mitral regurgitation (MR) is a serious and frequent complication of dilated cardiomyopathy and/or coronary artery disease. Patients with left-sided valvular heart disease, exercise pulmonary hypertension (ExPHT) was recently identified as a powerful marker of advanced risk of cardiac event. In secondary MR, exercise PHT is mainly determined by dynamic MR, which is involved in the pathogenesis of acute pulmonary edema (APE). Nevertheless, the impact of ExPHT on outcome in patients with secondary MR is unknown. We hypothesized that ExPHT is an independent predictor of the occurrence of APE, cardiac event and overall mortality.

Method and results: All patients with secondary MR, sinus rhythm, narrow QRS (<120ms) and referred for exercise stress echocardiography with quantifiable exercise systolic pulmonary arterial pressure (SPAP) were included in this study (n=159, 65±11 years, 66% of male). Resting and ExPHT were defined as a systolic pulmonary arterial pressure (SPAP) >50mmHg and >60mmHg, respectively. ExPHT was more frequent than resting PHT (40% vs. 13%, p<0.0001). There was no significant difference between patients with or without PHT regarding demographic and clinical data, as well as medication. Using multiple linear regression, exercise SPAP was determined by resting SPAP (β=0.94±0.01, p<0.0001), exercise MR severity as assessed using regurgitant volume (β=0.58±0.01, p<0.0001), and resting e’-wave velocity (β=1.3±0.4 p=0.004). During a mean follow-up of 35±11 months, 29 APE, 12 myocardial infarction and 23 deaths occurred. The incidence of combined cardiac event was significantly higher in patients with ExPHT as compared to those without ExPHT (2-year: 11±3% vs. 28±6%; 4-year: 20±5 vs. 40.7±% p<0.0001). Similarly, patients with ExPHT had a significantly reduced survival (2-year: 88±4% vs. 99±1%; 4-year: 62.8%±9.42%, p<0.0001). In multivariate Cox proportional Hazard model, after adjustment for age, sex, left ventricular volumes, both resting and exercise diastolic function and resting MR severity, ExPHT remains significantly associated with high risk of combined cardiac event (Hazard ratio=3.7, 95% CI of: 1.9-7.2, p<0.0001).

Conclusion: In patients with secondary MR, ExPHT may be frequent and mainly determined by resting SPAP. LV diastolic burden markers and exercise MR severity, ExPHT is a powerful predictor of poor outcome and is associated with a 3.7-fold increase in risk of cardiac event. These results further highlight the usefulness of exercise stress echocardiography for the management and the risk stratification of these patients.

Discrepancies between ESC and UK NICE guidance for predicted patient outcomes in subjects undergoing dobutamine stress echocardiography

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Introduction: NICE and ESC guidelines place different emphases on the modality of investigation for stable coronary artery disease. NICE recommends stress imaging for patients with pre-test probabilities (PTP) of 30-60% and invasive coronary angiography (ICA) for those with PTP of 60-90% as calculated from the NICE PTP tables derived from the Diamond/Forrester and Duke databases. The ESC guidelines provide their own PTP calculation, which systematically provides more conservative estimations of PTP, and recommends stress testing for those with a PTP of >60%.

Aim and methods: We hypothesised that using the ESC PTPs and adopting an extended role for dobutamine stress echocardiography (DSE) in higher risk patients was safe and obviated the need for unnecessary ICA. We retrospectively reviewed 121 consecutive patients who had a DSE between January to July 2013 in a UK district general hospital. The mean follow-up for MACE (STEMI, NSTEMI, UA, PCI or CABG) was 9.2 months from the date of the DSE.

Results: From the 121 patients 14 (11.6%) had positive DSE and 107 (88.4%) patients had negative DSE. Of the 14 positive DSE patients, 13 patients had at least moderate CAD on angiography that was revascularised (PPV 92.8%). Of the 107 patients with a negative DSE, one patient required three-vessel CABG and MV repair (NPV 99.1%). The PTP was significantly higher when calculated using NICE guidelines compared to ESC guidelines in both positive (91.6% vs 74.8%; p<0.001) and negative (65.5% vs 45.1%; p<0.001) DSE patients. Using the NICE PTP, 78 out of 121 (64.4%) patients should have undergone ICA instead of DSE. From these 78 patients, 14 (17.9%) had positive DSE with 13 (16.7%) had significant CAD on ICA. Using the ESC PTP, 6 out of 121 (0.5%) should have undergone ICA instead of DSE. From these 6 patients, 4 (66.7%) had positive DSE and all had significant CAD on ICA.

Conclusion: Our “real world” data shows that DSE has excellent negative and positive predictive values. The ESC guideline provides a more conservative risk score compared to NICE. Implementation of ESC guidelines in contrast to NICE can help avoid unnecessary invasive coronary angiograms.
terior mitral leaflet (PML). Resting and semi-supine bicycle exercise Dobutamine stress echocardiography were performed and MR was quantitated at rest and exercise with effective regurgitant orifice area (EROA) and regurgitant volume (RV) calculated with the proximal isovelocity surface area (PISA) and the quantitative Doppler methods.

Results: At rest, baseline echocardiographic parameters were not different between the two groups. During exercise, mean EROA and RV were markedly increased in patients with PML prolapse compared to those with AML prolapse. Moreover, exercise-induced change of RVSP was more significant in PML prolapsed compared to AML prolapsed. However, the prevalence of exercise-induced PHTN during the exercise was similar in both groups. Interestingly, PML prolapsed demonstrated more increase in LV cavity volume and LV spherical change during exercise compared with AML prolapse as shown in Table.

Conclusion: During exercise, MR prolapsed is associated with more increase of MR severity, more increased RVSP, and more significant LV remodeling compared to the AML prolapsed in patients with moderate to severe degenerative MR.

P651 | BEDSIDE
The prognostic value of dobutamine stress echocardiography among different ethnic groups
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Background: Cardiovascular disease mortality is different among ethnic groups. Populations referred for dobutamine stress echocardiography (DSE) are increasingly diverse and whether the prognostic information obtained from DSE provides differential information based on ethnicity is unknown. The aim of this study was to investigate the prognostic utility of DSE on non-fatal cardiac events (NFCE) and all-cause mortality in different ethnic groups.

Methods: We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality. We studied 5329 consecutive patients referred for DSE, of whom 8.1% were black, 41.6% were European white, and 50.2% were Indian Asian. End points included NFCE and all-cause mortality.

Results: During exercise stress echocardiography, in 23 (36.5%) patients WMA occurred (group with myocardial ischemia; MI), and 40 (63.5%) subjects were without ischemia (group without myocardial ischemia: NMI). Before starting the ESET, MI group patients had significantly higher values of QTdc (54.2±19.2 vs 39.8±12.4 ms; p<0.005) in comparison to NMI group patients. During the ESET, the QTdc significantly increased in MI group from 54.2±19.2 to 72.5±21.8 ms (p<0.005). In the NMI group there were no significant changes in the values QTdc during ESET (from 39.8±12.4 to 42.3±15.6 ms (p=NS).

Conclusions: Significant increase of QT dispersion is associated with the occurrence of myocardial ischemia during ESET in patients with LGL. This new diagnostic approach, of using QT dispersion, significantly improves the clinical usefulness of ESET in detecting myocardial ischemia in patients with LGL.

P564 | BEDSIDE
Exercise echo has superior cost efficacy compared to exercise ECG for the diagnosis of coronary artery disease in patients with new suspected angina: a randomised prospective study
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Purpose: Exercise Echo (ExECG) is still widely used to assess patients with coronary artery disease (CAD). We hypothesised that Exercise Stress Echocardiography (ExSE), by virtue of its superior diagnostic accuracy and feasibility, will convey a cost advantage over ExECG, when used as first line investigation in patients with new suspected stable angina.

Methods: Consecutive patients referred with suspected angina over a period of one year, with no known history of CAD, normal baseline ECG and a pre-test likelihood of CAD <10%, were randomised to undergo either ExECG or ExSE, on their first attendence. Test results were classified as positive, negative or inconclusive for ischaemia. Patients with positive tests were referred for Coronary Angiography (CA). Patients with inconclusive tests underwent further testing to establish presence of CAD. Cost to diagnosis of CAD was calculated for each patient by adding the cost of all tests up to and including CA, on an intention to treat basis.

Results: During exercise stress echocardiography, in 23 (36.5%) patients WMA occurred (group with myocardial ischemia; MI), and 40 (63.5%) subjects were without ischemia (group without myocardial ischemia: NMI). Before starting the ESET, MI group patients had significantly higher values of QTdc (54.2±19.2 vs 39.8±12.4 ms; p<0.005) in comparison to NMI group patients. During the ESET, the QTdc significantly increased in MI group from 54.2±19.2 to 72.5±21.8 ms (p<0.005). In the NMI group there were no significant changes in the values QTdc during ESET (from 39.8±12.4 to 42.3±15.6 ms (p=NS).

Conclusions: Significant increase of QT dispersion is associated with the occurrence of myocardial ischemia during ESET in patients with LGL. This new diagnostic approach, of using QT dispersion, significantly improves the clinical usefulness of ESET in detecting myocardial ischemia in patients with LGL.

Table 1. Cost to diagnosis of CAD

<table>
<thead>
<tr>
<th>Group</th>
<th>Unit cost (£)</th>
<th>Total cost (£)</th>
<th>Mean cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ExECG</td>
<td>145</td>
<td>202</td>
<td>178</td>
</tr>
<tr>
<td>SE</td>
<td>157</td>
<td>143</td>
<td>146</td>
</tr>
<tr>
<td>ESE</td>
<td>178</td>
<td>193</td>
<td>185</td>
</tr>
<tr>
<td>ExSE</td>
<td>178</td>
<td>193</td>
<td>185</td>
</tr>
<tr>
<td>Number of patients</td>
<td>158</td>
<td>143</td>
<td>146</td>
</tr>
</tbody>
</table>

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ExECC vs. ExSE groups respectively. Patients in the ExSE group had more negative tests 162 (95%) vs. 97 (54%) and fewer positive 7 (4%) vs. 14 (8%) and inconclusive tests 1 (1%) vs. 67 (38%) to those in the ExECC group.

As a result, the mean cost to diagnosis (Table) was significantly lower with ExSE ($259 6) vs. ExECC ($232.9) (p=0.02). All patients with positive ExSE had CAD on subsequent CA (77) compared with only 714 with positive ExECC (p=0.02).

**Conclusions:** In a first randomised study of patients with new suspected angina, ExSE demonstrated significantly lower cost to diagnosis and a higher positive predictive value for detection of CAD when compared to ExECC. This study suggests that ExSE should be the first line investigation in patients with suspected CAD.

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**P655 | BEDSIDE**

Two-dimensional longitudinal strain and torsion for the assessment of coronary artery disease during dobutamine stress echo: clinical tool or merely a research toy

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**Purpose:** The purpose of this study was to determine the diagnostic value of left ventricular (LV) longitudinal strain and torsion in order to diagnose coronary artery disease (CAD) during dobutamine stress echocardiography (DSE).

**Methods:** We studied ninety-two patients (mean age 60.5±11 years, 66 male) with known or suspected CAD, excluding those with prior history of transmural infarction. All of them underwent DSE and coronary angiography within 1 month. Left ventricular 2D global longitudinal strain (GLS) and torsion were measured off-line at rest and peak stress, while the respective differences (GLSΔ, TORSΔ) between rest and stress values were also calculated. Optimal cut-offs were derived from receiver operating characteristics curves (ROC) for strain and torsion values.

**Results:** Mean ejection fraction was 54.9±5.5%. Coronary angiography revealed CAD in 62 patients. Reported values regarding sensitivity, specificity and accuracy for DSE were 78%, 76% and 77% respectively. Global longitudinal strain (GLS) and torsion were measured off-line at rest and peak stress, while the respective differences (GLSΔ, TORSΔ) between rest and stress values were also calculated. Optimal cut-offs were derived from receiver operating characteristics curves (ROC) for strain and torsion values.

**Conclusions:** The combined assessment of the LV longitudinal strain and torsion during DSE could serve as an adjunct method for the echocardiographic assessment of CAD with high accuracy.

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**P656 | BEDSIDE**

A nationwide study on the utilization of stress echocardiography

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**Purpose:** Looking at non-invasive diagnostic methods in cardiology, stress echocardiography (SE) scores highly regarding sensitivity and cost-efficiency. Up to date no study has investigated the impact of genetic and environmental effects on left ventricular deformation profile.

**Methods:** We recruited 51 twin pairs (22 monozygotic and 29 same-sex dizygotic twin pairs, mean age 56.9±9 years). Siblings with coronary artery disease, any cardiomyopathy or severe valvular disease were not included. Beyond standard echocardiographic protocol, parasternal short axis- and apical views optimized for speckle tracking analysis were obtained. Using dedicated software (TomTec 2D Cardiac Performance Analysis), global circumferential (GCS), longitudinal (GLS) and radial (GRS) strains were calculated by averaging the segmental values of the 16 LV segments. Apical counter-clockwise, basal clockwise rotation and their net difference, the LV twist were also measured.

**Results:** The intraclass correlation coefficients for GCS were 0.94 for monozygotic twins (95% CI: 0.89 to 0.98) and 0.34 for dizygotic twins (0.18 to 0.52). After adjusting for age and sex, the univariate additive genetic (A), common (C) and unique (E) environmental effects model showed 94% genetic component in the variance of GCS (88 to 98%). Similarly high, but dominant genetic effects (D) were found regarding GLS, GRS, apical rotation, basal rotation, and twist (D: 91, 87, 81, 91 and 88%, respectively). Unique environmental effects were responsible for the rest of the variance (E: 6-19%). Common environment had no influence on these variables.

**Conclusions:** Clearly demonstrated a very dominant heritability of the LV deformation parameters with similar strength in all directions. Role of common and unique environmental factors is scant. These results urge to search for the responsible genes determining LV deformation.
peak LVF was lower than the baseline value. Patients were then followed-up for the composite end point of all-cause mortality or hospitalization for HF.

**Results:** At peak stress, LVF was 35±14 m/s² in patients with up-sloping FFR (n=70) and 17±6 m/s² in those with biphasic or flat FFR (n=30) (p<0.0001). During a mean follow-up of 710 days, there were 14 deaths and 14 hospitalizations for worsening HF. Using univariate and by segmental hazard analysis, the ratio of mitral blood flow to myocardial early diastolic velocities (E/e') (p<0.0001), LV EF (p=0.010) and abnormal FFR (p<0.0006) were associated with the combined end point. E/e' (p=0.0002) and abnormal FFR (p=0.008) were the only independent predictors of the adverse outcome of all-cause mortality or HF hospitalization. In patients categorized according to the FFR, those with an up-sloping response showed a significantly greater survival free from HF hospitalization than those with an abnormal FFR response at Kaplan-Meier survival curves (log rank test: p<0.032).

**Conclusion:** The ultrasound evaluation of the FFR during exercise stress echo-cardiography, as assessed from Newton’s second law, is an easy way to generate the FFR slope that can be used for the prognostic stratification of patients with advanced HF.

**P660 | BENCH**

**Treatment with anti-IL12/23 agents improves fetuin and oxidative stress in patients with endothelial glycocalyx, coronary function and myocardial twisting in patients with psoriasis**

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Fetuin inhibits vascular calcification. The role of treatment with biological agents on fetuin, oxidative stress, vascular and LV function in psoriasis is unclear.

**Methods:** 101 patients (age: 50±12yrs) with psoriasis (PS) (PASI-disease activity score) score=5.9±4.5) were randomized to an anti-TNFα (n=52), an anti-IL-12/23 regi-men (n=32) or a combined cyclosporine and methotrexate (n=38). At baseline and after 4 months of treatment, we measured a) augmentation index (AI) and central systolic blood pressure (cSBP); b) flow-mediated dilation (FMD); c) twisting (T w) and peak twisting (Tw-peaked) velocity, untwisting at mitral valve opening (unT w) and untwisting (unTw) velocity using speckle tracking echocardiography; d) coronary flow reserve (CFR); e) perfused boundary region (PBR) of the sublin-guvaral arterial microvessels (5-25 microns) using Sideview Darkfield imaging. The PBR includes the most luminal part of glycocalyx that does allow cell penetration. Increased PBR is an accurate index of reduced endothelial glycocalyx thickness because of a deeper RBC penetration in glycocalyx; fetuin and malondialdehyde serum levels (MDA).

**Results:** At baseline decreased fetuin and increased MDA were related with PASI (r=0.29 and r=0.30), PBR (r=-0.46 and r=0.28) and FMD (r=0.46 and r=-0.28) (p<0.05). PBR was related with PASI (r=0.25), cSBP (r=0.46, AI (r=0.32) and CFR (r=-0.35) (p<0.05). Increased MDA was with related reduced Tw (r=-0.42), unTw velocity (r=0.32) and unTw (r=-0.37) (p<0.05). Compared to base-line patients a) on anti-IL-12/23 had higher fetuin (28±6 vs. 28±32), cSBP (120±7 vs. 15±6), AI (15±6 vs. 17±7), T w (15±6 vs. 17±5), unT w velocity (97±45 vs. 110±48), unTw (8.3±3 vs. 9.4±3) and unT w velocity (100±44 vs. 120±60) (p<0.05). No differences between anti-TNFα and anti-IL-12/23 were detected. Af-ter treatment, patients on cyclosporine and methotrexate had no change in FMD, CFR and glycocalyx but an increase in AI, cSBP, T w and unT w velocity (p<0.05).

**Conclusion:** Decreased fetuin and increased oxidative stress are related with vascular and myocardial dysfunction.Treatment with anti-IL12/23 regimen improves fetuin levels and oxidative stress in addition to endothelial glycocalyx and vascular function leading to improved LV myocardial twisting.

**P661 | BEDSIDE**

**Evaluation of left atrial function using 2D speckle tracking echocardiography in patients with diabetes mellitus and diastolic dysfunction:**

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**Aim:** To evaluate left atrial (LA) function as assessed by strain derived from 2D speckle tracking echocardiography (SD-STE) and its association with markers of left ventricular diastolic dysfunction (LVDD) in patients with diabetes (DM) and preserved left ventricular ejection fraction (PLVEF).

**Methods:** A total of 113 age- and gender-matched pts with LVDD and PLVEF divided according to the presence of DM (55 with and 58 without) were enrolled in the study. Maximal LA volumes, LA ejection fraction as well as transmural inflow, pulmonary vein flow, and pulsed-wave Doppler tissue imaging parameters (DTI) were measured as expressions of LVDD. Peak atrial longitudinal strain (PALS) and time to peak longitudinal strain (TPLS) were measured using a 12-segment model for the LA. Values were obtained by averaging all segments (global PALS and TPLS). Comparison of LA dimension, LA volumes and LAAF as well as traditional transmural inflow parameters between pts with and without DM showed absence of significant differences although those with DM had values in addi-tion to more severe diastolic dysfunction. Average E/e' ratio was significantly higher in DM pts in comparison to pts without DM (p<0.031). The 4-chamber average PALS and global PALS were significantly lower in patients with DM compared to those without (20.61±1.7 vs. 24.33±7.8% vs. 24.14±6.6%, p<0.01; respectively). As for TPLS only 4-chamber average value was significantly shorter in patients with DM in comparison with those without (509.93±64.37 ms vs. 533.32±53.59 ms: p=0.036). In pts with DM global PALS correlated significantly with sepal (-0.367, p<0.0001), lateral (-0.207, p=0.027) and average E/e'ratio (-0.297, p=0.001). Logistic regression analysis showed that global PALS (OR = 0.928, 95% CI 0.874-0.985; p=0.015) and 4-chamber TPLS (OR = 0.993, 95% CI 0.987-1.000; p=0.044) were significant independent predic-tors of DM presence.

**Conclusion:** LA deformation mechanics are impaired in pts with diabetes mel-litus and diastolic dysfunction with preserved left ventricular ejection fraction. 2D speckle tracking echocardiography appeared as a useful additional tool for detec-tion of LA dysfunction in these patients especially prone to develop cardiovascular complications.

**P662 | BENCH**

**Myocardial strain and ventricular-arterial coupling in a rat model of heart failure with preserved ejection fraction**

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**Purpose:** Arterial stiffening and ventricular-arterial (VA) coupling has been pro-posed causative role in development of hypertensive heart failure, however, the analysis of association with myocardial strain is lacking.

**Method:** Dahl salt-sensitive rats were fed with high-salt (HT group, n=23), and with low salt (control group, n=24) from week 6. At week 10, 14, 18 and 20, speckle tracking echocardiography and invasive hemodynamic evaluation using conductance catheter were performed. Simultaneously, arterial pressure and stroke volume were measured to derive VA coupling as arterial to ventricular end- systolic elastance (Ea-Ees).

**Results:** In HT groups, blood pressure and left ventricular weight were gradu-ally increased and lung weight significantly increased from weeks 18, suggesting congestive heart failure development. Global longitudinal strain progressively im-paired from week 8 to 20, and circumferential strain and ejection fraction impaired from week 18. The Ea rose gradually and significantly elevated at weeks 18 in HT group compared to control (2.5±±1.2 vs. 7.0±3.3 mmHg/ml, p=0.018), while Ees showed no significant change during protocol.

**Conclusion:** Global strain was negatively correlated with LV end-diastolic %area fibrosis (r=-0.55, p=0.034, r=-0.69, p=0.029, respectively) and global longitudinal strain (r=-0.43, p=0.002, r=0.334, p=0.035, respectively), but not with circumferential strain.

**P663 | SPOTLIGHT**

**Native T1 values discriminate between health and disease in acute and convesal stage of disease in clinically suspected myocarditis**

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**Purpose:** Myocarditis is an important cause of morbidity and mortality. Charac-terised by a wide spectrum of clinical presentation, detection of disease can be chal-lenging and management pathway uncertain. T1 mapping by cardiovascular magnetic resonance (CMR) provides tissue-dependent relaxation times in line with the underlying composition. It may reflect evolution of disease and support clinical diagnosis independently of the stage of disease. Moreover, T1 mapping showed significant relation with LV end-diastolic %area fibrosis (r=0.55, p=0.034, r=0.69, p=0.029, respectively) and global longitudinal strain (r=0.43, p=0.002, r=0.334, p=0.035, respectively), but not with circumferential strain.

**Conclusion:** Global strain impairment may reflect elevated arterial stiffness, then may suggest abnormal VA coupling in hypertensive heart failure.
T2 values quantification was excellent (intra: r=0.978; P<0.001 and inter: r=0.948, P<0.001). Compared to controls, T2 values in remote myocardium were significantly different for acute myocarditis only (T2, msec: 48 ± 9 vs 51 ± 5, P<0.0001), whereas T2 values in involved myocardium differed between all groups. T2 values of complete M sepAI or involved areas were identified as the independent discriminators between active and chronic myocarditis. T2 values were concordant with T2 edema ratio (T2 involved, r=-0.42, P<0.001) and with native T1 (r=0.55, P<0.001). Inter and intra-observer reproducibility of T2 values quantification was excellent (intra: r=0.978; P<0.001; mean difference (MD): -0.05±1.18; inter: r=0.948, P<0.001; MD: ±0.01±2.5).

Conclusion: We demonstrate that quantitative T2 values are increased in patients with myocarditis. We further demonstrate that average mSAX and involved myocardium differed between all groups (T2, msec: 48 ± 9 vs 51 ± 5, P<0.0001). Similar, maximum P-wave duration and PWD were significantly longer in patients with sarcoidosis than control subjects (96.7±15.4 vs 94.7±17.1 ms, P<0.001, respectively).

Background: Cardiac involvement in pulmonary sarcoidosis is associated with adverse prognosis. The frequency and pattern of cardiac involvement in sarcoidosis patients without cardiac symptoms, however, is unclear. The aim of the present study was to screen patients with proven pulmonary sarcoidosis for potential cardiac involvement by cardiac magnetic resonance imaging (CMR) including late gadolinium enhancement (LGE) and to describe frequency and pattern of abnormalities.

Methods: We prospectively studied 76 patients with biopsy-proven pulmonary sarcoidosis (48.7% female, age 48.0±12.7 years, time since diagnosis of pulmonary sarcoidosis 6.7±6.2 years). Patients were followed for 21±10 months. Endpoints were defined as death and ventricular tachycardia (VT).

Results: All patients had normal systolic left and right ventricular function. CMR revealed positive LGE in 62 patients (81.6%). Only 14 patients (18.4%) had no LGE at all. 26 patients (34.2%) had minimal lesions (<2% LVM mass of left ventricular mass (LVM)). These 26 patients were also considered LGE negative. Two patterns of LGE were found. Type A: midmyocardial LGE in the left ventricular free wall (7 patients, 9.2%, LGE mass 3.5±2.7% of total left ventricular mass). Type B: LGE at the septal insertion of the right ventricle (29 patients, 38.2%, LGE mass 3.2±0.9% of total left ventricular mass). During follow-up 2 patients had documented VT (2.6%, both with type A lesions), but no sustained VT or death occurred.

Conclusions: The present prospective study shows that positive LGE is frequent in patients with systemic sarcoidosis and normal left ventricular function. However, LGE mass was limited (3.5±1.4% of LVM on average). The value of the small amount of LGE in patients with systemic sarcoidosis, who are otherwise healthy, remains to be determined, but mid-term prognosis appears to be good.

P665 | BEDSIDE

Assessment of atrial conduction time in patients with sarcoidosis

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Objective: Sarcoidosis is an inflammatory granulomatous disease of unknown etiology that involves multiple organ systems. Myocardial involvement is usually associated with poor prognosis but diagnosis of cardiac sarcoidosis is frequently difficult. The aim of this study was to investigate the atrial conduction time in patients with sarcoidosis by using high-usefulness tissue Doppler echocardiography (TDI).

Method: The study population included 49 patients with sarcoidosis (19 men; mean age, 40.5±9.8 years, and mean disease duration = 35.7±15.3 months) and 45 healthy control subjects (17 men; mean age = 40.7±7.2 years). From the 12-lead electrocardiogram P wave dispersion (PWD) was calculated. The timing of atrial contractions (PA) was measured as the intervals between the onset of P wave on electrocardiogram and the beginning of A-wave on TDI and atrial electrical delay (med) was calculated from the lateral (P1) and septal (PA septal) mitral annulus, and lateral tricuspid annulus (PA tricuspid).

Results: PA lateral and PA septal were significantly longer in patients with sarcoidosis than control subjects (67.9±16.1 vs 56.3±13.1, p<0.001 and 54.8±15.2 vs 45.1±14.2 ms, p=0.002, respectively). Intratrial (PA septal – PA tricuspid) and intratral (PA lateral – PA tricuspid) electrical delay (med) were significantly higher in sarcoidosis groups (12.6±7.5 vs 8.0±7.1, p<0.003 and 25.7±9.8 vs 19.3±7.7 ms, p<0.001, respectively). There were significant positive correlations between the disease duration and interatrial EMD (r = .56, p < .001) and intraatrial EMD (r=0.6, p<0.001).

Conclusion: Atrial EMD was found prolonged in patients with sarcoidosis. We have also demonstrated that PWD, inter- and intraatrial EMD were significantly correlated with disease duration. This study calls attention to measurement of atrial conduction time that may be clinically helpful in the recognition of cardiac involvement.
IMAGING AND VALVULAR HEART DISEASE

P669 | BEDSIDE
Three-dimensional strain in patients with aortic stenosis: a prognostic study
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Objectives: We hypothesized that global longitudinal strain (GLS) by 3D speckle tracking echocardiography (3DSTE) will be a significant predictor for future major cardiovascular events (MACEs).

Background: 2D GLS in patients with severe aortic stenosis (AS) and preserved left ventricular ejection fraction (LVEF) provides useful prognostic information. However, 3D strains by 3DSTE have not been studied extensively the usefulness for prognosis.

Methods: 3D echocardiographic volumetric measurements and strain analysis were performed in 108 AS patients with preserved LVEF and 62 normal subjects. MACEs were recorded in AS group. Using receiver operating characteristics with GLS of -14%, we performed survival analysis between symptomatic patients and asymptomatic patients.

Results: All strain components were significantly impaired in patients with AS compared to control subjects. During a mean follow up of 493 days, 46 AS patients had MACEs. GLS was significantly impaired in patients with MACE compared to those without MACE. Kaplan-Meier survival analyses showed GLS provides a significant difference in MACE rate in asymptomatic AS patients (p=0.0204).

Conclusions: In patients with severe AS, 3DSTE determined GLS is a powerful predictor of future MACEs in asymptomatic AS patients.

P670 | BEDSIDE
Evaluation of mitral regurgitation severity by proximal isovelocity surface area (PISA) method using cardiac magnetic resonance imaging 3D velocity vectors
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Purpose: Mitral Regurgitation (MR) is generally assessed semiquantitatively by echo-Doppler. The PISA method can be used for quantitative evaluation however it is based on simplistic assumptions, including hemispheric geometry. Cardiac magnetic resonance (CMR) enables detailed 3D evaluation of flow vectors making it theoretically suitable for MR quantification without any assumptions. We aimed to test the feasibility of calculating MR regurgitant volume (RVol) by the PISA approach, using CMR 3D velocity vectors, compared to Doppler and CMR volume-based RVol.

Methods: In a prospectively designed study, 19 patients with various grades of MR underwent CMR and echo-Doppler on the same day. By CMR, multiple slices were obtained parallel to the mitral valve by phase-contrast imaging, as well as short-axis cine images for left and right ventricular volume measurements. The area of proximal flow convergence was identified and, using dedicated software, the perimeter was automatically measured for each temporal phase. The 3D-RVol was calculated as the sum of PISA perimeters throughout systole, multiplied by slice width. CMR Volume-based RVol was calculated as the difference between left and right ventricular stroke volumes.

Results: For mild, moderate and severe MR, 3D-RVol was 20±11ml, 52±26ml and 82±38ml compared to Doppler-RVol 27±9ml, 38±18ml and 116±52ml. CMR 3D-RVol correlated well with Doppler-RVol (r=0.78) and with Volume-based RVol (r=0.77). On average 3D-RVol was 13ml less than Doppler-RVol, but 18ml larger than CMR-volume-based RVol. The observed 3D shape of the PISA envelope by 3D-CMR was closer to a hemiellipsoid than a hemisphere.

Conclusions: Three-dimensional echocardiography allows dynamic and detailed measurement of the distances between PM heads. These measurements depicted reduced mobility of PM heads in FMR not only inter but also intra PM direction. These findings should be taken into consideration in planning mitral valve repair targeting submitral apparatus for FMR.

P671 | BEDSIDE
Insights from three-dimensional transesophageal echocardiography into the cyclic motion of papillary muscle heads: inter and intra papillary muscle
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Background: Functional mitral regurgitation (FMR) is associated with altered dynamics of the mitral valve apparatus. Accurate characterization of changes in papillary muscle (PM) motion may contribute to better understanding of the specific pathology and thus help pre-surgical planning. The purpose of this study was to investigate the changes in the distance between PM heads of inter (=between anterior PM and posterior PM) and intra PM (=between anterior and posterior heads of each individual PM) in FMR using three-dimensional transesophageal echocardiography (3DTEE).

Methods: In 31 subjects [65.3±13.0 years old, 15 normal subjects (CTL) and 16 patients with FMR, volume datasets of submitral apparatus were acquired using 3DTEE from the transgastric approach. Using a commercially available quantitative software (4D Cardio view, Tom Tec), the coordinates of the point of each PM head that supports either the anterior leaflet or the posterior leaflet were obtained manually and the distance between the two heads was measured throughout the cardiac cycle.

Results: (Figure) In patients with FMR, the maximum distances of inter PM were significantly longer than CTL, while the distances of intra PM were not. On the other hand, all the minimum distances of inter and intra PM were longer in patients with FMR than CTL.

Conclusion: This feasibility study suggests that CMR-based 3D-PISA may be able to assess MR severity quantitatively without any geometric assumptions.
P672 | BEDSIDE
Gender difference in ventricular response to aortic stenosis: insight from cardiovascular magnetic resonance
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Aims: Although left ventricular hypertrophy (LVH) and remodelling is associated with cardiac mortality and morbidity, little is known about the impact of gender on the ventricular response in aortic stenosis patients. This study aimed to analyze the differential effect of gender on ventricular remodelling in moderate to severe AS patients.

Methods and results: A total of 118 consecutive patients (67±9 years; 63 males) with moderate or severe AS (severe 81.4%) underwent transthoracic echocardiography and cardiovascular magnetic resonance (CMR) within a 1-month period in this two-centre prospective registry. The pattern of LV remodelling was assessed using the LV mass index (LVMi) and LV remodelling index (LVRi; LV mass/LV end-diastolic volume) by CMR. Although there were no differences in AS severity parameters nor baseline characteristics between genders, males showed a significantly higher LVMi (102.6±29.1 g/m² vs. 86.1±29.3 g/m², p=0.003) and LVRi (1.1±0.2 vs. 1.0±0.3, p=0.018), regardless of AS severity. The LVMi was significantly associated with aortic valve area (AVA) index and valvuloarterial impedance in females, whereas it was not in males, resulting in significant interaction between genders (Pinteraction=0.007/0.014 for AVA index/valvuloarterial impedance, respectively). Similarly, the LVRi also showed a significantly different association between male and female subjects with the change in AS severity parameters (Pinteraction=0.033/0.001/0.029 for AVA index/transaortic mean pressure gradient/valvuloarterial impedance, respectively).

Conclusion: Males are associated with greater degree of LVH and higher LVRi compared to females at moderate to severe AS. However, females showed a more exaggerated LV remodelling response, with increased severity of AS and hemodynamic loads, than males.

P673 | BEDSIDE
Wilkins’ score as predictor of thromboembolic events in rheumatic mitral stenosis and normal sinus rhythm
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Purpose: Wilkins’ score is a widely used echocardiographic tool in evaluation of mitral stenosis (MS). It predicts the feasibility of balloon mitral valvuloplasty (BMV) through grading mitral valve leaflets mobility, thickening, calcification and sub-valvular involvement. Recent data suggest its utility as a predictor of atrial fibrillation (AF) in isolated MS. We examined the score as a predictor of left atrial (LA) thrombus formation and embolization in isolated MS and normal sinus rhythm (NSR).

Methods: Our study included 79 patients with isolated rheumatic MS in NSR. Case group (n=36) included patients with history of prior embolic events; while control group (n=43) included patients without history of embolization. All the studied population underwent history taking, clinical examination and ECG to rule out AF and confirm embolic manifestations. All patients underwent both transtheracic and transthoracal echocardiogram. Mitral valve area was measured using both planimetry and PHT. In addition to Wilkins’ score evaluation, LA volumes (LAV) were measured using both area-length and prolate-ellipsoid methods; LV maximum (end systolic; Vmax), LV minimum (end diastolic; Vmin) and LAV at onset of atrial systole (end of P wave on surface ECG;Vp) were measured by the two methods. We graded the spontaneous echo contrast (SEC) from 0 to 4+ according to its density, presence inside LA or LAA and its persistence throughout the cardiac cycle. LAA emptying velocity (LAAeV) was calculated.

Results: 53 (68.3%) were females. Both groups were age and gender matched and had comparable degree of MS. The case group had significantly higher Wilkins’ score than the control group (p=0.002). Wilkins’ score was positively correlated with SEC grade and the presence of LA thrombus (+0.374, p=0.001 and +0.340, p=0.002 respectively). However, it was negatively correlated with the LAAeV and the LAA FAC (+0.255, p=0.023 and +0.232, p=0.04 respectively). ROC analysis revealed that Wilkins’ score ≥8 had a sensitivity of 58% and a specificity of 75% for the prediction of thromboembolic events in rheumatic MS and NSR (AUC=0.681; 95% CI of 0.562-0.8). LAV was not statistically different between both groups.

Conclusion: The pathological affection of mitral valve; rather than degree of stenosis or LA enlargement; predicts thromboembolic risk in MS and NSR. Wilkins’ score may be a predictor of thromboembolic events in rheumatic MS and NSR. We recommend anticoagulant therapy in patients with MS and NSR if Wilkins’ score is ≥8.

P674 | BEDSIDE
Focused cardiac ultrasound for rheumatic heart disease screening: a prospective systematic evaluation of a simplified approach
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Background: Rheumatic Heart Disease (RHD) remains a major public health problem in the developing world. While early diagnosis by ultrasound may have a key role in developing active surveillance, systematic evaluation of simple approaches in resource poor settings are needed.

Methods: We prospectively compared Focused Cardiac Ultrasound (FCU) to a reference approach for RHD screening. FCU included (i) the use of a pocket-sized echocardiography machine, (ii) non-expert staff (two nurses with specific training), and (iii) a simplified set of echocardiographic criteria. The reference approach used high-technology portable echocardiography, a standardized echocardiographic examination reviewed by an expert cardiologist according to 2012 World Heart Federation criteria.

Results: Among the six different echocardiographic criteria first tested in a preliminary phase among 189 selected children, mitral regurgitation jet length ≥2cm or any aortic regurgitation was considered best suited to be FCU criteria, and was then prospectively used in school children. Mean scanning time per simplified echocardiogram was 5.9 min (1.7) and 7.0 min (1.9) for the two nurses, and 6.5 min (2.6) for the standard echocardiography. Of the 1,217 subjects enrolled (mean 9.6±1 years, 49.6% male), 49 (4%) were diagnosed with RHD by the reference approach. The sensitivity of FCU for the detection of any RHD was 83.7% (95% CI 73.3-94.0) and 77.6% (95% CI 65.9-89.2) according to nurses A and B, respectively. The combined criteria yielded a specificity of 90.9% (95% CI 89.3-92.6) and 92.0% (95% CI 90.4-93.5) according to users (kappa test 0.57). When restricted to definite RHD, the sensitivity increased to 93.3% (95%CI 80.7-100) and 86.7% (95%CI 69.5-100) according to users (kappa 0.53).

Conclusions: FCU by non-experts and using pocket-devices appears feasible and yields acceptable sensitivity and specificity for RHD detection when compared to a state-of-the-art approach. Mass screening for RHD in low-resource settings could be a viable option.

P675 | BEDSIDE
Does 3D echo impact upon the assessment of aortic valve stenosis using the continuity equation?
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Purpose: Quantification of true severity of aortic stenosis (AS) can be challenging; as the continuity equation (CE) relies on many assumptions, including the conservation of left ventricular outflow tract cross sectional area (LVOTr CSA). The aim of this study was to evaluate the clinical impact of 3D direct measurement of LVOT CSA, free from geometrical assumptions, on the assessment of the severity of AS using CE.
Results: 28 (56%) patients were male, 35 (70%) had good left ventricular systolic function. Mean (±SD) BSA was 1.7±0.2 m². Mean (±SD) AV gradient was 45±16 mmHg. There was a good correlation between AVA by 2D TTE [mean (±SD)=0.40±0.085 cm²/m²] and 2D TEE(0.40±0.088 cm²/m²) (r=0.85); and between 2D TTE and 3D TEE(43.0±0.11 cm²/m²) (r=0.7). However 2D TTE measurements were significantly underestimated L VOT compared to 3D TEE (p=0.007); equally 2D TEE compared to 3D TEE (p=0.001). The severity of AV was reclassified from severe to moderate using 3D L VOT CSA in 6 patients (12%) and from critical to severe in 5 (10%). 22% patients were reclassified.

Conclusions: Measuring L VOT CSA by 3D echo results in reclassification of AV severity in a significant number of patients as 3D avoids the potentially incorrect geometrical assumption of circularity of the L VOT.

P676 | BEDSIDE Direct measurement of proximal isovelocity surface area by single-beat three-dimensional color doppler echocardiography in mitral regurgitation

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Introduction: Two-Dimensional (2D) Proximal Isovelocity Surface Area (PISA) method has some technical limitations, mainly the geometrical assumptions of PISA shape required to calculate Effective Regurgitant Orifice Area (EROA). Recently developed single-beat real-time Three-Dimensional (3D) color Doppler imaging allows direct measurement of PISA without geometrical assumptions. Our aim is to validate this novel method in patients with chronic Mitral Regurgitation (MR).

Methods: Thirty-three patients were included: 25 (75.7%) had degenerative MR and 8 (24.2%) functional MR. EROA and Regurgitant Volume (RV) were assessed by transthoracic 2D and 3D-PISA methods. Quantitative Doppler method and 3D TEE planimetry in classifying severe MR. Good intra- and interobserver agreement for 3D-PISA measurements was observed, with an intraclass correlation coefficient of 0.93 and 0.90 respectively.

Conclusions: Measuring L VOT CSA by 3D echo results in reclassification of AV severity in a significant number of patients as 3D avoids the potentially incorrect geometrical assumption of circularity of the L VOT.

P677 | SPOTLIGHT Assessment of liver stiffness in patients with tricuspid regurgitation: relationship with disease severity

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Objective: Tricuspid regurgitation (TR) is known to be associated with liver cirrhosis. However, the pathophysiological effect of TR, right ventricular systolic pressure (RVSP) and the right ventricular (RV) function on the liver remains uncertain. The aim of this study was to evaluate the association between TR severity and the stiffness of liver.

Methods: A total of 105 patients with various degrees of (mild to severe) TR secondary to left heart disease were enrolled. Patients were divided into two groups based on their TR severity: 40 patients with mild-moderate TR (effective regurgitant orifice [ERO]≤0.4 cm²) and 65 patients with severe TR (ERO>0.4 cm²). Detailed transthoracic echocardiography was performed in all subjects. LV ejection fraction (LVEF), RVSP and RV systolic function assessed by tricuspid annular plane systolic excursion (TAPSE) were measured. Fibroscan transient elastography was used to estimate the level of liver stiffness and the threshold of significant fibrosis was defined as 7.5 kPa.

Results: There was no significant difference in age, gender and LVEF between patients with mild-moderate and severe TR. Compared to patients with mild-moderate TR, patients with severe TR had higher RVSP (50.17±14.48 vs. 20.78±11.93 mmHg, p<0.001) lower TAPSE (1.62±0.38 vs. 1.78±1.04 cm, p=0.042), and higher value of liver stiffness (20.83±14.46 vs. 9.14±7.02 kPa, p<0.001). Liver fibrosis was found in 16 (40%) patients with mild-moderate TR and 59 (89.8%) patients with severe TR. ERO was significantly correlated with liver stiffness (R=0.81, 95% confidence interval [CI] 0.81 to 12.3, p<0.001). In multivariate analysis, adjusting for age, TAPSE, LVEF and RVSP, ERO remained independently predictive of liver fibrosis (B=10.39, 95%CI 8.77 to 12.0, p<0.001).

Conclusions: Patients with TR have increased liver stiffness measured by fibroscan and was related closely with the severity of the TR, ERO remained an independent predictor of liver fibrosis in these patients after multivariable adjustment.

P678 | BENCH The echocardiographic and cardiac magnetic resonance grading of left ventricular dilatation and function is comparable in patients with severe aortic and mitral regurgitation

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Background and aims: Left ventricular (LV) size and ejection fraction (LVEF) is an independent predictor of liver fibrosis in these patients after multivariable adjustment.

Methods and results: Eighty-five individuals (AR, n=31; MR, n=34; controls, n=20) underwent prospectively echocardiography and CMR within 4 hours. The LV end-diastolic (EDV) and end-systolic volumes (ESV) by CMR (short-axis stack) and RT3DE (voxel counts) were measured in the papillary musculs and trabeculae included in the cavity. Volume by 2D was measured including the papillary muscles but excluding the trabeculae. For each patient, the expected EDV were predicted based on reference values and the Z-score (expected-observed/SD) was calculated. Volume assessment by 2DE was performed in 96% and by RT3DE in 71% of the patients and of these had 62% severe LV dilatation (Z-score>-5). Both 2DE and RT3DE significantly underestimated volumes (Figure). The LVEF was underestimated by RT3DE (mean difference ±SD: -7.8±5.4%, p<0.0001), but not by 2DE (mean difference ±SD: -5.5±4.4%, p=0.50). The agreement between 2DE and CMR was good for the categorical grading of LV
dilatation (normal, mild-moderate and severe, weighted kappa=0.77) and LVEF (<50%, 50-60% and >60%, weighted kappa=0.64).

Conclusions: The grading of severity of LV dilatation and function by 2DE is comparable with CMR. Compared with RT3DE, 2DE is more feasible and should still be considered the echocardiography method of choice in patients with valvular regurgitation.

PCI COMPLICATIONS IN THE SPOTLIGHT

P680 | BEDSIDE
Residual SYNTAX score and mortality after primary percutaneous coronary intervention for STEMI
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Purpose: The role of the SYNTAX score in guiding treatment decisions in revascularisable stable coronary artery disease is well documented. However, the predictive function of this score and importantly its residual has not been fully asssessed in the setting of primary PCI (PPCI) where controversy remains about the prognostic utility of the residual SYNTAX score in PPCI decision-making.

Methods: We reviewed the prospective PPCI database at our high-volume tertiary centre which operates a 24/7 STEMI service and performs 900+ PCI cases per year. The residual SYNTAX score was calculated for each patient based on the residual disease after PCI. Patients were excluded if they had presented >12 hours after the onset of symptoms, required intubation or cardiopulmonary resuscitation before arrival at the hospital, had culprit left main disease or had previous CABG. The primary outcome was cardiovascular death at 12 months.

Results: For year 2012, 202 cases met entry criteria and were followed up for 12 months to the end of 2013. All cardiovascular deaths occurred within 30 days. Overall, the median SYNTAX score was 12 and the median residual SYNTAX score was 2. Compared with survivors, the SYNTAX score in those who died was higher (22.5 vs 11.5, P=0.0225), as was the residual SYNTAX score (12.0 vs 1.0, P=0.0016). The degree of revascularisation was similar (9.25 vs 9.0, P=0.9988). There was also no difference in SYNTAX score between those who died and those with severe LV dysfunction (22.5 vs 20.5, P=0.5793). In contrast, the residual SYNTAX score was higher in those who died (12.0 vs 2.0, P=0.0067).

Conclusions: The residual SYNTAX score appears to be a simple tool that can help identify patients more likely to suffer cardiovascular death by 12 months indeed 30 days after PPCI. It may therefore be useful as a guide to whether and when more revascularisation is desirable. Whether such a reduction in residual SYNTAX score improves mortality deserves further investigation.

P681 | BEDSIDE
Clinical usefulness of the SYNTAX score for predicting outcomes after coronary intervention for chronic total occlusion
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Background: Chronic total occlusion (CTO) lesions remain a challenging issue. When dealing with complex CTOs in patients undergoing percutaneous coronary intervention (PCI), it is important to evaluate not only the CTO lesion itself but also atherosclerotic lesions of the whole coronary artery tree. The utility of the SYNTAX score in patients having CTO undergoing PCI is unclear.

Methods: This retrospective study included 304 consecutive patients with CTO lesions who underwent PCI. Primary endpoints were procedural and major adverse cardiac events (MACE) within 30 days. The SYNTAX and J-CTO scores were assessed before the procedures, and patients were divided into 2 groups according to SYNTAX criteria: high (>22; n=158) and low (≤22; n=146).

Results: Procedural success was obtained in 252 patients (82.9%). Patients with a high SYNTAX score had significantly lower procedural success than those with a low SYNTAX score (74.7% versus 91.8%, P<0.0001). There were 13 MACE (8.2%) in patients with high SYNTAX scores and 2 MACE (1.4%) in those with low scores. Both the SYNTAX and J-CTO scores had odds ratios of 1.39 (95%CI, 1.05-1.83) and 3.31 (95%CI, 1.16-9.47) for procedural failure. Higher SYNTAX scores were also an independent predictor of 30-day MACE after PCI (Odds ratio 1.65, 95%CI 1.50-1.82), though the J-CTO score failed to predict the development of MACE.

Conclusions: The SYNTAX score appeared predictive of procedural failure in patients undergoing CTO-PCI, to a similar degree as with the established J-CTO score. Furthermore, we observed that high SYNTAX scores were strongly associated with an increased risk of 30-day MACE. The SYNTAX score is useful for clinical decision making in patients with complex CTO to minimize PCI-related procedural complications and thrombotic events.

P682 | BEDSIDE
Incidence, predictors and clinical implications of peri-procedural myocardial infarction according to the 2007 and 2012 universal definitions

Background: Because high-sensitivity troponin (Tn) assays are too sensitive to detect peri-procedural MI (PMI) and its influence on clinical outcomes is questionable, this issue has led to adapt a more strict 2012 definition. We performed this study to evaluate incidence, predictors and prognostic implication of the 2012 3rd universal definition.

Methods: PCI-treated patients (n=539) with currently available laboratory and hemostatic measurements (CBC, lipid profile, chemical battery, BNP, light transmittance aggreometry, VerifyNow P2Y12 assay and fibrinogen) were prospectively enrolled. The 2012 definition includes elevation of cTnI values (>5x 99th Percentile URL) with accompanying clinical evidences (symptom, EKG change, and angiographic or imaging findings).

Results: The 2007 defined PMI was observed in 12.8% and 37.8% based on CK-MB and cTnI criteria (≤3 x 99th percentile), respectively. Based on 2012 3rd definition, PMI occurred in only 10.4% of patients. In multivariate analysis, the determinants of PMI were different according to the PMI definitions. Total stent length was only consistently associated with PMI based on all definitions. MACE occurred in 25 patients (5.0%) during follow-up, and median time to event was 9 months (IQR, 4-16). Compared with patients without PMI, MACE occurrence was higher in those with PMI (CK-MB >3 x URL) or the 2012 PMI definition (Fig.), not in PMI (cTnI >3 x URL).

Conclusions: Incidence and predictors of PMI are widely different according to the applied definitions. This is the first study to demonstrate the prognostic implication of the 2012 PMI definition in PCI-treated patients.

P683 | BEDSIDE
Multi-vessel intervention increased the risk of peri-procedural myocardial infarction in stable coronary artery disease patients
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Background: Troponin T elevation after elective coronary intervention, which indicates the occurrence of peri-procedural myocardial injury (PMI), is significantly associated with cardiac prognosis. Multi-vessel intervention at one time is common in coronary artery disease (CAD) patients. However, it is unclear about the association between multi-vessel intervention and incidence of PMI.

Objective: Our study was designed to clarify whether multi-vessel intervention in stable CAD increased the risk of PMI after elective coronary intervention.

Methods: From October 2011 to June 2012, stable CAD patients admitted for elective coronary intervention were included in our study. Cardiac troponin T measurement was obtained before PCI and 24 hours after coronary intervention. The main outcome is PMI, defined as troponin T after coronary intervention was at least one value above the 99th percentile upper reference limit (URL). Univariate and multivariate analysis were applied to analyze the risk factor of PMI, especially the characteristics of coronary angiography and coronary intervention.

Results: A total of 551 stable CAD patients with an average age of 64±9.3 years were enrolled. The incidence of PMI was 34.9% in our study. Compared with non-PMI patients, PMI patients had higher proportion of multi-vessel treatment (30.8% vs. 10.4%, P=0.01) and higher average number of diseased vessels (2.2±0.8 vs. 1.7±0.8, P=0.001), diseased lesions (3.6±2.0 vs. 2.5±1.6, P=0.001) and implanted stents (1.8±0.8 vs. 1.4±0.6, P=0.015). As concern to lesion characteristics, long lesion, unstenosed lesion and tortuosity were significantly common in PMI patients undergoing CTO-PCI, to a similar degree as with the established J-CTO score. Furthermore, we observed that high SYNTAX scores were strongly associated with an increased risk of 30-day MACE. The SYNTAX score is useful for clinical decision making in patients with complex CTO to minimize PCI-related procedural complications and thrombotic events.
patients. After adjusted by age, diabetes, severity of CAD (Gensini score), stent number and stent length, multi-vessel treatment still increased the risk of PMI significantly in stable CAD patients.

Conclusions: Multi-vessel treatment is one independent risk factor of PMI in stable CAD patients. Staging coronary intervention might improve cardiac prognosis by decreasing the incidence of PMI.

P684 | SPOTLIGHT
The current bleeding scores predict outcome in contemporary PCI? S. Khan, R. Morley, J. Carter, J. Hall, D. Muir, A. Sutton, N. Swanson, R. Wright, M. De Belder, P. Blowers. James Cook University Hospital, Middlesbrough, United Kingdom

Early invasive intervention and new anti-thrombotic therapies have reduced mortality and recurrent ischemia in patients with acute coronary syndrome (ACS) at the expense of higher bleeding events. We compared the predictive value of bleeding scores in a population treated predominantly from a radial approach.

Methods and result: We conducted a single centre, prospective, observational study enrolling 1567 consecutive patients with ACS and stable angina undergoing PCI from September 2011 to July 2012 at our hospital. The study cohort was: predominantly male, median age of 64 years (range 35-95), vast majority treated with glycoprotein inhibitor and none with bivalirudin. NSTEMI patients were treated upstream with fondaparinux or enoxaparin. 89% had PCI via the radial route. We evaluated the performance of Mehran and CRUSADE bleeding scores (BS) in predicting their own major bleeding events and TIMI major bleeding episodes. Calibration (Hosmer–Lemeshow test, HL) and discrimination (c-statistic) for the two BS were compared. Cumulative funnel plots were used to compare the predictive accuracy of these scores against observed bleeding outcomes. The calibration for the Mehran and CRUSADE for the total PCI population scores was fair (c-statistic Mehran c=0.66, p=0.02; CRUSADE c=0.61, p=0.63). The occurrence of in-hospital major bleeding was 2.7%. The cumulative plots showed that the overall observed bleeding rate was less than predicted (4.7% by Mehran, 6.9% by CRUSADE).

Conclusion: The Mehran and CRUSADE BS are useful but they over-predict the risk of bleeding in our population despite relatively high use of GPIs. Potentially this is explained by dominant use of radial access for PCI.

P685 | BEDSIDE
Development and validation of a scoring system to predict the risk of stent thrombosis
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Purpose: Coronary stent thrombosis (ST) is a rare but potentially lethal complication of PCI. Previous studies have identified various patient, lesion and procedure-related risk factors, but there are currently no risk scoring tools in clinical use. In this study, we aimed to develop a scoring system to predict the risk of ST at different time points following PCI.

Methods and results: Risk factors for ST and their associated odds ratios (ORs) were identified from a meta-analysis based on a systematic literature review, and from a panel of experts (Delphi-RAND method). The results were combined using Bayesian methodology to calculate risk scores for acute, early, late and very late ST. Risk scores were validated using patient level data from the TRITON-TIMI 38 study.

In total, 20 (9 patient-, 3 lesion- and 8 PCI procedure-related) risk factors were found to significantly influence the risk of developing ST. The following factors were found to be significant for the acute, early and late time points: diabetes mellitus, acute OR=1.64 (1.11-2.32), early OR=1.69 (1.29-2.18), late OR=1.53 (1.08-2.10); bifurcation stenting with two stents, acute OR=1.84 (1.20-2.70), early OR=1.76 (1.08-2.71), late OR=1.57 (1.00-2.43); incomplete stent expansion, acute OR=1.63 (1.08-2.38), early OR=1.73 (1.14-2.55), late OR=1.91 (1.19-2.94); undersized stent relative to vessel, acute OR=1.74 (1.03-2.75), early OR=2.00 (1.28-3.07), late OR=1.91 (1.17-2.96) and use of a covered stent, acute OR=2.08 (1.22-3.30), early OR=2.03 (0.20-3.20), late OR=2.03 (1.28-3.05). Incomplete duplication of anti-platelet therapy was noted to be a highly significant risk factor for early and late ST, early OR=3.49 (2.17-5.30), late OR=3.44 (2.09-5.36).

For very late ST, no meta-analysis was performed, as there was significant heterogeneity between studies. The Delphi-RAND process identified only 3 risk factors that were significant predictors of very late ST: diabetes mellitus, malignancy and thrombus at follow-up angiography. Therefore, no risk score was developed for this time point.

When the final risk scores were applied to the patient cohort in the TRITON-TIMI 38 study, increasing scores were associated with an increasing risk of ST.

Conclusions: In conclusion, published data were combined with expert opinion to produce a weighted scoring system to predict the risk of acute, early and late ST following PCI. This will be assessed prospectively in clinical use. Use of such a tool will be invaluable in combination with established bleeding risk scores to tailor the potency and duration of antiplatelet therapy in patients undergoing PCI.

P686 | BEDSIDE
IntraVascular UltraSound predictors of side branch occlusion in coronary bifurcation lesions after single stent crossover technique
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Background: In percutaneous coronary intervention (PCI), bifurcation stenting remains technically challenging and is a major problem of lower procedural success rates. Although a single-stent crossover technique is the most common approach to treating bifurcation lesions, the mechanism and predictors of side branch (SB) occlusions using this technique are unclear. The aims of this study are to identify the mechanisms and predictors of SB occlusions by intravascular ultrasound (IVUS) in bifurcation lesions after single stent-cross over technique.

Methods: For a total of 332 bifurcation lesions were enrolled. We excluded the left main lesions and SB which had a Thrombolysis in Myocardial Infarction (TIMI) flow 0 or 1. We pre-PCI, resulting 272 lesions enrolled in this study. All patients were performed pre-PCI IVUS examination in major branch (MB). SB was defined which ostium diameter had more than 1.5 mm at the junction site measured by IVUS and SB occlusion was defined as TIMI flow of <2 by post-stenting. We divided SB into two groups, occluded and non-occluded groups.

Results: There were 50 SB occlusions (18.4%) in this study. The rate of SB occlusion was similar between acute coronary syndrome and stable angina pectoris (24.6% vs. 16.1%, p=0.14). There were no significant differences between the two groups with regard to the clinical characteristics including coronary risk factors and PCI procedure including target vessel, stent size and length. In IVUS examinations, the MB plaque thickness of both sides of SB in junction was significantly higher in occluded group. Although the SB total diameter was similar between the two groups, the SB internal (media-media) diameter was significant lower in occluded group, indicating occluded group had a lot of plaque in SB os- tum. Multivariate logistic regression analysis revealed that independent factors were minimum plaque thickness of MB in junction and SB diameter ratio (SB total diameter/MB internal diameter). The best cut-off value of minimum plaque thickness was 0.79 mm from receiver operating curve (ROC), and the value of 0.79 mm had 71% of sensitivity and 89% of specificity to detect SB occlusion after SB crossover stent (area under ROC = 0.867). Besides, the best cut-off value of SB diameter ratio was 1.5 from ROC, and the value of ≤1.5 had 85% of sensitivity and 58% of specificity to detect SB occlusion after SB crossover stent (area under ROC = 0.842).

Conclusions: Our study suggested plaque thickness of MB in junction and SB plaque volume are predictors of SB occlusion for bifurcation lesion after single stent crossover technique.

P687 | BEDSIDE
Use of transradial access for PCI in clinical practice: results from the ALKK-PCI registry

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Background: European guidelines recommend the use of transradial access in patients with acute coronary syndrome (ACS). ACS. We examined the use of transradial access dependent on the indication for PCI from 2008-2012 in clinical practice in our country.

Methods and results: From 2008-2012 in 41 hospitals more than 13000 PCIs in stable coronary artery disease, more than 9000 PCIs in patients with Non-ST-elevation acute coronary syndrome (NSTE-ACS) and more than 5000 PCIs in patients with ST-elevation myocardial infarction (STEMI) have been performed per year. The time course of the use of radial access is shown in Table 1. The clinical events are given in Table 2.

Conclusion: Radial access is only used in 20% of patients, more often in sta-
P688 | BEDSIDE
Validation of a new risk score to predict contrast-induced nephropathy after percutaneous coronary intervention
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Purpose: Contrast-induced nephropathy (CIN) is a frequent, potentially lethal complication of percutaneous coronary interventions (PCI). We prospectively validated the diagnostic performance of a simple CIN risk score in a large multi-center international cohort of patients undergoing PCI.
Methods: 2,882 consecutive patients treated with elective or urgent PCI were enrolled. A simple CIN risk score was calculated for all patients by allocating points according to a pre-specified scale (pre-existing renal disease, 2; metformin use, 2; previous PCI, 1; peripheral arterial disease, 2; injected volume of contrast-medium >300 mL, 1). CIN was defined as an increase, compared to baseline, of serum creatinine by ≥25%, or by ≥0.5 mg/dL, 48 hours after PCI.
Results: CIN occurred in 15.7% of the study population. The predictive accuracy of the CIN risk score was good (c-statistic, 0.741; 95% CI, 0.713-0.763). ROC analysis identified a score of ≥3 as having the best diagnostic accuracy. Examination of the performance of the proposed risk score using different definitions of CIN yielded a robust predictive ability. The score exhibited good discrimination (All CIN) and good calibration across all pre-defined subgroups of the study population. Compared to two previously published risk scores for CIN, our score demonstrated higher discriminative ability and resulted in a net reclassification improvement and an integrated discrimination improvement (P < 0.001). Conclusion: The new risk score can easily be applied in the setting of urgent or elective PCI, allows for robust risk assessment and offers the potential to improve the interventional management of patients at risk for CIN.

P689 | BEDSIDE
Incidence and clinical significance of ischemic stroke following cardiac catheterization
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Background: Ischemic stroke is one of the most undesirable complications for patients receiving cardiac catheterization. The aim of the present study was to investigate the incidence, risk factors, and neurological outcome of ischemic stroke following cardiac catheterization.
Methods: A total of 2848 procedures of cardiac catheterization (69.1±11.1 years old, 2125 males) were performed from January 2011 to December 2013 in our hospital. The patients were divided into 3 groups according to the types of procedure: diagnostic coronary angiography (CAG group, n=1627), CAG plus internal thoracic arteriography before or after coronary artery bypass graft surgery (ITA group, n=301) and percutaneous coronary intervention (PCI group, n=920). We compared the incidence of stroke among the groups and determined the factors influencing on the occurrence of stroke. We also assessed neurological outcome after the onset of stroke using National Institutes of Health Stroke Scale (NIHSS) score and modified Rankin Scale (mRS).
Results: Thirteen patients (0.46%) developed ischemic stroke requiring stroke unit care. The incidence was significantly higher in ITA group (1.66%) compared to CAG group (0.25%) or PCI group (0.43%) (p=0.006 or p=0.034, respectively). Among possible factors contributing to the occurrence of stroke, age ≥75 (OR = 3.86, 95% CI [1.22-11.56], P=0.02) and additional internal thoracic arteriography (OR = 5.63, 95% CI [1.64-17.70], P=0.007) were found to be the independent risk factors by multiple logistic regression analysis. Initial NIHSS score immediately after the onset was 6.9±9.6 and the score was improved to 3.1±6.5 at discharge. Five patients obtained complete recovery (mRS = 0), whereas neurological deficits remained in 7 patients (mRS = 2.7±1.7) and 1 patient died in hospital (mRS = 6).
Conclusions: Ischemic stroke is a rare complication but is associated with significant mortality and morbidity following cardiac catheterization. The independent risk factors for this cerebrovascular event were found to be age ≥75 and additional internal thoracic arteriography for bypass grafts angiography.

STRATEGIES TO PREVENT PCI COMPLICATIONS

P690 | BEDSIDE
Remote ischemic preconditioning reduces peri-procedural myocardial injury in elective percutaneous coronary intervention: a meta-analysis
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Over one third of elective percutaneous coronary intervention (PCI) procedures are complicated by peri-procedural myocardial injury (PMI), detected by elevated biomarkers of myocardial necrosis. One approach to reducing PMI is by utilizing an intrinsic mechanism of cardioprotection termed remote ischemic preconditioning (RIPC). Since several studies have investigated the effects of RIPC before elective PCI with contradictory results, we conducted a meta-analysis of available data to determine whether RIPC before elective PCI reduces PMI.
Methods: We electronically searched Medline, EMBASE, Scopus, and Cochrane databases to identify studies investigating the following terms: “remote ischemic preconditioning”, “remote pre-conditioning”, and “percutaneous coronary intervention”. Eligible trials were those in which patients undergoing PCI were randomly assigned to receive either RIPC, or no RIPC. Primary outcome to be assessed was PMI, detected by troponin elevation at 16 or 24 hours post-PCI. A meta-analysis of non-redundant studies, reviews and duplicates, 8 studies were finally included in the meta-analysis, with a total number of 1066 enrolled patients, comprising 538 patients in the RIPC group and 528 patients in the control group. According to our analysis, RIPC reduced the incidence of PMI, which occurred in 217 (51.3%) patients in the control group (OR 0.57 [95% CI: 0.36, 0.90]; test for overall effect: Z=2.43 [P=0.02]).
In conclusion, the pooled analysis of all available studies suggests that RIPC before elective PCI is effective in reducing PMI. Even though, this may not be equivalent to reduction of major adverse cardiovascular events, RIPC is simple to apply, non-invasive, and virtually cost-free, and could be incorporated into clinical practice.

P693 | BENCH
Dynamic simultaneous hemodialysis for prevention of contrast-induced nephropathy during catheterization
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Objectives: The goal of the study was to examine the utility of prophylactic hemodialysis for prevention of contrast-induced nephropathy (CIN) in patients undergoing catheter angiography.

Methods: The subjects were 103 patients with chronic renal impairment (mean serum creatinine concentration 1.79 ± 0.72 mg/dl) who received prophylactic dynamic hemodialysis during diagnostic and interventional catheterization. In the hemodialysis procedure, blood was driven from the right atrium through a 7Fr introducer and returned to the saphenous vein after passing through an extracorporeal circuit. Serum creatinine was measured to evaluate renal function before and after the procedure.

Results: CIN developed in 6 (6%) patients who underwent percutaneous coronary intervention, including 4 (4%) urgent cases. Elective catheterization was performed in 87 cases and 2 (2%) of these patients developed CIN. No complications related to hemodialysis were observed.

Conclusions: In patients with reduced renal function, simultaneous hemodialysis during catheter angiography appears to be a safe and effective strategy for prevention of CIN.

P694 | BEDSIDE
What stent diameter should we select in order to prevent from stent edge dissection in OCT-guide?
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Background: To get better clinical outcome, biggest stent diameter without causing edge dissection should be selected. Optical coherence tomography (OCT) can show the lumen diameter of stent landing zone precisely and also show stent edge dissection clearly. We investigated the stent edge lesion in relation to stent diameter using OCT.

Method: From July 2012 to August 2013, we investigated 384 stent edge lesions without calcification treated with single 2nd generation drug-eluting stent (DES) under OCT guidance. Before and after deployment of DES with stent delivery balloon by 2 or 3 times inflations, diameter and area ratios of stent edge to reference lumen were analyzed by OCT. We compared these between edge dissection group and no-dissection group.

Result: The overall incidence of edge dissection was 23 lesions (6.0%). Comparison with no-dissection group, ratio of stent edge to reference lumen diameter (1.24 ± 1.12, p = 0.001) and area (1.56 ± 1.26, p = 0.001) were significantly larger in edge dissection group. Most of reference tissue character in edge dissection group was eccentricity (16/15 (69.6%) and lipid rich plaque (11/13 (85.2%).

Conclusion: We should select optimal stent diameter by up to quarter size-up to reference diameter in order to prevent from stent edge dissection.

P695 | BEDSIDE
Neutrophil gelatinase associated lipocalin (ngal), measured by a bedside assay, in the early detection of contrast-induced acute kidney injury in patients undergoing coronary stenting

Purpose: Contrast-induced Acute Kidney Injury (CI-AKI) is associated with high morbidity and mortality. It implies a damage but not necessarily a reduction in the overall renal filtration rate detected by serum creatinine (SCR); moreover SCR increases when the loss of greater than 50% of kidney function occurs. Thus, there is the urgency of more sensitive biomarkers to identify kidney damage. Neutrophil Gelatinase-Associated Lipocalin (NGAL) is the most promising biomarker because rapidly accumulated in urine and plasma after nephrotic and ischemic insults. The aim of our study was to evaluate the diagnostic accuracy of a "bedside" NGAL assay, compared to the standard SCR, in the early detection of CI-AKI in patients undergoing percutaneous coronary intervention (PCI).

Methods: 97 consecutive patients undergoing PCI were enrolled. Exclusion criteria were: GFR < 60 ml/min, left ventricular dysfunction, ST-elevation myocardial infarction, thrombocytopenia (< 70 to 109/L), sepsis, severe pulmonary disease, neoplasms. In all patients, blood samples were drawn before and 6 hours after PCI in order to detect NGAL levels by a bedside test. SCR was measured before and 24-48 hours after procedure and its clearance (CiCr) estimated by Cockcroft and Gault formula. CI-AKI was defined as SCR increase > 0.3 mg/dL within 48 hours from contrast administration. All patients were treated with saline hydration at 1 ml/kg/min.

Results: We found a significant correlation between pre-PCI NGAL and SCR (r=0.446, p<0.001) and CiCr (r=-0.405, p<0.001) at the baseline. A further correlation was found between 6-hours NGAL and both post-PCI SCR (r=0.339, p=0.001) and CiCr (r=-0.303, p=0.019). In the overall population, median post-PCI SCR increase (∆SCR) was 0.24 mg/dL; thus, in patients with ∆SCR exceeding 0.24 mg/dL (47%), a significant NGAL elevation (∆NGAL, 6.6±34.7 vs -11.2±40.5 ng/mL, p=0.048) and higher 6-hours NGAL values (107.6±49.1 vs 86.9±41.2 ng/mL, p=0.069) were observed. The ROC curve showed that 6-hours NGAL significantly discriminates between patients with and without ∆SCR > 0.24 mg/dL, with an area under the curve of 0.645 (p<0.034), identifying 96 ng/mL as the optimal cut-off to predict renal injury, with a sensitivity of 53% and a specificity of 74%.

Conclusion: This study confirmed the effectiveness of NGAL, detected by a bedside assay, in the early diagnosis of CI-AKI. This marker may play a crucial role especially in the identification of such patients who develop kidney injury regardless of significant increase in post-procedural SCR.

P696 | BEDSIDE
Impact on prognosis of periprocedural myocardial infarction after percutaneous coronary intervention (PCI)
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Purpose: Different definitions of periprocedural myocardial infarction (MI) after Percutaneous Coronary Intervention (PCI) have been provided, but their impact on prognosis remains to be determined.

Methods: All consecutive patients undergoing PCI in Our Institution from 2009 to 2011 were enrolled. Procedural data were revised to adjudicate definition of periprocedural myocardial infarction according to CK-MB increase (> 3 x URL and > 5 x URL), to troponin increase (> 3× 99th percentile URL and > 5× 99th percentile URL) and to recent ESC and SCI definitions. MACE (Major Adverse Cardiovascular events) was the primary end point, while its single components (death, myocardial infarction and target vessel revascularization) the secondary ones.

Results: 712 patients were enrolled: after 771 days, 115 (16.7%) patients experienced MACE. In 190 patients were diagnosed a periprocedural MI defined as elevation of troponin >5x99th percentile URL. When adjudicating ESC definition on these patients, 46 were excluded and 1.4% of them experienced a MACE and 0.3% died, while 144 with periprocedural MI, 2.9% reported a MACE and 1.3% died. After appraisal of SCI definition, 176 patients were excluded, 3.8% of them with a MACE and 1.4% died, and for with periprocedural MI, 0.5% experienced a MACE and 0.1% died. Similar low performance was appraised after reclassification of patients from more than 3 of upper limit of CK-MB and of troponin. At multivariate analysis, none of these definitions related to adverse events.

Conclusions: Periprocedural MI represents a frequent complication for patients undergoing PCI. At present definitions share a still not satisfactory discrimination between patients with and without adverse events at follow up, stressing the need for more accurate definitions.

P697 | BEDSIDE
Pretreatment with ivabradine reduces periprocedural myocardial injury and infarction in stable ischemic patients undergoing coronary intervention
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Purpose: Peri-procedural myocardial infarction (MI) in patients with stable angina undergoing percutaneous coronary intervention (PCI) is associated with long term survival. Iivabradine is an established anti-ischmic drug that reduces heart rate (HR) and subsequently alleviates symptoms of angina. There is no data that heart rate reduction reduces peri-procedural myocardial injury. In this study we sought to determine whether HR reduction via ivabradine attenuates peri-procedural myocardial injury.

Methods: 78 patients with stable angina and resting heart rate above 70 beats per minute (bpm) were randomly assigned to ivabradine 5 mg twice daily or no treatment. Patients were included 1 month before scheduled intervention. After admission troponin I levels were measured before the procedure and after 24 hours. We also collected data of any change in symptoms in both groups. MI was defined as an elevation of troponin > 3 x 99th percentile URL. When adjudicating ESC definition on these patients, 176 patients were excluded, 3.8% of them with a MACE and 1.4% died, and for with periprocedural MI, 0.5% experienced a MACE and 0.1% died. Similar low performance was appraised after reclassification of patients from more than 3 of upper limit of CK-MB and of troponin. At multivariate analysis, none of these definitions related to adverse events.

Results: Patients treated with ivabradine had more hypertension; otherwise there were no significant differences between both groups. We noticed significant reduction of heart rate and angina episodes per week in the ivabradine group compared to the control group (17.9 ± 7.1 BPM vs. 79.2 ± 12.0 BPM; p = 0.05 and 0.5 ± 1.5 vs. 2.4 ± 2.1; p = 0.05).

The mean troponin I levels after the procedure were significantly lower in the ivabradine group compared to the control group (0.12 ± 0.3 mg/L vs. 0.5 ± 0.9 mg/L). The incidence of cardiac troponin I elevation > 3x ULN was 18.4% in the
What is the optimal treatment for symptomatic patients with isolated coronary myocardial bridge? a systematic review and meta-regression

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Purpose: Myocardial Bridging (MB) represents infrequent common coronary anomaly, with few severe adverse events but a relevant symptom burden. Medical therapy, especially with beta-blockers, is the usual first-line treatment in symptomatic patients with bypass systole/myotony or stenting as secondary options, despite absence of randomized trials.

Methods: MEDLINE/PubMed was systematically screened for studies reporting on isolated MB diagnosed at coronary angiography or with coronary computed tomography in patients admitted for suspected angina or with an acute coronary syndrome. Baseline, treatment and outcome data were appraised and pooled according to treatment (medical therapy, bypass surgery/myotony or stenting)

Results: 831 patients in 15 studies were included, with a low prevalence of traditional cardiovascular/renal risk factors in the population. Baseline, treatment and outcome data were appraised and pooled according to treatment (medical therapy, bypass surgery/myotony or stenting). Baseline and procedural parameters

<table>
<thead>
<tr>
<th>Baseline and procedural parameters</th>
<th>Ivasdara group (N=38)</th>
<th>Control group (N=39)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>34 (89%)</td>
<td>27 (67%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11 (29%)</td>
<td>11 (27%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Antithrombolytic therapy</td>
<td>33 (87%)</td>
<td>30 (75%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>25 (66%)</td>
<td>22 (56%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Statins</td>
<td>21 (55%)</td>
<td>26 (65%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Number of lesions per patient</td>
<td>1.2 ± 0.5</td>
<td>1.1 ± 0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>PCI per patient</td>
<td>0.4 ± 0.5</td>
<td>0.5 ± 0.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Ivasdara group and 50% in the control group (odds ratio 0.23; 95% confidence interval 0.08 to 0.63; P 0.00).

Conclusions: Heart rate reduction achieved by Ivasdara reduces peri-procedural myocardial injury and MI in patients undergoing elective PCI.

P699 | BEDSIDE
Fluoroscopy time vs serum creatine kinase as a prognostic marker after percutaneous coronary intervention

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Purpose: Prolonged fluoroscopy time (FT) has been shown to be a promising marker of adverse long-term outcome after PCI. FT and serum creatine kinase (CK) both reflect procedural and patient complexity, operator skills and any acute procedural complications, all of which impact on prognosis. FT is routinely recorded and CK is easily measured, but it is not known which is better at predicting major hard clinical end-points after contemporary PCI. We therefore compared the ability of FT and CK in predicting long-term all-cause mortality and the need for coronary bypass grafting (CABG) after PCI.

Methods: We followed up 398 consecutive patients (mean age 61; range 33-86) at our high-volume tertiary centre who had PCI while under fluoroscopy. We compared the ability of FT and CK in predicting long-term all-cause mortality and the need for coronary bypass grafting (CABG) after PCI

Results: FT > 10 min predicted a nearly 3-fold risk of CABG or death by 5 years after PCI. In contrast, CK elevation after PCI was not associated with long-term all-cause mortality or need for CABG. Compared with CK, fluoroscopy time appears to be a superior marker of long-term outcome after PCI.

P700 | BEDSIDE
Neutrophil gelatinase-associated lipocalin (NGAL) as a marker of contrast-induced nephropathy in patients undergoing elective cardiac catheterization

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Purpose: Contrast-induced nephropathy (CIN) after cardiac catheterization is a common cause of hospital-acquired acute kidney injury and is typically diagnosed using creatinine or estimated glomerular filtration rate (eGFR) values. Prolonged fluoroscopy and contrast volume are usually used as surrogate markers of radiation exposure in patients undergoing cardiac catheterization. We evaluated the predictive value of urine NGAL in patients undergoing elective cardiac catheterization.

Methods: The study comprised 100 consecutive patients (64±9 years, 80% males) undergoing elective cardiac catheterization (coronary angiography plus angioplasty, if necessary). Serum creatinine, cystatin C and NGAL, eGFR, urine albumin-to-creatinine ratio (ACR) and NGAL levels and the prevalence of renal dysfunction (eGFR < 60 ml/min/1.73m²) and albuminuria (ACR>30 mg/g) were all determined at baseline and 24 hours post catheterization.

Results: The prevalence of traditional cardiovascular/renal risk factors in the population was: hypertension 68%, diabetes 26%, dyslipidemia 56%, smoking 7%, the body mass index of participants was 29.0 ± 4.4 kg/m². Angioplasty was performed in 57 patients while the administered contrast volume was 243 ± 155 ml. Minimal changes (p=NS) were noted 24 hours post catheterization in baseline (0.95 ± 0.23 vs 0.95 ± 0.24 mg/dl), cystatin C (0.94 ± 0.23 vs 0.94 ± 0.23 mg/dl), serum uric acid (370 ± 42 vs 383 ± 48 mg/dl) and eGFR (60 ± 15 vs 60 ± 15 ml/min/1.73m²). The prevalence of renal dysfunction occurred with a low rate (3.4%), with 78.7% [70.5-86.9; 95% CI] and those without, although absolute plaque area and volume were not significantly different between the two groups. The Δhs-TnT level was positively correlated with renal function 24 hours post catheterization (r: 0.188, 0.155, -0.059, 0.127, 0.498 and 0.334 for creatinine, cystatin C, ACR, albuminuria, and NGAL levels, respectively) were significant (p < 0.05).

Conclusions: Greater NA and CV observed by IMAP-IVUS may be related to the occurrence of PMI in SAP patients with normal hs-TnT level before PCI.

P701 | BEDSIDE
Myocardial Infarction in Patients with Stable Angina Pectoris: A Systematic Review and Meta-Regression Analysis


Purpose: Periprocedural myocardial infarction (PMI) is well known to occur after percutaneous coronary intervention (PCI) in patients with coronary artery disease. IMAP is a newly developed intravascular ultrasound (IVUS) tissue characterisation system. Few studies have shown the relationship between coronary plaque components on IMAP-IVUS and the occurrence of PMI. We assessed the prognostic of PMI in patients with stable angina pectoris (SAP) by the plaque components on IMAP-IVUS.

Methods: We investigated 50 consecutive coronary culprit lesions with 50 SAP patients (hs-TnT level <0.014 ng/ml before PCI) that underwent pre-intervention IMAP-IVUS. In the present study, patients with hemodialysis or multiple culprit lesions were excluded. Hs-TnT levels were measured on admission and 24 hours after PCI, and hs-TnT was defined as difference before and after PCI. All lesions were divided into lesions with PMI (hs-TnT levels after PCI >5 times of the upper reference limit) and those without.

Results: Hs-TnT level after PCI was 0.128±0.207 ng/ml, and PMI was observed in 22 (44%) lesions. Percentage necrotic area (%NA) (49.3±13.0% vs. 36.9±18.1%, p<0.01) and volume (%NV) (39.5±11.4% vs. 29.6±12.9%, p=0.01) on IMAP-IVUS were significantly greater in lesions with PMI than those without, although absolute plaque area and volume were not significantly different between the two groups. The Δhs-TnT level was positively correlated with renal function (r: 0.188, 0.155, -0.059, 0.127, 0.498 and 0.334 for creatinine, cystatin C, ACR, albuminuria, and NGAL levels, respectively) were significant (p < 0.05).

Conclusions: Greater NA and CV observed by IMAP-IVUS may be related to the occurrence of PMI in SAP patients with normal hs-TnT level before PCI.
Conclusions: NGAL emerge as a more sensitive marker of CIN 24 hours post elective cardiac catheterization compared to creatinine, eGFR and cystatin C.

P702 | BEDSIDE
Diverse role of prognostic factors in evaluating procedural success of percutaneous interventions for chronic total coronary occlusion

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Purpose: Chronic total occlusion (CTO) is one of the most technically challenging fields of interventional cardiology. Successful recanalization of chronically occluded vessels significantly improves the quality of life and perspectives in most patients. Since the risks of these interventions exceed those of a regular PCI, it is essential to evaluate the risk-benefit ratio before the procedure. Currently the J-CTO score is a generally accepted risk estimation method; calculated from various factors, including occlusion length, calcification, tortuosity, presence and shape of the stump, and previous recanalization attempt (each parameter counts 0 or 1, the score for most difficult lesions: 5). However, it is not clear which factors of J-CTO have more value than others in predicting procedural success. We intended to quantify the prognostic value of the different factors of J-CTO based on the CTO patient registry of our department.

Methods and patients: We calculated the J-CTO score in all the 168 CTO PCI procedures performed at our department from 2012 to 2013 and evaluated the procedural success predicting odds ratio (OR) of the different factors using logistic regression.

Results: The total procedural success rate was 70%. The average J-CTO score of the patients undergoing unsuccessful procedures was 1.86±1.05 (average±SD), the score in unsuccessful procedures proved to be significantly higher: 2.84±1.84 (p<0.001). Among the J-CTO score parameters, lesion length and tortuosity did not prove to be significant predicting factors. OR of the other factors are the following: calcification: 0.41 (p=0.031), absence of tapered stump: 0.40 (p=0.024), previous unsuccessful attempt: 0.09 (p<0.001).

Conclusion: (1) The J-CTO score is a good predictor of recanalization success rate, (2) certain factors of the score system are significantly more valuable that others in predicting the success rate, therefore we propose the development of a new scoring system, where certain factors are weighted differently for more accurate assessment of prognosis.

P703 | BEDSIDE
Large and macrophage-rich debris contribute to the filter no-reflow phenomenon during percutaneous coronary intervention

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Background: Filter-based distal protection devices are used to prevent no-reflow phenomenon by filtering potentially embolic atherothrombotic debris. Filter no reflow (FNR) is reduced flow that is reversible following removal of the filter, caused by plugging of atherothrombotic debris at the filter. We investigated the association among preintervention plaque characteristics, components of filtered debris, and FNR.

Methods: In 30 PCI patients with stable angina pectoris (SAP, n=11) or acute coronary syndrome (ACS, n=19), preinterventional debris were imaged by virtual histology intravascular ultrasonography (VH-IVUS). Coronary atherothrombotic debris were collected during PCI using a Filter (NIROPRO). The debris were imaged with ex vivo optical coherence tomography (OCT: LightLab), to determine its volume and macrophage contents.

Results: Compared to those without FNR (FNR−: n=16), patients with FNR (FNR+: n=14) showed larger debris volume (3.6±2.6 vs 1.1±1.6 mm3, p=0.01) and higher incidence of red thrombus (92.8% vs 43.8%, p=0.02). Moreover, macrophage contents were increased in FNR+ (n=14) than in FNR− (n=16) (2.5±3.8 vs 0.5±1.1%, p=0.05). In preinterventional plaque, patients with larger (> median) debris had larger necrotic core (27.4±8.4 vs 21.1±6.0%, p=0.03) but smaller fibrous component (55.2±3.7 vs 59.2±5.7%, p=0.04). Patients with increased (> median) debris macrophage contents had larger plaque burden (79.3±6.1 vs 57.3±3.9%, p=0.04).

Conclusion: Large and macrophage-rich atherothrombotic debris contribute to filter no reflow. These debris derived from large and necrotic core-rich plaque in their preinterventional culprit lesion.

P705 | BEDSIDE
Comparison of conventional versus patien haemostasis in patients undergoing transradial coronary angioplasty

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Purpose: Radial artery occlusion is the Achilles heel of trans radial coronary inter-ventions. We tested a hypothesis whether type of post procedural haemostasis is associated with lower incidence of radial artery occlusion in patients undergoing trans radial PCI.

Methods: 176 consecutive patients undergoing trans radial PCI were included. Patients were divided into 2 groups based on type of haemostasis following PCI. Patien haemostasis group (n=87, radial patency at the time of haemostasis as evident by pulsatile flow on plethysmograph in the banded arm) and conventional haemostasis (n=89, radial artery occluded: flat line on plethysmograph). Pre procedural Barbeau test and radial artery Doppler was done in all cases. The primary outcome was radial artery occlusion and secondary outcome was occurrence of arm hematoma and pain score (on a scale of 0 to 10). Radial artery occlusion was confirmed by Barbeau test and Doppler at 24 hours post procedure.

Results: The mean age of patients was 55.6±9.7 years, 14.8% were leision were diabetics,27.8% were smokers and 18.8% had history of prior transradial procedure. The mean radial artery diameter was 2.6±0.21 mm and 89% patients had Barbeau type A response. There was no difference between the two groups in terms of baseline and procedural characteristics. Radial artery occlusion at 24 hours occurred in 23 patients (13.1%) and was significantly higher in conventional haemostasis group as compared to patien group (17 vs 6, p<0.01). 16.5% patients developed arm hematoma and was similar between 2 groups (14 vs 15 p=NS).The mean pain score was higher in conventional group (5.6 vs 3.3; p<0.05). Diabetics, females, patients with prior radial intervention, radial diameter, phenotype of haemostasis, the radial artery diameter ratio were the variables associated with higher likelihood of developing radial artery occlusion, but smoking, creatinine, LDL, dose of heparin given and GPIb/IIa usage did not show significant correlation.

Conclusion: Patien haemostasis following transradial PCI is associated with lower incidence of radial artery occlusion as compared to conventional haemostasis without increase in arm hematoma and is associated with better patient comfort. Patien haemostasis is a simple measure in transradial PCI with better outcomes.

P706 | BEDSIDE
Longterm outcomes of iatrogenic coronary artery dissection: comparison based on dissection site


Background: Iatrogenic coronary artery dissection during coronary angiography (CAG) and percutaneous coronary intervention (PCI) is a rare but feared complication. When it occurs, bailout stent implantation is the most widely used therapy. However, its longterm prognosis remains uncertain.

Methods: From January 2000 to December 2013, CAG and PCI were performed on 67791 patients in our hospital (CAG, 48644; PCI, 19147). Among them, iatrogenic coronary artery dissection occurred in 89 patients and the incidence rate was 0.13% (CAG, 0.025%; PCI, 0.40%). In 9 patients, dissection was mild and did not require intervention. In the other 80 patients, 72 patients (90%) were treated by antipla- cial events (MACE) including a composite of cardiac death, nonfatal myocardial infarction (MI), and target lesion revascularization (TLR).

Results: Procedure-related death was nothing. Cardiac death occurred in 9 pa- tients (RCA, 3; LMT, 4; and ITA, 2). Nonfatal MI occurred in 2 patients (RCA, 1; LMT, 1). TLR was performed in 10 patients (RCA, 5; LMT, 3; and ITA, 2). The cumulative incidence of MACE is shown in the figure. It was significantly higher in the ITA group than in the RCA group (p=0.002). Also, it tended to be higher in the LMT group than in the RCA group, although it was not significant (p=0.097).

Conclusion: The longterm outcomes of iatrogenic coronary artery dissection were not good even after successful bailout procedure, especially in the ITA and LMT groups.

PREVENTION OF PCI COMPLICATIONS

P705 | BEDSIDE
Comparison of conventional versus patien haemostasis in patients undergoing transradial coronary angioplasty

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Purpose: Radial artery occlusion is the Achilles heel of trans radial coronary in-
P707 | BEDSIDE
Hemorrhagic versus thrombotic complications in patients undergoing primary percutaneous coronary intervention
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1Cardiology Clinic, Department of Cardiology, Clinical Center of Serbia, Belgrade, Serbia; 2Cardiology Clinic, Clinical Center of Serbia, Belgrade, Serbia; 3Cardiology Clinic, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; 4Center for Medical Biochemistry, Clinical Center of Serbia, Belgrade, Serbia
Purpose: The relative contribution of thrombotic versus hemorrhagic events to subsequent mortality of pts treated with primary percutaneous coronary interventions (PCI) is poorly understood. The purpose of this study was to investigate the incidence of in-hospital thrombotic and hemorrhagic complications and the association of these events with long-term mortality in patients with acute ST-elevation myocardial infarction (STEMI) undergoing primary PCI.
Methods: Consecutive STEMI pts who underwent primary PCI between 8/2009 and 1/2011 were enrolled in a prospective registry of high volume tertiary center. Bleeding events were assessed using Bleeding Academic Research Consortium (BARC) criteria. BARC class ≥2 bleeding were taken into consideration. Thrombotic complications involved reinfarction, target vessel revascularization for ischemia and stroke. The primary outcome was 1-year mortality.
Results: Of the 1808 STEMI pts with primary PCI, 115 (6.4%) experienced a BARC class ≥2 bleeding and 40 (2.2%) experienced thrombotic in-hospital events. Unadjusted 1-year mortality was the lowest in pts with thrombotic events only (8%) and the highest in pts with both thrombotic and hemorrhagic events (Table). After multivariable adjustment for demographic and clinical characteristics, the independent predictors of 1-year mortality were BARC class ≥2 bleeding (HR 1.94, 95% CI 1.24-3.02; p=0.004) and combined thrombotic and bleeding events (HR 4.60, 95% CI 1.74-12.16; p=0.002), but not the occurrence of thrombotic events only. Other independent predictors of 1-year mortality were heart failure, renal failure, advanced age, prior myocardial infarction, prior stroke and anemia.
Complications and mortality
1-year mortality
No thrombotic or hemorrhagic complications
Thrombotic complications only
Hemorrhagic complications only
Both thrombotic and hemorrhagic complications
P value
n=1644 (92.0%)
n=192 (11.6%)
n=104 (5.8%)
n=11 (0.6%)
All cause, %
11.4
17.2
19.2
36.4
<0.001
Cardiac, %
10.8
17.2
19.2
36.4
<0.001
Non cardiac, %
0.6
10.0
16.9
9.1
<0.001
Conclusion: Patients with in-hospital hemorrhagic complications after primary PCI have 2-fold higher risk of 1-year mortality than those without complications, and 4-fold higher risk with coexistence of thrombotic complications.

P708 | BEDSIDE
B-type NT-proBNP as a marker for contrast induced nephropathy in patients with primary percutaneous coronary intervention for ST-elevation myocardial infarction
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Purpose: Albuminuria has traditionally been associated with an elevated risk of cardiovascular events. However, there were few studies examining a potential relationship between albuminuria and peri-procedural risk of percutaneous coronary intervention (PCI). The aim of this study was to evaluate the impact of albuminuria on the incidence of peri-procedural myocardial infarction (PMI) in patients undergoing elective stent implantation.
Methods: The present study included 252 consecutive patients who underwent elective stent implantation at Nagoya University Hospital between September 2011 and June 2013. PMI was defined as an increase in high-sensitivity troponin T > 5 times (0.070 ng/ml) the upper normal limits of the reference range 24 hours after PCI. Albuminuria was defined as a urinary albumin-to-creatinine ratio (UACR) of ≥ 300 μg/g. Microalbuminuria was defined as a UACR of 30 to 300 μg/g. Patients with a UACR <300 μg/g were defined as normoalbuminuria.
Results: Albuminuria was detected in 67 of our patients (26.6%); 54 (21.4%) had microalbuminuria and 13 (5.2%) had macroalbuminuria. The incidence of PMI was significantly higher in patients with albuminuria compared to those with normoalbuminuria (31.9% vs 43.3%; p=0.014). An apparent dose-response relation was found between the severity of albuminuria and the incidence of PMI. The incidence of PMI increased significantly from 26.5% in patients with normoalbuminuria to 42.6% in patients with microalbuminuria, and to 46.2% in patients with macroalbuminuria (p for trend =0.037). After multivariate adjustment using logistic regression analysis, the presence of albuminuria predicted PMI [Odds ratio 2.02, 95% confidence interval: 1.03–3.97, p<0.029]. Age, total stent length, and high-density lipoprotein cholesterol level were also independent predictors of PMI. Furthermore, patients with albuminuria and preserved estimated glomerular filtration rate (eGFR) had a 4.2-fold higher risk for PMI compared to patients with normoalbuminuria and preserved eGFR.
Conclusions: Albuminuria is a strong predictive factor for the incidence of PMI in patients undergoing PCI, especially in patients with preserved eGFR. These findings emphasize that patients with early stage of chronic kidney disease should be considered as a high-risk population in PCI.

P710 | BEDSIDE
High platelet reactivity and periprocedural myocardial infarction: a significant correlation beyond definitions
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Background: Previous studies have established the role of high platelet reactivity (HPR) as a predictor of peri-procedural myocardial infarction (PMI) after percutaneous coronary intervention (PCI). We aimed to verify the correlation between HPR and PMI in the light of the several available definitions.
Methods: We enrolled 502 consecutive patients undergoing PCI on aspirin and clopidogrel. Pre-PCI platelet reactivity was measured using the VerifyNow P2Y12 assay (results expressed in P2Y12 reaction units, PRU). Primary endpoint was the incidence of PMI according to the presence of HPR. PMI was defined according to the 2007 and 2012 universal definitions of myocardial infarction (UMDI), and the 2013 Society for Cardiovascular Angiography and Interventions (SCAI) definition. HPR was defined as PRU ≥ 208 criterion, and 37.1% (186 patients) according to the PRU ≥ 235 criterion. The incidence of PMI was 41.0% (206 patients) according to the 2007 UMDI criterion, 33.2% (128 patients) according to the 2012 UMDI criterion, 24.1% (123 patients) according to the 2013 SCAI definition. The incidence of HPR was 53.4% (268 patients) according to the PRU ≥ 208 criterion, 38.6% (194 patients) according to the PRU ≥ 235 criterion, and 37.1% (186 patients) according to the PRU ≥ 240 criterion. The incidence of PMI was consistently higher in patients with HPR according to all definitions (Table). We performed a multivariate analysis. HPR and PMI remained strongly associated with the occurrence of PMI even after adjustment for risk factors, treatments, clinical, biological and angiographical variables (OR (95%CI): 1.76 (1.35-2.30)).
Conclusion: From this large contemporary prospective study, our work suggest that NT-proBNP levels at admission could help to identify patients at risk of CIN after PPCI beyond traditional risk factors.
Conclusion:

p=0.033), presence of hypertension (r=-0.228, p=0.008), diabetes mellitus correlated with the numbers of catheters (r=0.418, p<0.001) and the third quartile (16.9% vs. 6.7%, p=0.014, and 8.5% vs. 1.7%, p=0.016, respectively), and the third quartile (16.9% vs. 7.7%, p=0.031, and 8.5% vs. 2.6%, p=0.048, respectively).

Conclusions: Decreasing numbers of catheters and minimizing perception of pain during TRCAG may reduce the structural and functional changes of radial and brachial arteries.

PT712 | BEDSIDE
The SYNTAX score, not contrast media volume, predicts contrast induced nephropathy among the patients with acute coronary syndrome
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Purpose: Contrast-induced nephropathy (CIN) impairs prognosis of patients undergoing percutaneous coronary intervention (PCI). Only a few previous studies reported the predictors of CIN in patients with acute coronary syndrome (ACS). The aim of this study is to evaluate predictive value of coronary lesion complexity for CIN in patients with ACS undergoing emergency PCI.

Methods: Study population was 220 consecutive patients with ACS who underwent emergent PCI. Five patients with hemodialysis were excluded. CIN was defined as an increase in serum creatinine concentration ≥25% or >0.5 mg/dl above the baseline level within 72 hour of the administration of intravenous contrast.Delta creatinine (ΔCr) was defined as “subtract baseline creatinine from max creatinine value”. Study patients were divided into two groups (CIN-group and non-CIN-group). Coronary artery lesion complexity was evaluated by the SYNTAX score.

Results: CIN occurred in 28 patients (13.0%). Significantly higher SYNTAX score was observed in CIN-group than non-CIN-group (26.4±12.3 vs. 17.2±10.2, p<0.0001). The SYNTAX score showed significant independent predictive value for CIN after adjustment of age, sex, hypertension, dyslipidemia, diabetes mellitus, contrast media volume and pre-procedural estimated glomerular filtration rate (Odds ratio 1.061, 95%CI: 1.010-1.113, p=0.018). ΔCr presented significant correlation with the SYNTAX score (r=-0.231, p=0.0006).

Predictors for CIN

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.068 (1.014-1.0124)</td>
<td>0.012</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.848 (0.385-8.871)</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.744 (0.241-2.393)</td>
<td>ns</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.433 (0.454-4.524)</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.994 (0.993-9.031)</td>
<td>0.052</td>
</tr>
<tr>
<td>Contrast media volume</td>
<td>1.094 (0.993-1.071)</td>
<td>ns</td>
</tr>
<tr>
<td>eGFR</td>
<td>1.045 (1.013-1.078)</td>
<td>0.005</td>
</tr>
<tr>
<td>SYNTAX score</td>
<td>1.061 (1.010-1.113)</td>
<td>0.018</td>
</tr>
</tbody>
</table>

The SYNTAX score presented an independent predictive value for CIN.

Conclusions: The SYNTAX score is a useful tool to predict CIN in patients with acute coronary syndrome. The predictive value was independent from contrast media volume or pre-procedural estimated glomerular filtration rate.
PT15 | BEDSIDE
Uric acid levels and the risk of contrast induced nephropathy in patients with impaired renal function undergoing coronary angiography/pci
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Background: Contrast Induced Nephropathy (CIN) is a complication of procedure that forsee the use of contrast media, mediated by oxidative stress and re-active oxygen species. Uric acid is characterized by inhibited nitric oxide system and enhanced reactive oxygen species. Few studies have so far investigat-ed the association between hyperuricemia and CIN, that is the aim of the current study.

Methods: We analyzed 934 patients with impaired renal function (Creatinine clearance <60ml/min) undergoing coronary angiography/PCI. Patients were diveded according to tertiles of baseline uric acid (Group 1 = <5.74mg/dL; Group 2 = 5.7-7.4mg/dL; Group 3 = >7.4mg/dL). CIN was defined as an absolute >0.5mg/dL or a relative >25% increase of creatinine at 24-48h after the procedure.

Results: Patients with higher uric acid levels were more often of white and red blood cells, higher glycemia and glycosilated haemoglobin, higher triglycerides and lower HDL-cholesterol and creatinine clearance at admission. In addition higher uric acid levels were more often associated with dilated cardiomyopathy/valvular disease as indication for angiography, with history of previous smokers, with history of hypertension and diabetes. They had higher levels of white and red blood cells, higher glycemia and glycosilated haemoglobin, higher triglycerides and lower HDL-cholesterol and creatinine clearance at admission. CIN occurred in 12.6% of patients, and significantly associated with uric acid (11.2% in Group 2, 10.3% in Group 3 and 16.3% in Group 3; p=0.05); this association was confirmed by multivariate analysis after correction for base-line confounding factors.

Conclusions: This is the first large study showing that among patients with impaired renal function undergoing coronary angiography or PCI elevated uric acid level is independently associated with an increased risk of CIN.

PT16 | BEDSIDE
Contrast-induced nephropathy in patients undergoing primary percutaneous coronary intervention

Purpose: Contrast-induced nephropathy (CIN) is the third leading cause of acute renal failure in hospitalized patients and has a negative prognostic impact with increased mortality and hospital stay. The incidence of CIN in patients undergo-ing primary percutaneous coronary intervention (PCI) is higher than in programmed procedures. In them, CIN prevention measures are less applied than in programmed PCIs, probably because of the urgency of primary PCI and the intention to reduce ischemia times. Our aim was to analyze CIN in patients undergoing primary PCI and the role of hydration in its prevention.

Methods: 408 patients with acute myocardial infarction (AMI) who underwent primary PCI were randomly assigned to receive either hydration with normal saline: 1ml/kg/hour since the beginning of the procedure and 24 hours after it (SS group) or nesocin (SS+nc group). Contrast-induced nephropathy (CIN) was defined as a >25% or 0.5 mg/dL increase in serum creatinine within 48-72 hours following the procedure.

Results: Mean age was 63.1±13.6 years, and 73.4% of the patients were male. 47.2% had hypertension, 22.6% diabetes mellitus, 12.4% renal dysfunction and 12.4% anemia. Mean creatinine clearance was 88.6±38.46 ml/min. All patients received ioxilan contrast with a mean contrast volume of 326±72 cc. There were no significant differences between the two groups regarding baseline fea-tures. 45.4% of patients were included in SS group and 50.6% in NS group. An in-tention to treat analysis was performed with 28.4% of crossover between groups. NIC was observed in 14% of patients: 21.05% in the NS group and 10.92% in the SS group (p=0.0001). CIN was a predictor of death (15.2% vs 2.8%; p=0.0001) and extrarenal depuration measures (13.43% vs 0%; p<0.0001). The other pre-dictors of CIN in the univariate analysis were the feminine gender (p=0.005), advanced Killip class (p=0.025), hypertension (p=0.001), anemia (p=0.028), the higher age (68.5 vs 62.7; p=0.009) and the lower hemoglobin prior the proc-e-dure (13.1 vs 14.2; p<0.0001). In the multivariate analysis, the only predictors of CIN were the hydration [OR=0.29 (1.04-0.66); p=0.003] and the lower hemoglobin prior the procedure [OR=0.69 (0.59-0.88); p<0.0001].

Conclusions: Hydration during primary PCI, implies a relative reduction of risk of CIN of 48.12%. Patients who presented CIN had increased mortality and need of renal replacement depuration measures. Given the higher incidence of CIN in emergent procedures, and the morbidity that it implies, we should improve prevention measures in these patients.

PT17 | BEDSIDE
Impact of bifurcation lesion on long term clinical outcome in patient with acute myocardial infarction undergoing primary percutaneous coronary intervention

Aim: Bifurcation as culprit lesion is frequent in patients with STElevation acute myocardial infarction (STEMI). Purpose of this study was to evaluate the impact of bifurcation culprit lesion on clinical outcome in patients with STEMI undergoing primary percutaneous coronary intervention (PCI).

Methods and results: We retrospectively analyze 755 patients with STEMI who underwent primary PCI during the 2009. 230 (30.5%) of those patients had bifurcation as a target lesion (BL) compared with 525 (69.5%) pts. with no bifurcation as an infarct artery (BLN). Treatment goal was to stent the main branch and provide TIMI 3 flow without flow limiting dissection in the side branch (SB). There were no significant differences in baseline characteristics between the two groups except for higher rate of left anterior descending as infarct artery in the BL group (73.9% vs 22.9%, p=0.0001). Provisional SB stenting strategy was used in all patients, with side-branch wire protection in 40% of patients and SB dilatation with final kissing balloon inflation was necessary in 7.4% of lesions. At 4 years follow up, mortality rates were similar in the BL and the NBL groups (31.8% vs 30.7%, p=0.8).

Conclusion: In patients with bifurcation as a culprit lesion, a simple strategy with TIMI flow-guided provisional SB-PCI results in comparable four-year mortality rate as in patients without bifurcation lesions.

PT18 | BEDSIDE
Impact of incomplete revascularization in patients with multivessel disease following primary PCI on early and one-year clinical outcome
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Incomplete revascularization has a detrimental impact on long-term clinical out-comes, including mortality. Current guidelines recommend only culprit lesion revascularization during STEMI treatment in patients with multivessel disease (MD) and additional value and timing of complete revascularization is a matter of current debate. In a two year period 2009-2010, we identified 662 (29.5%) pts with MD of native coronary arteries, out of total 2246 pts who underwent primary PCI interventions in our center. We sought to investigate whether additional revascularization, per-cutaneous (PCI) or surgical (CABG) through achievement of complete revascu-larization (CR) affected short and long-term survival of patients.

In our study cohort, male population was predominant (70.8%) and average age was 63.4±11.3 years. Complete revascularization (CR) was achieved in 21% (32.8%) in total, with ad hoc PCI accounting for 15 (6.9%) cases, staged PCI for 167 (76.9%), while CABG was done in 35 (16.2%) pts. In hospital revascularization was performed in 127 pts in total (120 staged PCI and 7 CABG) with additional value and timing of complete revascularization of CR on early and one-year clinical outcome in patients with acute myocardial infarction undergoing primary PCI on early and one-year clinical outcome.

In our study cohort, male population was predominant (70.8%) and average age was 63.4±11.3 years. Complete revascularization (CR) was achieved in 21% (32.8%) in total, with ad hoc PCI accounting for 15 (6.9%) cases, staged PCI for 167 (76.9%), while CABG was done in 35 (16.2%) pts. In hospital revascularization was performed in 127 pts in total (120 staged PCI and 7 CABG) with additional value and timing of complete revascularization of CR on early and one-year clinical outcome in patients with acute myocardial infarction undergoing primary PCI on early and one-year clinical outcome.

The other pre-
related to mortality (21.9% vs 5.0%; p=0.006), alongside with CS - 6 (29.3% vs 5.1%; p<0.001), female gender (24.1% vs 13.1%; p=0.009), and presence of CTO as NC lesion (30.0% vs 9.9%; p<0.001).

Patients with multivessel coronary disease and complex anatomy who failed to achieve complete percutaneous or surgical revascularization, have unfavorable short term and long term outcomes following treatment of culprit lesions during STEMI.

P720 | BEDSIDE
Comparison of outcome in patients with ST-elevation myocardial infarction treated with PCI in Eastern Denmark with patients treated in Southern Sweden

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The prognosis of patients with ST-elevation myocardial infarction (STEMI) has improved significantly in the era of mechanical revascularization. Whether this improvement is similar in different countries remains unclear. We wanted to look at the difference in outcome between Danish and Swedish STEMI patients treated with percutaneous coronary intervention (PCI) in Eastern Denmark and Southern Sweden, respectively.

Methods: We included 16,776 consecutive STEMI patients from 2003-2012 (68,101 patient-years of follow-up) treated in Eastern Denmark and Southern Sweden with PCI from the Eastern Danish Heart Registry and the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Short- and long-term morality between Danish and Swedish STEMI patients was compared.

Results: We identified 9,595 (57.2%) Danish patients and 7,178 (42.8%) Swedish patients. The Danish patients were predominantly men (73.8% vs. 71.0%), younger (63.4 vs. 66.3 years) with a higher prevalence of smoking (53.6% vs. 36.1%) and hyperlipidemia (24.8% vs. 22.5%, all p<0.01). Swedish patients had a higher prevalence of hypertension (41.6% vs. 36.0%), diabetes (15.6% vs. 10.9%) and previous MI (16.7% vs. 7.9%, all p<0.01). During the follow-up time 21.9% of the Danish patients died compared to 19.4% of the Swedish patients, p<0.01. Danish patients had a higher risk adjusted 30-day mortality (adjusted hazard ratio [HR] =1.8, CI 1.4-2.2, p<0.001) as well as long-term mortality (HR = 1.2, CI 1.1-1.4, p<0.001, Figure).

Conclusions: Danish STEMI patients treated with PCI have significantly higher short-term as long-term mortality compared to Swedish STEMI patients. The difference in mortality could not be explained by traditional risk factors, but may be due to unmeasured confounding.

P721 | BEDSIDE
Chronic total occlusion in a non-infarct coronary artery exacerbates the prognosis of patients with acute myocardial infarction

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Purpose: Several observational studies suggest that the co-existence of significant stenosis in the non-infarct related coronary artery worsened the clinical outcomes of patients with acute myocardial infarction (AMI). However, data on the impact of chronic total occlusion (CTO) of a non-infarct coronary artery on the prognosis of patients with AMI are scarce.

Methods: We retrospectively evaluated 429 consecutive patients with AMI who underwent primary percutaneous coronary intervention (PCI) from January 2008 and December 2012. We excluded AMI patients with out-of-hospital cardiopulmonary arrest, those with a culprit lesion in the left main trunk, and those diagnosed after 24 hours from symptom onset.

Results: In total, 41 (9.6%) patients had CTO lesions in a non-infarct related artery (CTO patients). These patients were significantly more likely to be associated with cardiogenic shock (30.2% vs. 11.6%, respectively; p<0.01) and to require extracorporeal membrane oxygenator (ECMO) treatment due to cardiopulmonary arrest in the emergency department or catheterization laboratory (12.2% vs. 2.3%, respectively; p<0.001) when compared to patients without a CTO lesion (non-CTO patients). Moreover, intraaortic balloon pump use was required in 28 (68.3%) CTO patients. Although the peak creatinine kinase levels between the CTO and non-CTO patients were similar (2815 U/L vs. 2116 U/L, respectively), the left ventricular ejection fraction, estimated by echocardiography after primary PCI, was significantly lower in the CTO patients compared to that in non-CTO patients (45.3% vs. 54.8%, respectively; p<0.0001). In-hospital mortality and 30-day mortality were significantly higher in the CTO patients than in the non-CTO patients (19.5% vs. 4.6%, p<0.0001; 14.6% vs. 3.4%, p<0.001, respectively).

Conclusions: AMI patients with CTO lesions are more likely to require assist device use and have a significantly poorer outcome as compared to those without CTO lesion.

P722 | BEDSIDE
One-year results of the taxus liberte post-approval study: comparison with the ARRIVE registry

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Purpose: The TAXUS Liberté Post-Approval Study (TL-PAS) is a prospective, multicenter US registry. Unique features include the TL stent and >12 months of prasugrel as part of dual antiplatelet therapy (DAPT) after stenting. Previously, in-hospital MACE were similar to the ARRIVE registries, which utilized the TAXUS Express stent and clopidogrel as part of DAPT. One-year outcomes in TL-PAS versus the ARRIVE registries are presented for the first time.

Methods: A total of 4119 patients (pts) were enrolled; 1592 pts were considered on-label for stent use. Pts were prescribed aspirin and prasugrel for 12 months. All major cardiac, cerebrovascular, and bleeding events were independently adjudicated. Overall and on-label patient outcomes were compared in TL-PAS and ARRIVE with unadjusted and propensity-score matched analyses.

Results: The overall rate of 1-year MACE in TL-PAS was 7.2% with ST 0.9% compared with 9.4% and 1.7%, respectively, in ARRIVE. MACE, its components and ST were significantly reduced when compared with ARRIVE (Table) and were consistent in unadjusted or adjusted analyses. Similarly, on-label pt cardiac endpoints were significantly better when compared to ARRIVE (Table).

Conclusions: One year TL-PAS registry results show excellent MACE and ST outcomes demonstrating statistically significant improvements when compared to a prior registry using a previous-generation paclitaxel-eluting stent and clopidogrel. These favorable results may reflect the utilization of a more modern stent platform coupled with a prasugrel-based DAPT regimen.
**P723 | BEDSIDE**

Distal left main coronary artery disease; does the localization of the lesion determine the success of the percutaneous intervention in the current era?

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**Purpose:** To analyze clinical, technical and prognostic characteristics of percutaneously revascularized (PCI) patients with left main (LMCA) disease according to the lesion localization.

**Methods:** All patients with LMCA consecutively treated with PCI in a high volume tertiary center between June 1997 and October 2011 were prospectively included in a data base. Follow-up information was obtained between January and May 2013 with a mean follow-up of 4.5±2.8 years. The IBM SPSS 20.0 was used for the statistical analysis.

**Results:** Total of 570 patients were included in the study, with distal LMCA lesion (D-LMCA) in 72.3% of them, 25.7% with Medina 1-1-1. D-LMCA were more frequently older (69.4±10.9 vs 66.5±12.8 years), men (81.1% vs 63.6%), anemic (39.1% vs 26.0%) and required intra-aortic balloon pump (IABP) in more cases (8.8% vs 5.6%) as compared to non-distal (ND) lesions (p =0.05 for all). Moreover, D-LMCA patients presented associated lesions in other main coronary vessels in 80.8%, as compared with 62.8% observed in the ND group and more angiographic complexity: AHA type C lesions in 54.2% vs 20.9% (p=0.001 for both). Technically, double stenting was used in 4.9% vs 0.7% in D-LMCA and ND group (p=0.03), with kissing balloon applied in 52.9% and 27.7% of cases in both groups (p=0.001), with longer stents used in the former group (19.8±5.6mm vs 14.4±5.4mm, p<0.001). Intravascular ultrasound was applied in 36.8% of patients of the whole group without any differences between D-LMCA and ND group (p=0.2). At the end of follow-up events rates in the group of D-LMCA and ND were as follows: mortality 30.7% vs 20.7%, p=0.03; non-fatal myocardial infarction 17.9% vs 11.3%, p=0.096; non-fatal cerebrovascular event 3.7% vs 2.9%, p=0.35. In the multivariable analysis not the localization of the lesion but clinical variables such as the age, presence of anemia and IABP were significantly associated with higher mortality. Among those with anterior STEMI and at least 1mm ST-elevation in aVR, ORs for non-fatal myocardial infarction and intra-procedural ventricular fibrillation (VF) were 1.05 (95%CI 0.62-1.73) and 1.88 (1.01-3.61), respectively. The adjusted ORs for inferior STEMI -80mmHG and intra-procedural VF or sustained VT were 2.01 (1.10-3.69) and 2.28 (1.05-5.20), respectively. Adjustments for age and co-morbidities were performed.

**Conclusions:** Not the distal localization of the LMCA disease per se determines higher mortality rates among these patients but the worse clinical profile that they present is responsible for the worse prognosis.

**P724 | BEDSIDE**

Multi-vessel coronary artery disease is associated with early, but not late, mortality following primary percutaneous coronary intervention

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**Background:** A third of ST-elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PCI) have multi-vessel coronary artery disease (MVD). The PRAMI study has suggested that prevention of non-culprit lesion associated mortality is the key to improve survival. However, optimal timing of non-culprit lesion PCI remains controversial.

**Aim:** To assess early (<30 days) and late (30 day – 1 year) mortality following PCI in the pre-PRAMI era, according to MVD status.

**Methods:** A total of 3566 STEMI patients underwent PCI at two large tertiary centres between 2008 and 2011 and were included in this study. Patients were divided into 2 groups: 1) single vessel disease (SVD); 2) multivessel disease (MVD) group. The MVD group was further subdivided into those who had single vessel PCI (MV-SVPCI) and those who had multivessel PCI (MVD-MVPCI) during the index PCI.

**Results:** The MVD group consisted of 1201 patients (33.7%), who were older and had a smaller proportion of females (66.2±12.7 years, 26.4%) compared to SVD group (61.3±12.2 years, 33.2%). In the MVD group, 21.1% of patients underwent MVP PCI. Compared to MVD-SVPCI group, the MVD-MVPCI group had similar age and proportion of females but a higher percentage of cardiac shock (13.2% vs. 4.45%, p<0.001) Overall 30-day mortality rate was 5.9% (4.3%) in SVD group, 7.4% in MVD-SVPCI group and 15.8% in MVD-MVPCI group. In a logistic regression model for several confounders, MVD-MVPCI and MVD-SVPCI had similar 30-day mortality compared to SVD with odds ratio (95% confidence interval) of 1.63 (1.13-2.30) in MVDSVPCI and 2.89 (1.39-4.32) in MVD-MVPCI group. Overall 30-day to one-year mortality rate was 3.4% (3.0%) in SVD group, 4.5% in MVD-SVPCI and 3.4% in MVD-MVPCI. In the Cox proportional hazard model, neither MVD alone nor MVD subgroups were associated with 30-day to one-year mortality.

**Conclusions:** In this large observational study of unselected PCI-treated patients who were associated with increased in-hospital mortality but not with mortality beyond 30 days. Although, the optimal timing of staged PCI for MVD following PCI remains to be determined, the current study suggests that it should be performed early following index PCI for it to have an impact on mortality.
did not show the significant difference compared to those in non-oldest patients. (P=0.06)

Conclusion: In this study population, aggressive primary PCI for the oldest old AMI patients may provide the better 30days and 1 year prognosis similar to the younger patients.

P727 | BEDSIDE
Impact of the CABG SYNTAX score in patients with acute coronary syndrome and previous CABG undergoing percutaneous coronary intervention (PCI).

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Purpose: Limited information exists regarding clinical outcomes in patients with acute coronary syndrome (ACS) and previous CABG undergoing percutaneous coronary intervention (PCI). Recently the CABG SYNTAX Score, an objective measure of anatomical complexity and revascularisation post CABG surgery was reported in stable ischemic heart disease patients. In this context we sought to analyse the prognostic role of the CABG SYNTAX score in patients with ACS and previous CABG surgery undergoing PCI.

Methods: Between January 2012 and July 2013, 106 patients with previous CABG were referred to cardiac catheterisation in our centre due to moderate- and high-risk ACS (UA-44, NSTEMI=44 and STEMI=18 patients). The study’s population was subdivided into those that had low-risk (-22) and those that had high-risk CABG SYNTAX score (n=45 and n=61, respectively). The primary endpoint was all-cause mortality at a median follow-up of 11.6 months (IOR range: 10.2-13.1 months).

Results: Mean CABG SYNTAX score was 32.5±6.0 and 14.6±4.9 in the high-risk and low-risk group, respectively. There were no differences in baseline characteristics and clinical presentation between groups. Patients in the high-risk group had a larger number of unprotected coronary lesions (2.6±1.2 vs. 1.9±1.0; p<0.01), fewer patient grafts (0.6±0.7 vs. 1.1±0.7; p<0.01) and a higher standard SYNTAX score (45.9±9.0 vs. 28.7±10.1; p<0.01) than patients in the low-risk group. There was no difference in the incidence of secondary revascularisation between groups (59% in the high-risk group vs. 49% in the low-risk group; p=0.30), and PCI was the preferred technic in both groups (94% in the high-risk group and p=0.8). Thirty-day mortality was higher in the high-risk group (21.5% vs. 0%; p<0.01). Kaplan-Meier analysis revealed that patients with high-risk CABG SYNTAX score had significantly higher all-cause mortality rates (39.3% vs. 8.9%, p<0.01) during follow up. Multivariable analysis identified age (OR: 1.06 [CI: 1.01-1.12]; p=0.018) and CABG SYNTAX score (OR: 7.19 [CI: 4.9 in the high-risk group - 2.04-25.26]; p<0.01) as independent predictors of mortality during follow-up.

Conclusions: In patients with prior CABG surgery and acute coronary syndrome undergoing PCI, the anatomical coronary disease complexity and the degree of revascularisation measured by the CABG SYNTAX score is an independent predictor of 1 year all cause mortality.

P728 | BEDSIDE
Decreasing educational inequalities in percutaneous coronary intervention (PCI) utilization following an incident acute myocardial infarction (AMI) in Norway 2001-2009: a CVDNOR project

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Purpose: To explore national trends and educational differences in PCI utilization in patients with an AMI during 2001-2009. Methods: Hospitalisations for an incident AMI in Norway were explored using multivariable Poisson regression. Educational differences and trends were analyzed by Joinpoint regression. Results are expressed as average annual percentage change (AAPC). Results: Of 104,836 patients (mean age (SD) 71.1 (12.7) years; 62.7% men), 30.4% underwent PCI within 28 days. In men, PCI rates increased during 2001-2009 in all education levels) (Fig. 1).

Conclusions: Small but significant decrease of P2Y12 inhibition is observed during elective PCI and the decrease is associated with reticulated platelets.

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Purpose: We evaluated whether P2Y12 inhibition is affected by elective percutaneous coronary intervention (PCI) in patients prepaid with clopidogrel. The study also aimed to investigate role of reticulated platelets (RPs) on periprocedural changes of platelet inhibition.

Methods: In a prospective single-center study 91 patients underwent elective PCI with stenting. All patients were preloaded with 300 mg of clopidogrel on the day before PCI and one 75 mg maintenance dose on the day of PCI. Arterial blood samples were taken exactly before and immediately after PCI from the arterial sheath. Platelet reactivity index (PRI) was measured by the vasodilator-stimulated-phosphoprotein (VASP) flow cytometry test. Reticulated platelet count was performed in 86 patients before and after PCI. Results: The median increase of PRI was 31%p (interquartile range -2 to 7, p<0.001). The absolute number of RPs decreased from 9.33±4.82 x10^9/L to 8.08±4.29 x10^9/L (p<0.001). Patients with baseline RPs below median had greater increase of PRI (31%p [-1 to 15] vs 17%p [-6 to 46], p=0.015). Individuals with elevation of RPs during PCI (n=8) had significantly more pronounced median increase of PRI (6%p [3.5 to 19.75]) compared to those with fall of RPs (n=78, 21%p [-3 to 6], p=0.045). Both baseline number of RPs and their change during PCI were associated independently with the increase of PRI (Fig. 1).

Reference:
K. Amemiya, K. Yamashita, M. Yamamoto, S. Ebara, T. Okabe, K. Hoshimoto, T. Yakuashii, N. Isomura, H. Araki, M. Ochiai. Showa University Northern Yokohama Hospital, Division of Cardiology and Cardiac Catheterization Laboratories, Yokohama, Japan

Purpose: The coronary thin-foil fibrotheroma (TCFA) estimated by optical coherence tomography (OCT) is a major determinant of vulnerable plaques.

P731 | BEDSIDE
Impact of statin therapy on coronary thin-foil fibrotheroma in patients with stable coronary artery disease: a 3 vessel optical coherence tomography study

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Purpose: The coronary thin-foil fibrotheroma (TCFA) estimated by optical coherence tomography (OCT) is a major determinant of vulnerable plaques. The...
**P732 | BEDSIDE**

Early benefit of cangrelor in patients undergoing PCI in CHAMPION PHOENIX


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**Purpose:** CHAMPION-PHOENIX showed that cangrelor, an intravenous P2Y12 inhibitor, reduced death, MI, ischemia-driven revascularization, or stent thrombosis at 48 hours in patients undergoing PCI. We aimed to further characterize the benefit attributed to either cangrelor or 600 mg clopidogrel in the cangrelor arm.

**Methods:** A total of 11,145 patients undergoing PCI were randomized in a double blind, double dummy fashion either to cangrelor transitioned to clopidogrel 600 mg after the end of the 2 hour infusion or to 300 or 600 mg of clopidogrel as soon as possible after randomization, which was after the need for PCI was established at the time of angiography. Timing and dose of clopidogrel administration in the comparator arm were at the investigator’s discretion. The primary endpoint was the composite of death, MI, ischemia-driven revascularization, or stent thrombosis at 48 hours. A landmark analysis at 2 hours was performed to reflect a comparison prior to the administration of the clopidogrel 600 mg transition dose in the cangrelor group.

**Results:** At 2 hours, cangrelor significantly reduced death, MI, ischemia-driven revascularization, or stent thrombosis (4.1% vs. 5.4%; HR 0.76; 95% CI 0.64, 0.90; p=0.002) compared with clopidogrel (Figure). The results were similar in both the 300 mg and the 600 mg placebo subgroups. Between 2-48 hours, there was no difference in outcomes between patients randomized to either cangrelor or clopidogrel (0.7% vs. 0.6%; HR 1.16; 95% CI 0.70, 1.90; p=0.57).

**Conclusions:** In the CHAMPION-PHOENIX trial, the benefit seen with cangrelor was driven by cangrelor administration and occurred very early before administration of clopidogrel in the cangrelor arm.
post-procedural index of microcircular resistance (IMR) value as an index of microvascular function.

**Methods:** This study consisted of 56 patients (56 lesions) with stable angina pectoris who were planned coronary stent implantation. Patients were assigned to receive either EPA (1800mg/daily) with statin (EPA group, n=33) or statin only (Control group, n=23) more than 2 weeks before procedure. In all lesions, integrated backscatter intravascular ultrasound (IB-US) measurements were performed before stenting and the IMR was measured immediately after stent implantation using a pressure-temperature sensor wire. We compared to IVUS parameters and the IMR between the 2 groups.

**Results:** There were no different in clinical characteristics except for eicosapentaenoic acid to arachidonic acid ratio between EPA and Control group (1.07 [0.79, 1.47] vs 0.32 [0.21, 0.49], p<0.0001). IB-US parameters were not different between EPA and Control group (total plaque volume: 154±106mm$^3$ vs 164±131mm$^3$, p=0.8, 5lipid volume: 46±15% vs 44±12%, p=0.6). Post-procedural IMR was significantly lower in EPA than in Control (20.6 [12.9, 24.8] vs 30.6 [16.5, 42.4], p=0.01).

**Conclusions:** Pre-treatment with EPA in addition to statin reduced microvascular dysfunction induced by PCI. The mechanism was not associated with coronary plaque characterization. This favorable effect with EPA to coronary microcirculation could contribute to the prevention of post-procedural myocardial injury and the better clinical outcomes.

**P736 | BEDSIDE**

**Long-term compliance of secondary prevention treatment - females and males with stable angina in clinical practice: Results of the STAR-Registry**

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**Background:** Patients with coronary artery disease need live-long medical treatment with multiple agents for secondary prevention. Little is known about the compliance to long-term secondary prevention treatment of stable coronary artery disease (CAD) in clinical practice.

**Methods:** Between Sept 2001 and March 2003, a total of 2,022 consecutive patients with angina pectoris and first angiographic diagnosis of CAD were enrolled in the STAR-Registry (50 centres). We examined the compliance to guideline recommended medical treatment over a 5-year-follow-up in stable CAD in clinical practice in Germany, separated by gender.

**Results:** Current practice guidelines recommend long-term treatment with aspirin, ACE-inhibitors and statins for patients with stable coronary artery disease. The use of these drugs was high in both females and males but declined over the time of 5 years of follow up after the first angiographic diagnosis of CAD. The decline in aspirin treatment might be partly compensated by an increase in the use of VfK-antagonists probably due to a higher rate of atrial fibrillation over time. We found an increase in the use of calcium-blockers which might be seen as an aggravation of anti-anginal treatment over time.

**Table 1**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Females, n=600 (30%)</th>
<th>Males, n=1402 (70%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline 1-year 5-year</td>
<td>Baseline 1-year 5-year</td>
</tr>
<tr>
<td>Aspirin</td>
<td>89.3% 73.4% 75.7% 90.3% 78.8% 79.9%</td>
<td>89.3% 73.4% 75.7% 90.3% 78.8% 79.9%</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>77.5% 74.0% 80.0% 77.1% 71.0% 75.2%</td>
<td>77.5% 74.0% 80.0% 77.1% 71.0% 75.2%</td>
</tr>
<tr>
<td>ACE-inhibitor</td>
<td>61.3% 50.8% 48.9% 59.3% 52.4% 52.0%</td>
<td>61.3% 50.8% 48.9% 59.3% 52.4% 52.0%</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>16.8% 18.0% 26.3% 12.7% 15.0% 19.2%</td>
<td>16.8% 18.0% 26.3% 12.7% 15.0% 19.2%</td>
</tr>
<tr>
<td>Statin</td>
<td>73.3% 61.0% 67.2% 73.8% 63.5% 66.8%</td>
<td>73.3% 61.0% 67.2% 73.8% 63.5% 66.8%</td>
</tr>
<tr>
<td>VfK antagonist</td>
<td>4.0% 5.9% 13.7% 3.4% 5.5% 11.0%</td>
<td>4.0% 5.9% 13.7% 3.4% 5.5% 11.0%</td>
</tr>
</tbody>
</table>

**Conclusion:** Five years after the first angiographic diagnosis of CAD only 77% of patients stayed on aspirin, 50% on ACE-inhibitors and 67% on statins. There is need for improvement towards better long-term compliance to guideline recommended drug treatment.

**P737 | BEDSIDE**

**Withdrawal of angiotensin converting enzyme inhibitor or angiotensin receptor blocker before coronary angiography reduces contrast-induced nephropathy from meta-analysis of 4483 patients**

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**Objectives:** To investigate whether stopping or starting ACE/ARB before contrast procedure might influence the occurrence of contrast-induced nephropathy (CIN).

**Methods:** RCTs or non-RCTs comparing incidence of CIN in the patients undergoing contrast-using procedure with or without pre-procedural discontinuation of ACEI or ARBs. The pre-specified primary endpoint was overall post-procedural incidence CIN according to the status of withdrawing ACE/ARB in chronic users or new intervention with these medications before coronary angiography. The OR with 95% confidence interval was the effect measure.

**Results:** This analysis included 12 studies, 4,493 total adult patients receiving CAG. Continuation of ACEI/ARB in chronic users or administration of ACEI/ARB as a preventive measure in the naïve patients before AG showed no effect in the incidence of post-procedural CIN in the random effect model (OR 1.27, 95% CI 1.77-2.11, p<0.351, I2=61.9%). However, for the patients with chronic users, the continuation of ACEI/ARB before CAG is significantly associated with higher incidence of CIN (OR 2.06, 95% CI 1.62-2.61, p<0.001, I2=0.0%), and the hazard of continuation were marked in the subgroup of older patients (age >80 OR 2.00, 95% CI 1.51-2.66, p<0.001, Pinteraction=0.009) and chronic kidney disease (estimated GFR <60 ml/min; OR 2.70, 95% CI 1.52-4.79, p<0.001, Pinteraction=0.111). Administration of ACEI/ARB as a preventive measure in the naïve patients showed no impact on the development of CIN (OR 0.52, 95% CI 0.23-1.16, p=0.108, I2=34.2%).

**Conclusions:** Discontinuation of ACEI/ARB in chronic users is associated with significantly lower incidence of CIN, however administration of ACEI/ARB as a preventive measure did not showed any effect in the occurrence of CIN in this meta-analysis.

**P738 | SUSTAINED**

**Sustained reversal of apixaban anticoagulation with andexanet alfa using a bolus plus infusion regimen in a phase 2 placebo controlled trial**

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Increased use of novel oral anticoagulants couples with the lack of a reversal agent presents an unmet medical need for bleeding patients. Andexanet alfa (AnXa) is a modified recombinant human fXa that is catalytically inactive but retains high affinity for fXA inhibitors. Previously reported data in apixaban anticoagulated healthy subjects demonstrated a dose responsive reversal of anticoagulation as measured by anti-fXa activity after a single intravenous (IV) bolus administration of AnXa.

In this study we examine sustained reversal of apixaban-mediated anticoagulation using a 420 mg bolus plus continuous infusion regimen of AnXa for 45 min or 2 hrs at 4 mg/min, utilizing a 6:3 ratio of AnXa to placebo-treated subjects. Subjects were administered apixaban 5 mg BID on Days 1-6 and then dosed with IV AnXa or placebo on Day 6.

At 2 min following the completion of the AnXa bolus, mean anti-fXa activity decreased by >90% and this level of reversal was sustained throughout the infusion period for both regimens (p<0.0001). Similarly, plasma concentrations of unbound (free) apixaban decreased immediately after AnXa bolus and paralleled the anti-fXa activity profile. For the 2-hr infusion cohort, complete reversal of inhibition of thrombin generation was sustained throughout the AnXa infusion and remained within the normal range for 2 hrs post cessation of infusion. AnXa was well tolerated with no SAE's or severe AE's.

These data demonstrate that a bolus plus infusion regimen of AnXa provides a rapid and sustained reversal of anticoagulation as measured by anti-fXa activity, unbound fraction of apixaban in plasma, and thrombin generation. These properties of AnXa are likely to provide flexibility in dosing regimens for various clinical indications requiring different durations of reversal.
P739 | BEDSIDE
Safety and efficacy of hemostatic patch for post procedural hemostasis

Purpose: Hemostasis using hemostatic patch after cardiac interventions has been developed but its safety and efficacy is unclear. The purpose of this study is to investigate success of hemostasis rate and to investigate-difference of it among different access sites.

Methods: 100 consecutive puncture sites which were used for CAG, PCI or structural heart intervention with radial artery (RA), femoral artery (FA) or femoral vein (FV) were included in the study. Activated clotting time (ACT) was measured at the end of the procedure. Hemostasis was performed using manual pressure with hemostatic patch (Algimelt, Kaneka). Time to achieve hemostasis was measured. When hemostasis was not obtained even after 15 minutes manual pressure, radiula band was added. Successful hemostasis was defined as no bleeding condition was achieved without adding a radlula band. Re-bleeding and hematoma rate were calculated. Difference of successful hemostasis rate, rate of successful hemostasis which did not need protamine and time until complete hemostasis and frequency of bleeding/hematoma between FA, FV and RA was compared.

Results: RA, FA and FV access was included in 48 (48.0%), 33 (33.0%) and 19 (19.0%) sites. Mean ACT was 231 ± 220.6 and 221.0 sec (p=0.80). Mean sheath size was 5.3 and 7.1FR (-0.091). Borderline significant difference was ob-
served in successful hemostasis rate (85.4%, 97.0% and 100%, p=0.061). When adjusted for confounding factors, significance disappeared (p=0.15). Borderline significant difference was also observed in successful hemostasis which did not need protamine within 15 minutes (45.8%, 66.7% and 68.4%, p=0.003). Difference became signifi-
cant when confounding factors were adjusted (p=0.031). Similar result was ob-
served when femoral artery and vein access were combined and compared to radial artery access (p=0.013). Significant difference was observed in time until hemostasis (13.6, 10.4 and 9.4min, p=0.003) as well. Significant difference was not changed even when confounding factors were adjusted (p=0.008). Similar result was observed when femoral artery and vein access were combined and compared to radial artery access (p=0.001). No difference was observed in re-
bleeding and hematoma rate (4.1%, 6.1% and 5.3%, p=0.64). Conclusion: FA and FV access showed significant higher rate of success-
ful hemostasis which did not need protamine and shorter time until complete hemostasis than RA access.

A POTPOURRI OF ACUTE CORONARY SYNDROMES

P741 | BEDSIDE
Prognostic implication of the new peri-PCI (type 4a) myocardial infarction definition according to the third universal definition of myocardial infarction in patients with NSTEMI ACS
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Purpose: The definition of peri-PCI MI (type-4a) and its prognostic implication are controversial. Traditionally, type-4a MI was defined by CK-MB >3xULN after PCI. The 3rd universal MI definition introduced key changes: troponin (cTn) as the preferred biomarker; cTn (or CK-MB) threshold >5xULN; need for evidence of PCI-related clinical/angiographic complication. The prognostic implication and incidence of type-4a MI with the new criteria are not defined.

Methods: In the TRACER trial, 7479 of 12,944 NSTEMI ACS pts underwent PCI. CEC-ajudicated type-4a MI definition was: new CK-MB increase >3xULN post-PCI (normal/ falling biomarkers pre-PCI). CRFs collected investigator-reported PCI complications, including clinical instability or ischemia and angiographic complications (dissection, branch closure, no-reflow, TIMI flow decrease, emboliza-
tion, abrupt vessel closure). We assessed 1-y death rates following type-4a MI within 30d using these definitions: 1) TRACER definition; 2) TRACER definition with PCI complications; 3) cTn>CK-MB >5xULN; 4) 3rd universal type-4a MI definition. 1-y death was assessed in pts with spontaneous MI within 30d (n=98) and in pts without MI (n=6922) for comparison.

Results: Type-4a MI rates were 4.0% with the TRACER definition, 0.99% with the TRACER definition plus PCI complications, 3.7% with the >5xULN biomarker-only definition, and 0.95% with the universal type-4a MI definition. Mortality through 1-y follow-up MI didn’t change substantially by adding clinical and angiographic complications to biomarker criteria and was several folds lower than mortality after spontaneous MI.

Conclusion: Incorporating clinical or angiographic complications in addition to

P742 | BEDSIDE
Impact of invasive strategy in elderly patients referred for Acute Coronary Syndrome
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Background: Limited data are available in elderly patients admitted for acute coronary syndromes. The purpose of this study is to assess the beneficial impact of aggressive treatment strategy (defined by percutaneous coronary angiogram and eventually revascularization) on outcome in elderly patients.

Method: 1702 patients consecutive patients admitted for acute coronary syn-
drome were screened. Of these 1702 patients, 294 patients were ≥80 years old. Acute coronary syndrome was defined as chest pain associated with either tro-
ponin rise and fall or new change in ST segment or T wave. Patients with ST elevation were excluded and 235 patients -80 years old with non STEMI (85.3% of patients＜60 years old, 14.7%＜70 years old) were finally retrospectively analyzed. All patients received anti-platelet and anti-coagulant treatment according to ESC guidelines. We com-
pared outcome defined by death and emergency readmission in cardiology ac-
cording to treatment strategy (conservative or invasive).

Results: Coronary angiography was performed in 146 patients while 88 received medical treatment alone. Patients with angiography performed were younger (84.5±3.2 years vs. 85.6±1.9 years) but had similar event risk estimated by GRACE score (174.2±26 vs. 179.3±33). During follow up (median=496 days), one year mortality and emergency readmission was similar regardless of decision to perform coronary angiogram or not (41.2% vs. 43.6%, p=0.7) but in hospital stay was longer when angiography was performed (4.1±3.7 vs. 2.9±2.8, p<0.01).

Among the 146 patients who underwent coronary angiography, revascularization was performed in 98. Revascularization was not influenced by age (84.1±3.0 vs. 84.7±3.4) but GRACE score was higher in patients with revascularization per-
formed (177.2±26 vs. 167±30). Importantly, only patients with Left main (LM) or proximal left anterior descending artery (LAD) disease benefited from revascu-
larization (1-year free event survival 26% vs. 79%, p<0.0003) whereas patients without LM/LAD disease did not. Kaplan Meier mortality and emergency readmission analysis during follow up con-
firmed that patients with non revascularized LM or proximal LAD disease had worse outcome (LogRank p=0.009).

Conclusion: Invasive management of acute coronary syndromes in elderly pa-
tients improves survival in patients with Left main or proximal LAD disease. In other patients, invasive strategy does not improve outcome and results in pro-
longed in-hospital stay. Upstream stratification may be useful to identify patients with suspected Left main or proximal LAD disease.

P743 | BEDSIDE
Use of copeptin for the early diagnosis of acute myocardial infarction in patients with just minimally elevated high-sensitive troponin T

Background: High-sensitive troponin (hs-cTn) assays have markedly increased the number of patients with elevations of hs-cTn levels above the 99th percentile in the emergency room. The early diagnosis of acute myocardial infarction (AMI) in the subset of patients with just minimal elevations in hs-cTn is particularly dif-
ficult. Copeptin, a marker of endogenous stress, might be of added value in this patient group.

Methods: In a prospective multicenter study, we enrolled 1990 consecutive pa-
tients with symptoms suggestive of AMI. Levels of hs-cTn and Copeptin were measured at admission. Final diagnoses were adjudicated by two independent cardiologists according to the universal definition of AMI and hs-cTnT levels. For this analysis, we focused on patients with a hs-cTnT level at admission between 14 ng/l (99th percentile) and 50 ng/l.
Results: Of the 1990 patients enrolled, 22% had a hs-cTnT level at admission between 14 ng/l (99th percentile) and 50ng/l. Of these patients, 32%, had a final adjudicated diagnosis of AMI, while 19% were diagnosed with unstable angina, 21% with other cardiac disorders and 34% with non-cardiac causes of chest pain. Levels of Copeptin were significantly higher in patients with AMI compared to those without (17.5 pmol/l vs. 11.0 pmol/l, p=0.001). The area under the ROC curve for the diagnosis of AMI of hs-cTnT was (AUC of 0.66). The combination with Copeptin did not significantly improve the diagnostic accuracy (AUC for combination 0.68).

Conclusion: Of all patients presenting with symptoms suggestive of AMI, one quarter shows a minimal elevation in hs-cTnT between 14ng/l (99th percentile) and 50ng/l at admission. In this difficult subset of patients, the additional use of Copeptin did not improve the early diagnosis of AMI compared to the use of hs-cTnT alone.

P744 | BEDSIDE
Optimal cutoff-value of a prototype high-sensitivity cardiac troponin I assay in patients with kidney disease for the early diagnosis of acute myocardial infarction

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Purpose: The recent introduction of high-sensitivity cardiac troponin (hs-cTnI) assay has improved the early diagnosis of acute myocardial infarction (AMI). However, its diagnostic utility has never been tested in patients with kidney disease (KD), who are known to have elevated levels of cTn already in the absence of AMI, which may lead to a lower diagnostic value of more sensitive cTn in this high-risk subgroup.

Methods: We conducted an international multicenter study to examine the diagnostic accuracy of the prototype Siemens hs-cTnI Vista assay in 1885 patients presenting to the emergency department with symptoms suggestive of AMI, of whom 283 (15%) were determined to have KD (MDRD GFR -60ml/min/1.73m2) and to derive the optimal cutoff value for the diagnosis of AMI in patients with KD. The final diagnosis was adjudicated by two independent cardiologists based on high-sensitivity cardiac troponin (hs-cTnT).

Results: The final diagnosis was the final diagnosis in 33% (n=93) of all KD-patients as compared to 17% in patients with normal kidney function (p<0.001). Among KD patients with other diagnoses than AMI, baseline hs-cTnI-levels were elevated above the 99th percentile in 44%, in patients with KD the diagnostic accuracy at presentation, quantified by the area under the receiver-operator-characteristic curve (AUC), was 0.89. In patients presenting within three hours after the onset of chest pain, the AUC remained high with 0.88. In KD, the optimal hs-cTnI cutoff derived from the ROC curve was 32.0ng/l compared to 12.9ng/l in patients with normal kidney function (standard 99th percentile 9ng/ml, provided by the manufacturer).

Conclusions: The investigated prototype hs-cTnI assay has a very high diagnostic accuracy also in KD-patients. Mild elevations are common in non-AMI patients. However, the test-specific optimal cutoff-level in KD-patients seems to be more than three times as high as the standard 99th percentile level.

ClinicalTrials.gov number, NCT00470587

P746 | BEDSIDE
Spontaneous coronary artery dissection: angiographic diagnosis and contribution of optical coherence tomography

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Purpose: We aimed to assess the incidence of spontaneous coronary dissection (SCAD) and to determine the typical characteristics revealed by angiography and optical coherence tomography (OCT) observations with angiography and optical coherence tomography (OCT).

Methods: We performed a prospective single centre study of SCAD during usual care practice. Consensus management was adopted as appropriate. OCT was performed selectively for diagnostic purposes and/or to guide the management of complex cases.

Results: Between 2005 and 2013 SCAD was diagnosed in 40 patients (mean age 49 years, all women), representing 0.8% of all acute coronary syndrome patients managed invasively. Three quarters of these patients had ≤1 cardiovascular risk factors. 16/40 (40%) SCAD patients presented with ST-elevation myocardial infarction and 7/40 (17%) had concomitant cardiogenic shock. The final treatment plan was: 60% medical therapy; 30% PCI, 10% surgical (CABG or heart transplant). Two (5%) patients died acutely and all of the other women are currently alive (median follow-up 27 months).

Angiography: On retrospective review of the angiograms, we observed 5 features indicative of the pathophysiology of SCAD: 1) absence angiographic evidence of coronary disease; 2) an intimal flap; 3) extravasation of contrast; 4) smooth reduction of lumen caliber or coronary artery occlusion; 5) start/end of angiographic ambiguity distal to a collateral branch. 3 of these 5 signs were present in 95% of the cases.

OCT was performed in 10 cases (25%). OCT imaging revealed an intramural hematoma, an intimal flap and the total extent of vessel dissection extension. OCT confirmed the position of the guide-wire in the true lumen in 2 cases, which in turn facilitated an uncomplicated successful PCI.

Conclusions: In this large series of consecutive SCAD, we report angiographic signs helpful for the diagnosis. In complex or ambiguous cases, OCT is safe and it helps to optimise successful PCI.
nary intervention were prospectively enrolled. Echocardiography was performed to evaluate left ventricular diastolic function, LA volume, and LA function. Systolic (LAS) and late diastolic (LAA) LA strain were measured using speckle tracking echocardiography. Echocardiographic data was compared regarding culprit lesion locations and clinical characteristics.

Results: Global LAS strain was significantly lower in patients with a culprit lesion in the left circumflex branch than in patients with culprit lesions in other vessels (left anterior descending, 27.3±6.8%; left circumflex, 20.1±6.9%; right coronary artery, 23.3±6.5%; p<0.007). LA volume index did not differ significantly (left anterior descending, 34.3±11 mL/m²; left circumflex, 34.1±11 mL/m²; right coronary artery, 32.9±11 mL/m²; p=0.093). Other clinical and conventional echocardiographic parameters, including Doppler measurements, did not differ significantly.

Conclusion: Global LAS strain was lower in AMI patients with a culprit lesion in the left circumflex branch than in patients with culprit lesions in other vessels, with no significant difference in LA volume index. The lower global LAS strain might suggest decreased LA function resulting from ischemic insult by AMI with culprit lesions in the left circumflex branch.

P748 | BEDSIDE
Microvascular obstruction in patients with non-ST-elevation myocardial infarction - A contrast-enhanced cardiac magnetic resonance study

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Objectives: The aims of the study were to assess the frequency and predictive factors of microvascular obstruction (MVO) in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Background: The frequency and predisposing factors of MVO in patients with NSTEMI are unknown.

Methods: This study included 190 consecutive patients with NSTEMI who underwent coronary angiography, percutaneous coronary intervention (PCI) within 24 hours after admission and cardiac magnetic resonance (CMR) imaging after a median of 4.1 days after angiography. MVO was defined using the CMR criteria.

Results: MVO was detected in 26 (13.8%) patients with CMR late-gadolinium enhancement images. Patients with MVO were more likely to be men (88% vs 7%; P<0.008) and to have higher peak high-sensitivity troponin T, creatinine kinase (CK) and creatinine kinase-myocardial band levels, baseline Thrombolysis in Myocardial Infarction (TIMI) flow grade <1, absence of collateral circulation, post-PCI TIMI flow grade <3, microvascular blush grade <3 and angiographic no-reflow (58.3% vs 18.7%) than patients without MVO. Patients with MVO had a significantly larger myocardial edema extension which corresponds to the area at risk (16.4%±16.0% vs. 10.7%±13.7% of the left ventricle, P<0.016) and larger infarct size (13.6%±8.8% vs 3.5%±5.6% of the left ventricle, P<0.001). In multivariable analysis, the culprit lesion localization in the circumflex coronary artery (adjusted odds ratio [OR]=13.71, 95% confidence interval [CI] 2.91-64.58, P<0.001) and the infarct size (adjusted OR=3.37, 95% confidence interval [CI] 80-2.69, P<0.001 for each 5% of the left ventricle) were independently associated with the increased risk for MVO.

Conclusions: In patients with NSTEMI undergoing early PCI, the MVO defined by CMR imaging was present in 13.8% of the patients. The localization of culprit lesion in the circumflex coronary artery and larger infarct size were independently associated with the increased risk for MVO in these patients.

P749 | BEDSIDE
Absolute or relative deltas for diagnosis of myocardial infarction and how should they be calculated

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Objective: To compare delta values with peak troponin for the diagnosis of myocardial infarction when more sensitive troponin assays are used for the diagnosis of acute myocardial infarction (AMI) utilising laboratory measurements of cardiac troponin performed at different timepoints.

Methods: This was a sub-study of the point of care assessment of the RATPAC trial (Randomised Assessment of Treatment using Panel of Cardiac markers), set in the emergency departments of six hospitals. Prospective admissions of chest pain and AMI-diagnostic electrocardiogram had an additional blood sample taken at admission and 90 minutes from admission, and the serum stored frozen until subsequent analysis. Samples were analysed for cardiac troponin I (cTnI) by Laser Stratus CS (CS) (Siemens Healthcare Diagnostics), 99th percentile 0.01 ng/mL (3437); acute TnI (B) (Accumetrics), 99th percentile 40 ng/mL (Siemens Ultra S) (ADVA Centia, Siemens Healthcare Diagnostics); 99th percentile 50 ng/L and cardiac troponin T (cTnT) by the Roche high sensitivity cardiac troponin T assay hs-cTnT (Elecsys 2010, Roche diagnostics) 99th percentile 14 ng/L. The universal definition of myocardial infarction (MI) utilising laboratory measurements of cardiac troponin performed at the participating sites together with measurements performed in a core laboratory was used for diagnosis. Delta troponin was calculated as follows (a = 0 and b = 90 minutes): absolute-delta (b-a), absolute positive delta (b - a b - a for b-a) and %delta (b-a)/a, %positive delta (b-a)/a for b-a and (a-b)/b for a-b. Diagnostic accuracy was compared by receiver operator characteristic (ROC) curve analysis for diagnosis by each delta calculation and for peak troponin value.

Results: Samples were available from 617/1132 patients enrolled in the study, 357 male age 23.7-92.8 years median 53.8 years. Delta troponin was diagnostically equivalent to peak troponin for all four troponin methods. Absolute delta was superior to relative delta for cTnI (P ≤ 0.0007) and cTnT (p = 0.0049) and just failed to reach significance for cTnT CS (p = 0.064). Absolute and positive positive delta had equivalent diagnostic performance for all methods. For all methods, expressing relative delta as a positive percentage made diagnostic performance worse when compared to absolute delta or peak troponin or both. Absolute positive delta was superior to relative positive delta for cTnI and cTnT. Conclusion: Absolute delta appears more useful for relative delta for diagnosis of MI. The calculation should be the subtraction of the two values in temporal sequence.

P750 | BEDSIDE
The more you see the worse you get: institutional experience as a predictor of evidence based care in acute coronary syndromes

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Purpose: Variations in evidence based care for patients with Acute Coronary Syndromes (ACS) exist between hospitals. Gaps in care are prevalent and prognostic in important among highest risk patients. We hypothesised that “institutional experience” reflected by the proportion of high to non-high risk patients seen in hospitals contributes to inter-institutional variation in care.

Methods: Receipt of evidence based care (invasive management (cath), reperfusion therapy or more evidence based therapies (EBT)) according to patient risk was documented in the Co-operative National Registry of Acute Coronary Care, Guideline Adherence and Clinical Events (CONCORDACE). Hospitals were stratified according to proportion of high risk patients treated in discrete clinical categories (Median Grace Risk Score (GRS), Chronic Kidney Disease (CKD), age ≥ 80-85 years, Killip ≥ 1). For each category, receipt of care was compared between hospital groups. Hospital characteristics were entered into multivariate models to identify the predictors of care.

Results: 4969 ACS patients recruited into 33 Australian hospitals from February 2009-December 2013 were included. Comparing hospital performance, there was an inverse relationship between high risk patients and care:Highest vs lowest hospital quartiles: GRS > 130, cath 70% vs 89% p<0.0001, >4 EBT 72% vs 80%, p=0.06, CKD, cath 56% vs 71% p<0.001, >4 EBT 60% vs 78% p=0.0009, ≥80 yrs cath 35% vs 66% p<0.0001, >4 EBT 62% vs 56% p=0.41, K-1 cath 53% vs 80% p=0.01, >4 EBT 64% vs 64% p=0.98. After adjusting for catheterisation laboratory and hospital location, care of high risk patients remained inversely associated with hospital experience (Table).

Conclusion: Institutions that treat higher proportions of high risk patients are less likely to offer them evidence based care. Risk adverse behaviour therefore appears to be reinforced by clinical experience and constitutes a novel important barrier to improvement in evidence based care.

P751 | BEDSIDE
Heart rate at hospital discharge predicts long term prognosis in patients with acute coronary syndrome

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Purpose: Heart rate is a clear prognostic marker in patients with coronary artery disease. But the prognostic value of heart rate at hospital discharge in acute coronary syndrome patients is not very well known. So we tried to identify the prognostic value of heart rate in this setting.

Methods: We collected information from 525 consecutive acute coronary syndrome patients hospitalised in our hospital between December 2010 and December 2011 who survived and had a hospital discharge heart rate record in their files. The heart rate values, laboratory measurement values, demographic and echocardiographic parameters were recorded. Fifty-three (10%) of the patients had unstable angina pectoris, 290 (55%) had non-st elevated myocardial infarction and 182 (35%) had ST elevation myocardial infarction. The mean age of the three groups were 64. Three hundred ninety patients (74%) were men and 135 (26%) were women. The patients were divided into two groups according to their heart rate at hospital discharge: the patients in the first group had heart rate >70 beats/minute and the ones in the second group had heart rate <70 beats/minute.
of 2-year mortality after acute coronary syndrome.

Results: The patients in the first group who had discharge heart rate $>70$ beats/minute had lower ejection fraction, higher admission heart rate values, higher troponin I values, higher admission serum glucose levels than the patients in the second group. According to Spearman’s correlation analysis, discharge heart rate was positively correlated with serum troponin I, CK-MB, glucose and creatinine values and negatively correlated with ejection fraction and serum haemoglobin values. Ninety-seven patients died during the 2 year follow-up. The mortality rate in the first group was significantly higher than in the second group (87 vs. 10, p value=0.04). Univariate logistic regression analysis showed age, discharge heart rate, sex, ejection fraction, troponin I value, serum haemoglobin and creatinine values as independent predictors for 2-year mortality after acute coronary syndrome. But at the multivariate logistic regression analysis only discharge heart rate (odds ratio=1.047, CI: 1.005-1.09, p=0.027), age, ejection fraction and serum haemoglobin value persisted as independent predictors of mortality.

Conclusions: Hospital discharge heart rate of the patients is a strong predictor of 2-year mortality after acute coronary syndrome.

COMORBIDITIES AND CORONARY ARTERY DISEASE

P753 | BEDSIDE
How common is significant coronary artery disease in patients with type 2 myocardial infarction? Data from the SWEDGEHEART registry 2011-2013

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Aim: To assess the prevalence of significant coronary artery disease (CAD) in patients with type 2 acute myocardial infarction (AMI) and compare it with the prevalence in type 1 AMI.

Methods and results: A total of 59,685 hospitalizations with a discharge diagnosis of AMI were registered from 2011 until 2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEPHEART). The AMI type 1-5, locally classified in accordance with the universal definition of MI from 2007, and the result of any performed coronary angiography during hospitalization were noted in the registry. Significant CAD were defined as at least one coronary stenosis $\geq 50\%$ in the coronary angiogram. Type 2 AMI was present in 6.8% (n=4,036), while 89.1% (n=53,207) AMIs were classified as type 1. Patients with type 2 AMI underwent invasive coronary angiography less frequently compared to patients with type 1 AMI, 33.1 vs 78.9% (p<0.001), respectively. Proportions of the coronary angiography findings in relation to AMI type are shown in the figure.

Conclusions: Of the one third of the patients with type 2 AMI that underwent invasive coronary angiography in this real life study, almost half had no significant stenosis. On the other hand, among type 2 AMI patients with significant CAD, 3-vessel disease were relatively more common than among type 1 AMI patients. Hence, the type 2 AMI population is very heterogeneous regarding the occurrence and severity of CAD.

P754 | BEDSIDE
Prognostic impact of contrast volume on the basis of renal function regardless of SYNTAX score in patients with coronary artery disease

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Purpose: To investigate the association among clinical outcomes, contrast volume on the basis of renal function, and lesion characteristics due to SYNTAX score in patients undergoing percutaneous coronary intervention (PCI) with coronary artery disease (CAD).

Methods: A cohort of 1701 patients (69.7±10.7 years old, 77% male) who underwent PCI for CAD was analyzed from ICAS multi-center registry between April 2007 to April 2010. We divided patients into 3 groups according to tertile of SYNTAX score: Low SYNTAX score (0-8: n=567), Mid SYNTAX (9-15: n=567), and High SYNTAX (≥16: n=567). And we also divide into 3 subgroups on the basis of contrast media volume / e-GFR ratio (tertile, CV/GFR, low: <2.21, mid: 2.21-3.32, high: >3.32).

Clinical outcomes were defined as Major adverse cardiovascular event (MACE) which included all cause death, myocardial infarction, stroke, or hospitalization for worsening heart failure.

Results: Mean follow up period was 440 days. Incidence of MACE was significantly increased according to increasing CV/GFR ratio in high SYNTAX group, and according to increasing SYNTAX score in mid and high CV/GFR groups (Fig. 1).

Receiver operating characteristics curve (ROC) showed area under the curve (AUC) was larger in CV/GFR than SYNTAX score for MACE (0.641 vs. 0.498). CV/GFR was an independent predictor of MACE after adjustment of multiple co-founders (per increase, OR: 1.51, 95% confidence interval: 1.24-1.83, p<0.01) but not SYNTAX score (per increase, OR: 0.93, 95% confidence interval: 0.78-1.12, p=0.46).

Figure 1. Incidence of MACE (%).

Conclusions: High CV/GFR provides worse clinical outcome regardless of SYNTAX score in patients with CAD in this registry.

P755 | BEDSIDE
Impact of diabetes mellitus on long-term prognosis in patients with ischemic heart failure - a report from the Swedish Heart Failure Registry (S-HFR)

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Purpose: In an everyday life setting, we investigated the impact of diabetes on long-term prognosis in patients with heart failure of ischemic origin.

Methods: Patients clinically judged to have ischemic heart failure, of whom 50% were previously revascularised with (n=5265) and without (n=12 408) type 2 diabetes, included in the Swedish Heart Failure Registry (S-HFR) 2003-2011 were followed for mortality until 30 September 2011 (median 22.5 months). Differences in background characteristics were adjusted for in a logistic regression model.

Results: Patients with diabetes were younger (75 vs. 77 years) and more often had preserved renal function (60 ml/min; 44 vs. 38%), however hypertension
Results: Our cohort included >1,200,000 patients (32% young, 26% elderly) with a mean age of 49.6±17.0 years and mean GFR of 93.0±17.1 ml/min/1.73m². During a median follow up of 96.0 months and >10 million patient-years of follow-up, incident CVD rate was 0.4%, 3.8% and 10.5% in the young, middle-aged and elderly, respectively. Adjusting for gender and CVD risk factors, an increase of 10 units in GFR using CKD-EPI formula was independently associated with a decrease of 6.0%, 3.9% and 6.3% in incident CVD, in the young, middle-aged and elderly, respectively (p<0.001 for all; p for interaction=0.015). However, by using the MDRD formula, an increase of 10 units of GFR was associated with a decrease of 3.5% in incident CVD only in the elderly (p<0.001), but not in the other age groups (p for interaction=0.001).

Conclusion: An increase in GFR in the normal or mildly impaired range is independently associated with reduced incident CVD in all age groups using the CKD-EPI formula but only in the elderly using the MDRD formula.

P758 | BEDSIDE
Clinical and angiographic characteristics in patients with acute myocardial infarction without any cardiovascular risk factors

Purpose: Although cardiovascular (CV) risk factors are well established, some patients experience acute myocardial infarction (AMI) even without any risk factors. We analyzed clinical and angiographic characteristics in patients with AMI and without any CV risk factors. Also, we analyzed in-hospital and 1-year clinical outcomes between the patients with and without any CV risk factors.

Methods: We analyzed consecutive 11,997 AMI patients. CV risk factors were defined as any previous history of angina, MI, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), hypertension, diabetes mellitus, dyslipidemia, smoking and family history of CV disease. Patients were divided into 2 groups according to the presence of any CV risk factors (Group I, no risk factor; n=1,303; Group II, any risk factors, n=10,694). 1-year clinical outcome was analyzed in the patients who survived at hospital discharge and defined as the composite of 1-year major adverse cardiac events (MACE) including death, recurrent MI, and target vessel revascularization (TVR) and CABG.

Results: Group I was older (70.5±12.8 vs. 66.4±12.6 yrs old, p<0.001) and had higher prevalence of female gender (52.9% vs. 26.9%, p<0.001), and less previous history of chronic kidney disease (0.9% vs. 2.4%, p<0.001), cerebrovascular accidents (4.2% vs. 7.3%, p<0.001) than the group II. Group I experienced more cardiac pulmonary resuscitation during hospitalization (3.2% vs. 2.3%, p=0.047) and showed more anterior wall ischemia or infarction in electrocardiographic finding (49.0% vs. 45.0%, p=0.007). Angiographic findings showed more severe vessel involvement (55.6% vs. 48.7%, p<0.001), left anterior descending artery involvement (52.2% vs. 46.8%, p<0.001), total obstruction (49.2% vs. 45.2%, p=0.018) and lower PCI success rate (93.8% vs. 96.2%, p<0.001) in the group I. In-hospital mortality was higher in the group I (8.7% vs. 5.8%, p<0.001). However, in-hospital complications were comparable between the 2 groups including acute renal failure, multi-organ failure, new onset heart failure, cardiogenic shock, and major bleeding. Kaplan-Meier estimation showed no difference in the rate of in-hospital mortality of the 2 groups, although re-MI was lower in the group I (0.7% vs. 1.5%, log-rank p=0.039).

Conclusions: Elderly female patients were prone to develop AMI even without any known CV risk factors. Because AMI patients without any CV risk factors had higher in-hospital mortality, more intensive care is needed in AMI patients without any CV risk factors during hospitalization.
renal functions. In multivariate analysis, GI-3 was the only independent predictor for overall postoperative complications, while TN-c and hematocrit were independently associated with occurrence of AKI. No significant associations were observed between UT and postoperative complications.

**Conclusions:** TN-C and GI-3 are useful biomarkers for early detection of postoperative kidney damage. Although the incidence of diffuse CAS and ESC change in the DES-CAS group, those patients with higher incidence of coronary revascularization, recurrent chest pain and major adverse cardiac events (MACES). Table.

**Results:** In this study, DES-related CAS was related to higher incidence of adverse 3-year clinical outcomes. Special caution should be exercised in this particular subset of pts.

**P762 | BEDSIDE**

**Pregnancy losses in women and risk of myocardial and cerebral infarction in their parents**

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**Purpose:** Previous studies have linked pregnancy losses with increased risk of later myocardial and cerebral infarction in the woman. To shed light on whether a common underlying mechanism with a genetic component could link the two events, we conducted a familial aggregation study examining whether miscarriages, stillbirths and/or live singleton births between 1977 and 2008, and their parents. We then followed the parents for incident myocardial and cerebral infarction. Using Cox regression with parental age as the underlying time scale, we estimated hazard ratios (HRs) for each outcome by history of pregnancy loss in one or more daughters. All estimates were adjusted for parental sex, birth year, and number of children.

**Results:** Our cohort included >1 million parents. During almost 10 million person-years of follow-up, the parents experienced more than 50,000 myocardial infarctions and over 30,000 cerebral infarctions. Overall, parents with 1, 2 and ≥3 miscarriages among their daughters had 1.01 (95% CI 0.97-1.05), 1.04 (95% CI 1.02-1.11) and 1.10 (95% CI 1.02-1.19) times the rate of myocardial infarction, respectively, as parents who have not had miscarriages. When stratified by number of daughters contributing pregnancies, the results were similar for parents with 0 or 1 daughter, whereas for parents with ≥3 daughters the HRs for 1, 2 and ≥3 miscarriages among those daughters were 1.12 (95% CI 1.02-1.24), 1.29 (95% CI 1.13-1.48) and 1.33 (95% CI 1.12-1.57), respectively. HRs for cerebral infarction in parents with 1, 2 and ≥3 miscarriages among their daughters were 1.04 (95% CI 1.04-1.07), 1.08 (1.03-1.14) and 1.14 (1.04-1.24). Parents with ≥1 stillbirths among their daughters had 1.14 (95% CI 1.05-1.24) and 1.07 (95% CI 0.96-1.18) times the rates of myocardial and cerebral infarction, respectively, as parents whose daughters had no stillbirths.

**Conclusion:** Our findings are consistent with a common underlying etiology for both pregnancy losses and for myocardial and cerebral infarction. This hypothesis is supported by the fact that both events occur in the brain, and imply that in families with vascular/atherosclerotic disease, women may also be predisposed to miscarriage and stillbirth.
**CHALLENGES AND NEW CONCEPTS IN ACUTE CORONARY SYNDROME**

**P765 | BEDSIDE**

Incidence and prognosis of type 2 acute myocardial infarction in patients admitted to the emergency department in a university hospital

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Introduction: Type 2 myocardial infarction (MI) is defined as myocardial necrosis in circumstances that would cause the balance between supply and demand oxygen in the absence of a complicated atherosclerotic plaque. There is little information on the true incidence of type 2 MI and even less information about its prognosis compared to patients with type 1 acute MI. The objective of our study was to determine the incidence and prognosis of type 2 MI in relation to type 1 MI.

Methods: Of the 30,000 adult admitted to the emergency department during the first half of 2012, 1063 patients that had at least one determination of troponin I, were included. The diagnosis of type 1 and type 2 MI was established by three independent physicians according to the data obtained in medical records. We excluded patients with raised troponin who did not meet diagnostic criteria for MI type 1 or type 2 (n=144).

Results: A total of 191 patients satisfied the criteria of MI: Type 1 in 121 patients (63%) and type 2 in the other 70 patients (37%). Patients with type 2 MI were older (77 vs 69 years, p<0.001), more frequently female (41% vs 26%, p<0.018), previous history of heart failure (17.1% vs 4.1%, p<0.018) and higher comorbidity (worse renal function and less hemoglobin levels). On presentation, these patients had less chest pain (30% vs 88%, p<0.001) but more dyspnea (44% vs 15%, p<0.001). 1-year follow-up mortality was higher in type 2 than type 1 MI (Long Rank, p<0.001). However, multivariate Cox regression analysis adjusted by age and sex couldn’t find significant differences between both groups.

Conclusion: Type 2 MI patients have increased one year mortality than type 1 MI, probably due to their high comorbidity.

**P766 | BEDSIDE**

Is it still legitimate to recognize and differentiate the type of unstable angina?

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Purpose: Unstable angina (UA) and non-ST-segment-elevation myocardial infarction (NSTEMI) constitute a clinical syndrome subset of acute coronary syndromes and they are considered together in the guidelines. Although these clinical syndromes have a similar pathophysiology, they may be different with regard to risk stratification. We sought to identify clinical, laboratory and ECG features during admission and hospitalization to determine risk of new stratification of patients with UA.

Methods: We enrolled 986 consecutive patients admitted to 21 Italian cardiology centers (Stratificazione Prognostica Angina instabile; SPAI) for suspected UA. On admission, patients were categorized according to the following three types of UA: 1) de novo, 2) destabilizing, 3) post-infarction myocardial infarction (post-MI). Patients with UA post-MI and destabilizing UA also constitute the non de novo UA group. All patients completed standardized angina questionnaires,12-lead ECG, 24-H in-hospital Holter ECG, high-sensitivity C-reactive protein (hs CRP), and cardiac troponin I measurement at study entry. They were managed at the physician’s discretion during follow-up (F-up).

Results: The final diagnosis of UA was confirmed in 831 patients (84.3%). A total of 321 (39.6%) had de novo angina, 464 (56%) destabilizing angina and 46 (5.5%) post-infarction angina. Patients with non de novo UA were older, had significantly higher incidence of hypertension, diabetes, family history for coronary artery disease whereas patients with de novo UA had higher admission Tnl levels and similar levels of hsCRP. Instability at 48 hours occurred in 81 of 321 patients who had de novo UA (25.2%) and 193 of 510 non de novo UA (37.8%) during hospitalization. De novo UA was a negative predictor of instability at 48 hrs (p=0.005); the number of chest pain episodes in the month before admission was an independent predictor of instability at 48 hrs in both groups (p<0.001). After six-month F-up, 40 deaths and 34 non-fatal myocardial infarctions (MIs) had occurred (1.6% vs 6.9% deaths and 3.8% vs 4.5% non-fatal MIs in de novo and non de novo respectively). At multivariate analysis, non de novo UA, instability during the 48 hrs after admission, increased age and elevation of troponin were all independently associated with an adverse outcome at 180 days F-up (all p<0.05).

Conclusions: This study identified a subgroup of patients with either UA or NSTEMI having a high risk of cardiac events by evaluating clinical presentation, instability during the first 48 hrs and biochemical markers.
angina (PIA) have a smaller infarct and better in-hospital outcome after ST segment elevation myocardial infarction, than those without PIA. However, the impact of PIA on infarct size in patients with non-ST-segment elevation myocardial infarction (NSTEMI) has not been fully explored, and we aimed to determine the predictive value of PIA on infarct size and clinical outcome in NSTEMI patients.

Methods: From January 2013 to December 2013, 299 consecutive NSTEMI patients who presented with chest pain and underwent coronary angiography within 5 days after presentation were retrospectively reviewed. Of 299 patients, 7 individuals were excluded because 5 patients had recent cocaine use and 2 patients had a history of previous PCI. PIA was defined as experiencing separate episodes of chest pain within 7 days prior to the episode leading to admission. Revascularization procedures including percutaneous coronary intervention and coronary artery bypass grafting were performed at the discretion of the treating physician. Clinical and angiographical characteristics, length of stay (LOS), and in-hospital major adverse cardiac event (MACE) including death, recurrent myocardial infarction, target vessel revascularization, major ventricular arrhythmias, and shock, were compared between the patients with and without PIA.

Results: Among 292 patients, 144 (49%) patients experienced PIA. Clinical characteristics were similar except that, compared to the patients without PIA, those with PIA were more likely to be younger than 65 (54% vs. 42%, p=0.04) and less likely to be taking an ACE inhibitor (17% vs. 30%, p=0.009) or calcium-channel blocker (13% vs. 24%, p=0.02) despite the similar prevalence of hypertension. Patients with PIA had a higher AF in a precatheterization period (median 0.23 [0.07-1.86] vs. 0.85 [0.20-3.67] mg/l, p<0.001) and lower peak troponin values (median 0.39 [0.07-3.81] vs. 1.75 [0.25-7.47] mg/l, p<0.001) compared with patients without PIA. There was no significant difference between the two groups in the use of antiplatelet medication (p=0.30), in-hospital MACE (4.3% vs. 4.2%, p=0.73), and LOS (5.5 days vs. 5.4 days, p=0.83).

Conclusions: PIA in patients with NSTEMI was associated with smaller infarct as indicated by lower pre-catheterization and peak troponin values. There was no significant difference in the rate of revascularization, in-hospital MACE and LOS.

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Early Diagnosis of Myocardial Infarction in Patients with Atrial Fibrillation by Multiple Biomarkers

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Objective: Atrial fibrillation (AF) is a common condition in patients presenting to a chest pain unit. Early diagnosis and treatment of myocardial infarction (MI) strongly relies on blood biomarkers. Biomarkers may be elevated in AF patients due to the underlying disease. In our study we therefore sought to evaluate the ability of new troponin assays and novel cardiac biomarkers for rapid diagnosis of MI in AF patients presenting with a chest pain unit.

Methods: 14 established and new biomarkers (creatine kinase, myoglobin, troponin I, BNP, copeptin, soluble vascular endothelial growth factor receptor 1 (sFL T1), growth differentiation factor-15, troponin I, troponin T, heart type fatty acid binding protein, myoglobin, glycogen phosphorylase BB, midregional pro-atrial natriuretic peptide and B-type natriuretic peptide) were determined in 1802 patients with acute chest pain, mean age 61±14 years, 66% men. Among those, 313 patients (17.4%) presented with AF. All biochemical biomarker measurements were performed on admission, at 3 hours and 6 hours.

Results: On admission, patients with AF showed higher concentrations of all evaluated biomarkers. In AF patients, highest AUCs (area under the curve) for the diagnosis of MI were observed for troponin I and hsTnI. Admission hsTnI performed similarly in AF patients compared to individuals without the disease. The change in hsTnI concentration between 0 and 3 hours revealed a significantly higher AUC (0.98 in individuals with AF versus 0.84 in patients without AF; p<0.001). All other tested biomarkers showed comparable AUCs in patients with and without AF. None appeared to be superior to troponin measurements.

Conclusions: Troponins revealed very good discriminatory characteristics for the early diagnosis of MI in AF patients with suspected acute coronary syndrome. Serial measurement of a broad range of novel cardiac biomarkers did not show a benefit in the early diagnosis of MI. The change of hsTnI concentration after 3 hours seemed to be more diagnostic in AF patients.

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Frailty is common among older patients referred for invasive treatment in the setting of non-ST elevation acute coronary syndrome

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Objectives: To determine the prevalence of frailty in ≥75 year old patients presenting with NSTEACS managed by invasive treatment in a tertiary cardiac centre.

Methods: Over a period of 12 months from February 2013 to January 2014, 110 ≤75 year old consecutive patients admitted for invasive management of NSTEACS were recruited into an ongoing study (ICON1-A Study to Improve Cardiovascular Outcomes in High Risk Patients with Acute Coronary Syndrome) to a tertiary cardiac centre. Frailty was evaluated using the Fried criteria. A score of ≥3 is classified as frail, 1 or 2 as pre-frail and 0 as robust.

Results: The mean age was 81.6 years (standard deviation [SD] 4.3 years). 55 (50%) were females. 95 (86%) were managed by PCI, 5 (4%) by CABG (1 patient had staged CABG after PCI) and 11 (10%) patients were managed by medical treatment after CA. As per Fried Frailty Criteria; 36 (32.7%) were frail, 58 (52.7%) pre-frail and 16 (14.5%) were robust. All patients in the robust group were managed by invasive strategy (PCI) while only 88.3% frail/pre-frail patients were managed invasively. Previous MI was more common in the frail group versus pre-frail or robust (52.8% vs. 32.8% vs. 6.3%; p<0.05) groups respectively, as was previous cerebrovascular disease (33.3% vs. 17.2% vs. 6.3%; p=0.05), chronic obstructive pulmonary disease (30.5% vs. 12% vs. 12.5%; p=0.06) and chronic lung disease (22.2% vs. 17.5% vs. 0%; p=0.10). MVR (707pts.), 2 - patients with moderate MVR (205pts) and 3 - with severe MVR (29 pts.).

Results: Grade of MVR correlated positively with medical history of diabetes mellitus (p<0.001), heart failure (p<0.001), renal failure (p<0.001), previous myocardial infarction (p<0.001) and coronary-artery bypass grafting (p=0.001). Patients with higher grade of MVR were older (p<0.001). At admission the rate of atrial fibrillation (p<0.001) and pulmonary oedema (p<0.001) was higher in patients with more severe MVR. They also had more often chronic total occlusion (p<0.001) and multivessel coronary artery disease (p<0.001) diagnosed in angiography. According to the echocardiographic evaluation, patients with higher grade of MVR had lower left ventricular ejection fraction (p<0.001) and larger end-systolic (p<0.001) and end-diastolic (p<0.001) volumes of left ventricle. During hospitalization higher grade of MVR was related with higher rate of inhospital myocardial infarction (p<0.004), ventricular fibrillation (p=0.003), necessity of use intra-aortic balloon pump (p=0.05), respirator (p<0.001) and blood transfusion (p<0.001). The percentage of inhospital (p<0.001), 1-month (p<0.001), 6-month (p<0.001), one-year (p<0.001) and two-years mortality (p<0.001) was also higher in those patients.

The independent prognostic factors in this group of patients were: age (HR: 1.03; 95%CI: 1.00-1.05; p=0.022), female sex (HR: 1.94; 95%CI: 1.21-3.12; p=0.006), minimal hemoglobin (HR: 0.75; 95%CI: 0.63-0.89; p<0.001), minimal glomerular filtration rate (HR: 0.87; 95%CI: 0.79-0.96; p=0.006), hypertension (HR: 1.69; 95%CI: 1.04-2.73; p=0.034), smoking (HR: 2.04; 95%CI: 1.33-3.12; p=0.001) and performed preoperative coronary intervention (HR: 0.49; 95%CI: 0.31-0.79; p=0.003).

Conclusions: According to increase of MVR severity, clinical characteristic and prognosis in patients with NSTE-ACS deteriorate. MVR is not an independent prognostic factor in this group of patients.
In patients with GRACE hospital mortality (OR 0.45, IC95% 0.16-1.27, p=0.131).

Results: From 8186 patients included in the Registry, our sample included 2616.

The majority of patients (709 [80%]) was diagnosed with non-ST-segment elevation acute coronary syndromes (ACS) includes the administration of one anticoagulant at diagnosis. Switching a previously initiated heparin to another in the catheterization lab (CC) is discouraged in current guidelines because of increased bleeding reported in clinical trials. We sought to analyse a real-world population for an impact in mortality and bleeding associated with HC during percutaneous coronary intervention (PCI).

Conclusions: In this population, angiography timing had no significant influence in mortality. There was a tendency towards higher mortality with EIS, which could be explained by an eventual selection of sicker and unstable patients for an EIS.

Conclusions: In this population of contemporary patients with NSTACS, an elevated HC rate did not translate into increased mortality or bleeding rates.

Impact of total coronary occlusion of an infarct-related artery on outcomes in NSTE-MI patients treated with percutaneous revascularization (Pi-ACS)

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Purpose: The main purpose of this study was to define prevalence and predictors of total occlusion (TO) of an Infarct-Related Artery (IRA) in patients with NSTE-MI undergoing PCI. The second aim was to evaluate the clinical impact of preprocedural TIMI flow 0 in in-hospital outcomes and long-term mortality.

Methods: A total of 2767 pts with NSTE-MI enrolled in the Polish Registry of Acute Coronary Syndromes who underwent an invasive strategy with percutaneous coronary revascularization (PCI) were analyzed. Patients were divided in 2 groups according to preprocedural culprit vessel TIMI flow. TIMI flow 0 – total coronary occlusion (TO): 728 pts – 26.3%, and TIMI flow 1-3 – non-TO: 2039 pts – 73.7%.

Methods: We performed a retrospective analysis of patients admitted with NSTE-MI included in a National Acute Coronary Syndrome Registry in October 1st 2010 and October 1st 2013. We selected the patients admitted to angiography less than 24 hours after first medical contact (EIS) and between 24 and 72 hours (CIS) and determined in-hospital mortality associated with each strategy. We calculated each patient’s C-ACS and GRACE scores and determined the in-hospital mortality associated with EIS and CIS specifically in patients with C-ACS>1 and in patients with GRACE>140.

Purpose: Patients admitted with non-ST-elevation myocardial infarction (NSTEMI) may be submitted to angiography in an urgent invasive strategy, early invasive strategy (EIS) or conventional invasive strategy (CIS). The primary objective of this study is to determine how angiography timing affects in-hospital mortality in patients with NSTEMI. The secondary objective is to determine whether high risk NSTEMI patients, determined with the GRACE and with the C-ACS scores, benefit from a different approach.

Methods: We analyzed 889 consecutive patients admitted in a large-volume center to evaluate the safety and the efficacy of the stent. The device was successfully implanted in 100% of targeted lesions. Complete revascularization was achieved in 71% (n=635) of patients. Complete revascularization was defined as residual stenosis <50%.

Conclusions: Only Cx as a culprit lesion was an independent predictor of total occlusion in infarct-related coronary artery. NSTEMI pts with TO had higher in-hospital and one-month mortality, but long term outcomes were similar to non-TO pts.

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Conclusions: In this population of contemporary patients with NSTACS, an elevated HC rate did not translate into increased mortality or bleeding rates.

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Prognostic impact of heparin crossover across the spectrum of non-ST-elevation acute coronary syndrome patients

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Purpose: The invasive strategy for non-ST-segment elevation acute coronary syndromes (ACS) includes the administration of one anticoagulant at diagnosis. Switching a previously initiated heparin to another in the catheterization laboratory (CC) is discouraged in current guidelines because of increased bleeding reported in clinical trials. We sought to analyse a real-world population for an impact in mortality and bleeding associated with HC during percutaneous coronary intervention (PCI).

Methods: We analyzed 889 consecutive patients admitted in a large-volume center to evaluate the safety and the efficacy of the stent. The device was successfully implanted in 100% of targeted lesions. Complete revascularization was achieved in 71% (n=635) of patients. Complete revascularization was defined as residual stenosis <50%.

Conclusions: In this population of contemporary patients with NSTACS, an elevated HC rate did not translate into increased mortality or bleeding rates.
or transfusions. At one month, no events were reported. 6-month results will be presented.

Conclusion: Those Results are very promising in real world and complex patients (Diabetes, AF, Acute MI, Unstable Angina, Bifurcation, VKA). The COBRA P2F stent is safe and effective in routine practice. These preliminary data and the rapid reendothelialization observed in preclinical will serve as an impetus for a multi-center randomized study of short DAPT.

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Thrombus aspiration in thrombus containing culprit lesions in NSTEMI
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Objectives: Aim of this trial was to assess the effect of aspiration thrombectomy on no-reflow in patients with non-ST-elevation myocardial infarction (NSTEMI) in comparison to standard percutaneous coronary intervention (PCI).

Background: Aspiration thrombectomy in patients with STEMI is recommended by current guidelines based on several randomized trials, but there are no randomized trials assessing aspiration thrombectomy in patients with NSTEMI.

Methods: This prospective, controlled, multicenter study randomized 440 patients to adjunctive thrombectomy (n=221) in comparison to conventional PCI (n=219) in patients with thrombus containing lesions. The primary endpoint extent of microvascular obstruction (MO) in % of the left ventricle (LV%) was assessed by cardiac magnetic resonance (CMR) within 4 days. Secondary endpoints included infarct size, myocardial salvage index, and angiographic parameters including myocardial blush grade and TIMI flow grade. The combined clinical endpoint consisted of death, reinfarction, target vessel revascularization, and new congestive heart failure within 6 months.

Results: The primary study endpoint MO was not different between the thrombectomy and the standard PCI group with 2.0%LV (interquartile range [IQR] 0.8-4.1) versus 1.4%LV (IQR 0.7-2.6; p=0.17). Similarly, no significant differences were observed in infarct size (8.6%LV; IQR 4.0-14.7 versus 7.4%LV; IQR 4.1-13.1; p=0.46), myocardial salvage index (63.3; IQR 35.4; 87.2 versus 65.6; IQR 0.8-4.1) versus 1.4%LV (IQR 0.7-2.6); p=0.17. Similarly, no significant differences were observed in infarct size, myocardial salvage index, and angiographic parameters including myocardial blush grade and TIMI flow grade. The combined clinical endpoint consisted of death, reinfarction, target vessel revascularization, and new congestive heart failure within 6 months.

Conclusion: Aspiration thrombectomy in conjunction with PCI in NSTEMI with thrombus containing lesions does not lead to a reduction in microvascular obstruction.

STEMI
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The magnitude of ST elevation prior to primary PCI predicts ventricular fibrillation at reperfusion in patients with acute myocardial infarction
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Purpose: Ventricular fibrillation (VF) during reperfusion in ST-elevation myocardial infarction (STEMI) is an infrequent event, however it contributes to increased in-hospital mortality. Our aim was to analyse electrocardiographic (ECG) characteristics associated with VF during reperfusion in an unselected population of STEMI patients treated with percutaneous coronary intervention (PCI).

Methods: Consecutive STEMI patients admitted to a tertiary care hospital for primary PCI during 2007-2012 were retrospectively assessed for the presence of VF during reperfusion. Medical records were analysed for the presence of VF in relation to opening of infarct-related artery (IRA). Admission ECG stored in digital format, were analysed for a maximal ST elevation in a single lead (maxST), sum of ST -deviations in all leads (sumST), Anderson-Wilkins acuteness score and characteristics associated with VF during reperfusion in an unselected population of STEMI patients admitted to a tertiary care hospital for primary PCI during 2007-2012. 71 (1.9%) suffered from VF during reperfusion. In 56 of them, ECGs before reperfusion were available. 513 consecutive patients admitted to a university hospital for primary PCI during 2007, and not suffered from reperfusion arrhythmias comprised the control (No VF) group.

Results: Among 3724 STEMI patients admitted during 2007-2012, 71 (1.9%) suffered from VF during reperfusion. In 56 of them, ECGs before reperfusion were available. 513 consecutive patients admitted to a university hospital for primary PCI during 2007, and not suffered from reperfusion arrhythmias comprised the control (No VF) group.

MaxST was 498 (350-680) in VF group vs 300 (190-450) μV in NoVF group, p<0.001. SumST was 2289 (1714-3647) vs 1522 (975-2186) μV, correspondingly, p<0.001. Despite shorter time from symptom onset to PCI in VF group (185 (127-291) vs 227 (154-408) min, p<0.001), neither Anderson-Wilkins acute- ness score (2.6±0.9 vs 2.5±1.0, ns), nor the percentage of patients with grade 3 ischemia (45% vs 40%, ns) differed significantly between VF and NoVF groups. MaxST–300 μV remained an independent predictor of reperfusional VF in a multivariate analysis (OR=2.2, 95%CI 1.6-3.3, p<0.001), along with clinical characteristics such as the history of myocardial infarction (OR=2.3, 95%CI 1.1-5.0, p<0.03) and right coronary artery as the IRA (OR=2.2, 95%CI 1.2-4.1, p=0.012).

Conclusion: The magnitude of ST-elevation in patients with STEMI predicts reperfusional VF during primary PCI independently from other clinical characteristics and should be considered in assessment of periprocedural arrhythmic risk.

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Risk factor paradox in patients with acute myocardial infarction: Multicenter registry from Tokyo CCU network database

Background: Few studies have evaluated the relationship between the number of coronary artery disease (CAD) risk factors and mortality in patients with acute myocardial infarction (AMI).

Methods: We extracted data from Tokyo CCU Network Database (68 centers-Rainbow registry) in 2009-2011 and identified 7,650 AMI patients. We examined the presence and absence of 5 major CAD risk factors (Male, Hypertension, Dyslipidemia, Diabetes, and Smoking) among them. We assessed all-cause in-hospital mortality within 30 days.

Results: We followed up 6,923 patients. Most patients (95.2%) had at least 1 CAD risk factor. Number of fatalities for all cause was 513. All-cause mortality was significantly higher in the “no risk factor” group (23.8%, 19.5%, 15.0%, 10.1%, 10.0%, and 6.3% for patients with 0, 1, 2, 3, 4, and 5 risk factors, respectively, p for trend <0.001, Figure). Multivariate Cox regression analysis, which adjusted for age, Killip class on admission and other clinical factors, showed a clear inverse correlation between the number of CAD risk factors and all-cause mortality. Hazard ratio was 4.359 (p=0.009, 95% CI: 1.435 – 13.244) among group with 0 vs 5 group.

Conclusion: In AMI patients, lower number of CAD risk factors was associated with higher short-term mortality. These data strengthen the concept of the risk factor paradox and the mechanism should be elucidated.

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Factors associated with infarct-related artery patency before primary PCI for STEMI: Results from the FAST-MI 2010 registry
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Purpose: Early infarct-related artery (IRA) patency is associated with better clinical outcomes in STEMI patients. Using the FAST-MI 2010 STEMI cohort, we investigated factors related to IRA patency (TIMI 2 or 3 flow) at the start of procedure in patients admitted for primary PCI.

Methods: Consecutive STEMI patients treated with primary PCI in the FAST-MI registry was a nationwide French registry recruiting consecutive STEMI and NSTEMI patients (-48 hours from onset) in 213 centers in November 2010. Of 1452 STEMI patients with primary PCI, 466 (32%) had TIMI 2/3 flow of IRA before the procedure.

Results: Median age (62±14 years in both groups), GRACE score (141±31 vs 142±34) and time from onset to angiography (472±499 vs 451±479 min) did not differ according to IRA patency (TIMI 2/3 vs TIMI 0/1). Likewise, risk factors, medical history, and location of infarct were similar. Patients with a patent IRA had higher SBP and heart rate on admission (145±29 vs 141±28 mm Hg, and 79±20 vs 76±20 bpm, p=0.004 and 0.007, respectively). TIMI flow 2/3 did not differ according to antplatelet regimen before angiography: none 29%, ASA alone 28%, clopidogrel 31.5%, prasugrel 37%, GPIb-IIIa inhibitors 36.5%; in contrast, more patients had a patent IRA when receiving anticoagulants before angiography: none 24%, UFH 31%, LMWH, bivalirudin or fondaparinux 35% (P<0.03).

Conclusion: In patients with STEMI in patients having called earlier (<75 min, median time from symptom onset: OR 1.60, 1.26-2.04), or receiving anticoagulants before angiography: UFH
OR 1.52 (0.96-2.40), LMWH or newer anticoagulants OR 1.66 (1.05-2.63). Increasing time from diagnostic ECG to angiography was also associated with IRA patency: compared with first quartile of time from ECG to angiography, OR 1.39 (0.99-1.95) for Q2, 1.53 (1.02-2.14) for Q3 and 1.70 (1.20-2.41) for Q4.

**Conclusion:** Pre-procedural IRA patency is observed in one third of STEMI patients, it is not influenced by antplatelet therapy administered prior to angiography, but is more frequently found in patients having received anticoagulants, as well as in patients having called early. Higher IRA patency with increasing time delays from qualifying ECG to angiography suggests an additional role of spontaneous or medication-mediated fibrinolysis.

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**Impact of delays on mortality in women with STEMI: insights from the e-MUST STEMI registry**

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**Purpose:** The mortality rate in patients with STEMI is higher in women than in men. This higher mortality rate is partly accounted for by certain known characteristics inherent in the female population (age, diabetes, cardiogenic shock...). The purpose of our study based on the e-MUST registry of the Agence Régionale de Santé Ile de France (2006-2010) was to investigate the differences between men and women with respect to the time to initiation of reperfusion treatment strategies.

**Methods:** The study population included 5840 males (78.9%) and 1557 females (21.1%) with a higher median age in women: 72.1 [58.3–81.5] vs. 58.0 [50.1–67.8] (p < 0.0001).

**Results:** In-hospital mortality was significantly higher in women than in men: 254 (4.4%) vs. 143 (9.4%), p < 0.0001. Time to treatment initiation was significantly longer: Symptoms to Call (1.3 hrs [0.5–3.3] vs. 0.9 [0.4–2.4], p< 0.0001); Symptoms to First Medical Contact (FMC) (1.8 hrs [1.0–3.8] vs. 1.3 hrs [0.8–2.8], p< 0.0001). Call to FMC: (20 min [14–30] vs. 20 min [14–27], p<0.02). In addition to excess mortality, our results clearly show that the time to initial treatment is longer in females, partly due to the delay in calling the emergency units. After adjustment for clinical factors, severity, therapeutic strategies and time to first medical call, mortality remains higher in women than in men with an Odd Ratio of 1.43 [1.06–1.88], p < 0.01. The impact of time was more important in women with a symptoms to call delay of less than 90 min.

**Conclusion:** This study shows the important impact of time on mortality in women treated for STEMI especially when the symptoms-to-call delay is less than 90 min.

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What predicts acute kidney failure in patients with ST-elevation myocardial infarction?: Quantity of contrast agent or severity of myocardial infarction?

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**Introduction:** Deterioration of renal function is a common problem in patients with ST-elevation myocardial infarctions (STEMI). The purpose of the present study was to assess the association between the occurrence of acute kidney injury (AKI) in STEMI-patients and severity of myocardial infarction, comorbidities and treatment modalities including amount of contrast agent used.

**Methods:** All patients with STEMI from the metropolitan area of Bremen, Germany are treated at the Bremen heart center and since 2006 documented in the Bremen STEMI Registry (BSR). An increase of >25% or >0.5 mg/dl from baseline creatinin was interpreted as acute kidney injury (AKI).

**Results:** Data from 2538 patients and documented creatinin-values of a timespan > 48 hours after STEMI were included. At baseline 78% (n=1990) of pts. showed a normal renal function (eGFR >60 ml/min) while in 22% (n=548) renal function was initially impaired (kidney disease (KD)). An AKI was observed in 21% (n=522) of patients which was associated with a marked increase in 30-day (33 vs. 4%) and 1-year mortality (37 vs. 6%) after STEMI. A multivariate analysis showed that preexisting KD, age > 70 yrs., Killip Stage II/III as well as size of STEMI (CKmax) were predictive for developing an AKI while amount of contrast agent (CA) was neither in unadjusted data (CA >100 ml: OR 1.0, 95%CI 0.5-1.4, CA <300 ml: OR 1.2, 95%CI 0.6-1.5) nor in a multivariate model associated with higher rates of AKI (Table). TIMI-3-flow after primary PCI however was independently associated with a lower risk of developing an AKI equally in pts. with KD (OR 0.43, 95%CI 0.3-0.5, p < 0.01) and without prior KD (OR 0.63, 95%CI 0.5-0.8, p < 0.01).

**Conclusion:** In 21% of patients with STEMI an acute kidney injury could be observed which was associated with a marked elevation in short and long-term mortality after STEMI. However deterioration of renal function should be interpreted as a surrogate parameter indicating severity of STEMI while patients with a TIMI-3 flow after primary PCI showed lower rates of kidney injury. An association to the amount of contrast agent used could not be observed.

**P783 | BEDSIDE**

Impact of the Clinical SYNTAX score on four-year mortality in STEMI patients undergoing primary PCI


**Purpose:** Clinical Syntax Score (CSS) has been shown to predict adverse clinical outcomes after percutaneous coronary intervention (PCI). Our aim was to evaluate the ability of CSS to predict very long-term mortality in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI.

**Methods:** We analyzed records of 534 STEMI patients who underwent primary PCI, from a databank of a high-volume catheterization laboratory for the year 2009. CSS was calculated as Syntax Score (SXscore) x (modified age, creatinine and left ventricular ejection fraction (ACEF) score). SXscore was determined by scoring the culprit lesion just before stent implantation. Predictive accuracy was analyzed by determining c-statistic and goodness-of-fit of the model by the Hosmer-Lemeshow test. Kaplan-Meier cumulative survival curves for CSS tertiles were compared with the log-rank test.

**Results:** We divided patients into three categories according to the calculated tertiles: CSS-LOW < 7.56, 7.56 < CSS-MID < 19.30 and CSS-HIGH > 19.30. Four-year mortality rate in the studied population was 18.4% and it increased with the higher category of CSS (7.3% for CSS-LOW, 11.2% for CSS-MID and 36.7% for CSS-HIGH). Log-rank test showed significant difference between the cumulative mortality curves of different CSS tertiles (p < 0.001) (Figure). The continuous CSS had good discriminating power (C=0.756, 95%CI 0.701-0.812, p < 0.001) (Figure) and Hosmer-Lemeshow test showed good agreement between expected and observed data (χ² = 9.94, p = 0.27).

**Conclusion:** Clinical Syntax Score appears to accurately predict four-year mortality in STEMI patients undergoing primary PCI with the mortality rate gradually increasing across the tertiles of the score.

**P784 | BEDSIDE**

Long term clinical outcomes of newly diagnosed diabetes and prediabetes among patients with acute myocardial infarction


**Background:** Recent studies have demonstrated that newly diagnosed diabetes mellitus and prediabetes is common among patients with acute myocardial in-
Conclusion: Even though all three equations are predictive of one-year mortality, discriminatory power of the MDRD equation seems inferior to Cockcroft-Gault and the new CKD-EPI formula.

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Shorter ischaemic time and improved survival with ambulance activated primary PCI
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Purpose: In primary PCI (PPCI) for STEMI, reductions in door to balloon time have not resulted in lower mortality and the focus is increasingly on total ischaemic time. We sought to determine if our regional program for STEMI diagnosis by ambulance paramedics and direct transfer for PCI was associated with shorter ischaemic times and improved survival compared with ED diagnosis.

Methods: STEMI diagnosis was made in local EDs or by ambulance paramedics depending on patient presentation. Ambulance ECGs were transmitted to our ED for cath lab activation. Patient demographics, procedural variables and treatment times were prospectively recorded. Follow up was after 12 months by letter, phone call, clinical review or review of files.

Results: We treated 783 consecutive patients with PPCI during January 2008 - June 2013. Cath lab activation was initiated by Ambulances (Amb) in 24% cases and by ED in 76% cases. The patients were well matched with regards to age, sex, risk factors and prior revascularization. Mean age was 62.2±13.4 yrs for Amb versus 62.0±13.2 yrs for ED patients (p=0.84). Cardiac arrest prior to PCI occurred in 1.1% of Amb and 2.2% of ED patients (p=0.37). Prasugrel was used in 38% of Amb patients and 18% of ED patients (p=0.0001). Severity of coronary disease, lesion complexity and procedural variables were similar in the 2 groups. Initial TIMI 0 flow was present in 60.0% Amb and 59.7% of ED patients (p=0.93). Diameter, length and type of stent used (bare metal or drug eluting) as well as deployment pressures were almost identical in the 2 groups. Median total ischaemic time was 159 min for Amb and 210 minutes for ED patients (p=0.0001). The proportion of patients with first medical contact to balloon time of <120 min was 84% for Amb and 65% for ED patients (p=0.0001). Mean follow up was 324 days in both groups (p=0.99). Overall mortality was 7.3% in the Amb group compared with 47.7% (95%) in the ED group (p=0.036). Cardiogenic shock occurred in 2 patients (1.1%) in the Amb group and 33 patients (5.5%) in ED group (p=0.003). There were no significant differences in the incidence of stent thrombosis, MI or revascularization. On multivariate co-regression analysis including baseline and procedural variables, ambulance activation remained an independent predictor of mortality (HR 0.42, 95% CI 0.16-0.92, p=0.029).

Conclusions: Ambulance diagnosis of STEMI and direct transfer to the cath lab reduced total ischaemic time by 51 minutes and mortality by ~50% following PPCI. Efforts are needed to increase the proportion of STEMI patients treated using this strategy.

CORONARY ARTERY DISEASE IN THE REAL WORLD

P787 | BEDSIDE
The clinical benefit of ultrasensitive cardiac troponin I in the detection of exercise induced myocardial ischaemia

Background: Cardiac Troponin is the preferred biomarker in the diagnosis of acute myocardial infarction. We hypothesized that the development of a novel “ultrasensitive” cardiac Troponin I (us-cTnI) assay that allows quantification of minimal amounts of cardiomycocyte injury in the “normal range” of cTnI might allow the non-invasive detection of exercise-induced myocardial ischaemia.

Methods: We included 819 patients with suspected exercise-induced myocardial ischaemia referred for evaluation by rest/bicycle myocardial perfusion single-photon emission computed tomography (SPECT). All clinical information available to the treating cardiologist was used to quantify the clinical judgment regarding the presence of myocardial ischaemia using a visual analogue scale twice: once prior and once after bicycle exercise stress testing. Us-cTnI measurements were performed before, immediately after peak stress and 2h after stress testing in a blinded manner. The presence of myocardial ischemia was adjudicated based on perfusion SPECT combined with coronary angiography findings.

Results: Exercise-induced myocardial ischaemia was detected in 278 (34%) patients. Us-cTnI levels were significantly higher at all time points in patients with myocardial ischemia as compared to those without (p<0.001 for all). Combining clinical judgment prior exercise testing with baseline us-cTnI levels increased diagnostic accuracy quantified by the area under the ROC curve (AUC) from 0.672 to 0.757 (p=0.001). Combining clinical judgment after exercise testing (AUC 0.692) with us-cTnI levels at rest, peak stress and 2h after stress testing also increased the diagnostic accuracy (AUC 0.760-0.786, p<0.001 for all).

Conclusion: Combining clinical judgment with us-cTnI levels at rest, immediately after peak stress and 2h after stress testing substantially increased the diagnostic accuracy regarding the presence of myocardial ischemia. This novel strategy offers new avenues in the non-invasive assessment of cardiac patients.
Impact of left main stenosis on one-year mortality in patients undergoing coronary angiography

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Aim: The aim of this study was to investigate the relationship between left main (LM) stenosis and one year mortality in patients undergoing coronary angiography.

Methods and results: We extracted data from SCAAR (Swedish Coronary Angiography and Angioplasty Registry) and identified 294,928 patients between 2003 and 2013 who underwent coronary angiography. In 3,870 patients the extent of coronary artery disease was unknown and these were excluded. The indication for coronary angiography was stable angina in 29%, NSTEMI in 34%, STEMI in 17%, cardiac arrhythmia in 2%, valve disease in 8%, heart failure in 4% and aortic aneurysm in 0.4%. 21,758 (7.4%) of these patients had a LM stenosis.

The primary treatment decision was medical therapy in 15% (n=3,285), CABG in 55% (n=11,724) and PCI in 29% (n=6,219). One year mortality in patients with LM stenosis was 10.3% (n=2,031) compared to 4.2% (n=10,110) in patients with no LM stenosis (p < 0.001).

Adjusted multivariate logistic regression was used to compare one-year mortality between the groups. The following variables were entered into the model: age, gender, previous myocardial infarction, previous CABG, occlusion/stenosis in CABG graft, previous PCI, indication of angiography, smoking status, treated hypertension, treated hyperlipidaemia, diabetes and primary treatment decision. Adjusted odds ratio (OR) was 2.1 (95% CI 1.9-2.2; P < 0.001) if LM stenosis was present.

Intra-dia-stenosis test between LM stenosis, prior CABG, indication for angiography and primary treatment decision has shown that presence of LM disease had most impact in patients without previous CABG (OR 2.2, 95% CI 2.0-2.3, P < 0.001), with STEMI (OR 2.3; 95% CI 2.0-2.7, P < 0.001) and where primary treatment decision was medical therapy (OR 2.6 95% CI 2.2-3.0, P < 0.001) or PCI (OR 2.45 95% CI 2.2-2.7, P < 0.001).

Conclusions: In this large and unselected cohort of patients undergoing coronary angiography, presence of LM-stenosis was associated with increased risk of one year mortality compared to no LM stenosis. LM stenosis had most impact in patients without previous CABG, in patients with STEMI and in patients where primary treatment decision was medical therapy. This study confirms the results of previous historical studies that have shown LM stenosis negative impact in prognosis.

P791 | BEDSIDE
Defining clinical and biological predictors of high on-aspirin platelet reactivity: insight from a real life population of high risk cardiovascular patients


Purpose: Aspirin is a key treatment of atherothrombosis. Inter-individual variability of the effect of aspirin is linked to a higher risk of ischemic events. The aim of this study was to identify main factors linked to high on-aspirin platelet reactivity (HPR) in a large real-life population.

Methods: Between November 2011 and July 2013, in patients with coronary or cerebrovascular disease chronically treated with aspirin. Platelet reactivity testing was performed for the following reasons: high risk coronary or cerebrovascular angioplasty, recurrent acute coronary syndrome or ischemic stroke despite aspirin treatment. HPR was measured 24h after last aspirin intake and defined as maximal aggregation intensity >20% using light transmission aggregometry with arachidonic-acid 0.5mg/mL (LTA-A). Collagen-epinephrine platelet function analyzer (PFA-EPI) was also performed to evaluate global platelet reactivity (threshold <165%) and was combined with LTA. Cardiovascular risk factors, usual biological parameters and anti-platelet treatment were recorded and predictive factors of HPR were analyzed using multivariate logistic regression.

Results: 1508 patients (mean age 63±13y.o., 71% male, 23% diabetics, 23% active smokers) were explored. Antiplatelet treatment was aspirin alone in 333 patients (20.1%), associated with clopidogrel in 787 (52.2%), prasugrel in 269 (17.8%) or ticagrelor in 119 (7.9%). HPR was found in 11.1% patients using LTA-AA and in 5.2% patients combining LTA-AA and PFA-EPI. In multivariate analysis, independent predictive factors (OR [CI]) of HPR using LTA-AA were diabetes mellitus (2.10 [1.39-3.16]), age/10y. (1.25 [1.06-1.47]), fibrinogen level (2.57 [1.28-1.79]). Similar results were observed in patients treated with aspirin or dual antiplatelet therapy. The association between HPR and fibrinogen was not found significant in older patients (>75y). A fibrinogen level >4.00g/L was associated with 3.9-fold increased risk of HPR in patients aged >75y.o.

Conclusion: Diabetes, age and fibrinogen are the major predictor of HPR on aspirin in a real-life large population.

P792 | BEDSIDE
Galectin-3 predicts long term cardiovascular mortality in high-risk coronary artery disease patients of the GENICA study

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Purpose: Galectin-3 (Gal-3) can affect atherogenesis by inducing chemotaxis of monocytes, stimulation of phagocytosis, and proliferation of vascular smooth cells and fibroblast. However, data on its role in atherosclerosis and its complications lack, even though it has been extensively studied in heart failure patients. We therefore, investigated if Galectin-3 predicts cardiovascular (CV) death in patients at high risk.

Methods: The plasma levels of Gal-3 were measured in 1023 randomly selected patients of the GENICA study, who underwent coronary angiography and as- sumptively had a CV event within 3 years. After patients treated with CABG or with PCI, CV mortality was compared across groups by Kaplan-Meier analysis. The impact of Gal-3, as a continuous variable, was also examined using multivariable Cox's regression.

Results: During long-term (median 7.2 years) follow-up CV deaths occurred in 115 patients (15.2%), more commonly in the high and intermediate Gal-3 (25.2% vs. 13.6%, respectively) than in the low tertile (7.5%; p < 0.001). The adverse prognostic effect of high Gal-3 was confirmed also in subgroups analysis of the population with angiographically documented CAD and with a normal left ventricular ejection fraction (LVEF). Along with age, LVEF, and coronary atherosclerotic burden Gal-3 was one of the strongest predictors of CV mortality (HR 1.79, 95% CI 1.10-2.93, p = 0.020) at Cox's regression analysis.

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Conclusions: Gal-3 is a major predictor of CV mortality in patients at high CV risk, with angiographically documented CAD, and normal LVEF.

P793 | BEDSIDE
Right ventricular dysfunction following acute myocardial infarction with and without ST segment elevation: differences in predictors and prognosis

Introduction: The occurrence of right ventricular dysfunction (RVD) in the context of acute myocardial ischemia is associated with high morbidity and mortality, requiring early clinical recognition to choose the appropriate therapeutic strategy.

Objective: To identify the clinical differences and prognostic impact of RVD in ST elevation and non-ST elevation acute myocardial infarction (STEMI and NSTEMI, respectively).

Methods and results: Retrospective observational study including 1969 consecutive patients admitted in a Coronary Unit for the period of 4 years, since 2009, with the diagnosis of AMI (52% with STEMI and 48% with NSTEMI; mean age 64 years, 77.2% male). RVD incidence was more frequent in STEMI than in NSTEMI (6.9% vs. 4.1%, p=0.008) and also more severe (p=0.026). The independent predictors of RVD in STEMI were heart failure at presentation (OR 5.3, p=0.026), culprit lesion in right coronary artery (OR 19.2, p=0.004). The independent predictors of RVD in NSTEMI were previous history of atrial fibrillation (OR 19.2, p=0.004). The independent predictors of RVD in STEMI were heart failure at presentation (OR 5.3, p=0.026) and lower left ventricle ejection fraction (OR 0.93, p=0.023). Although it was not an independent predictor, right coronary artery stenosis ≥70% was very prevalent in those with NSTEMI and RVD (76.3%). Apart from AMI type, patients with RVD presented, during hospitalization, higher prevalence of cardiac shock (21.2% vs. 3.6%, p<0.001) and rhythm disturbances, as new onset atrial fibrillation (19.5% vs. 8.8%, p<0.001) and high degree atrioventricular block (22.1% vs. 4.3%, p<0.001). Only in the group with RVD and STEMI the mortality during hospital stay was significantly higher (15.7% vs. 3.2%, p<0.001) and related to RVD severity (mild, moderate or severe dysfunction). During follow-up, no differences were registered concerning mortality.

Conclusion: RVD is more frequent, more severe and has a worse prognosis in the acute phase of STEMI than in NSTEMI. It is associated with failure of primary angioplasty to restore effective blood flow on the right coronary artery in the majority of times.

P794

P795 | BEDSIDE
Impact of SYNTAX score for predicting contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention
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Objectives: We investigated the association with coronary complexity and contrast-induced acute kidney injury (CI-AKI) among coronary artery disease (CAD) patients undergoing percutaneous coronary intervention (PCI).

Methods: A total of 1701 CAD patients who underwent PCI, except for hemodialysis, were analyzed from ICAS (Ibaraki Cardiovascular Assessment Study) multicenter registry. Analyzed subjects were divided into 3 groups according to SYNTAX score: low (score<22, n=1435), moderate (score 23-32, n=184), and high score (≥33, n=82). CI-AKI was defined as an increase in serum creatinine of more than 25% or 0.5 mg/dl from the baseline within 1 week of contrast-medium exposure.

Results: A total of 133 patients (7.8%) developed CI-AKI among whole subject. The incidence of CI-AKI was 6.8%, 12.0%, and 15.9% for the group with low, moderate, and high SYNTAX score, respectively (Fig. 1). There was a stepwise increase in CI-AKI with increasing SYNTAX score and Mehran risk score (Fig. 2). After adjusting for baseline characteristics, multivariate analysis revealed SYNTAX score was an independent predictor of CI-AKI (odds ratio: 1.017, 95% confidential interval: 1.000-1.035, p=0.048).

Conclusion: SYNTAX score was a useful information for predicting CI-AKI among CAD patients undergoing PCI.

P796 | BEDSIDE
The clinical, angiographic characteristics and the 24-month clinical outcomes of Korean patients with vasospastic angina

Background: Vasospastic angina (VA) has been reported to be more frequent in the East than in the West. However, in Korea, a grand scale analysis has not been done yet. We planned to set the multi-center registry for Korean VA.

Methods: Total 11 centers of 9 universities participated in prospective, web-based VA-KOREA (Vasospastic Angina in KOREA) registry and the enrollment of patients newly diagnosed as VA using same diagnostic protocol started in July 2010. We only used intracoronary ergonovine, not acetylcholine, in provocation. Positive result of the provocation is defined as development of total or subtotal occlusion accompanied by angina and/or ECG changes. We got information about medical history, laboratory and angiographic findings, treatment, and prognosis. In this analysis, we determined the clinical, angiographic characteristics and prognosis using data-sets of VA-KOREA.

Results: A total of 2107 patients were enrolled to the registry. 432 patients (20.5%) demonstrated positive result on provocation and 693 patients (32.9%) showed negative. In positive group, the numbers of male and current smokers were higher than in negative group (p<0.05). Baseline hsCRP and triglyceride were higher in positive group (0.9±0.2 vs 0.6±0.4 mg/dl, 151±198.6 vs 129.3±86.1mg/dl, p<0.05). In angiographic analysis for 432 “positive”, multi-vessel spasm occurred in 106 patients (24.5%). Right coronary artery (RCA) was the most common coronary artery for provoked spasm (58.1%). Diffuse type of spasm is more frequent than focal type (69.9% vs 34.1%). Out of 634 coronary segments on which spasm was provoked, 365 segments (57.6%) were associated with minimal fixed atherosclerosis. The most frequently prescribed drug was diltiazem (347, 80.3%). During the 24-month follow-up (mean 26.7±8.4 months), 23.7% of patients had re-hospitalization or visited to emergency room due to repeated angina. However, the rate of cardiac death was very low (0.9%). Additionally, the cumulative incidences of newly developed acute coronary syndrome and arrhythmia were only 1.9% and 1.1%.

Conclusions: In clinical and angiographic analysis, positive group had more male, smokers, and higher baseline hsCRP. Positive rate of ergonovine provocation was 20.5% and RCA was the most common artery for coronary spasm. Coronary spasm was more frequently provoked on the segment with minimal stenosis than on the segment without atherosclerosis. During the 24-month follow up, the prognosis was excellent by conventional medical treatments. The VA-KOREA registry will be helpful for the establishment of clinical guidelines for VA.
Combination of impaired insulin sensitivity and decreased insulin secretion predicts both the onset of diabetes and cardiovascular events in patients with CAD and newly detected hyperglycemia.

The effects of diabetes mellitus on long-term prognosis in acute myocardial infarction (AMI) patients with atrial fibrillation (AF) who underwent percutaneous-coronary intervention (PCI).

Background: The aim of this study was to investigate whether diabetes mellitus (DM) has the effects on long-term outcomes in acute myocardial infarction (AMI) patients with atrial fibrillation (AF) who underwent percutaneous-coronary intervention (PCI).

Methods: We selected 1,129 consecutive AMI patients (70±10.2 years, 87.1% male) with AF who underwent primary PCI and divided them into 2 groups according to the presence of DM (DM group: n=545, non-DM group: n=584) and followed them up for 24 months. The primary outcomes were 24-month major adverse cardiac events (MACES), a composite of death, fatal and non-fatal MI, and target vessel revascularization, and coronary artery bypass grafting.

Results: There were no significant difference in ejection fraction (EI) (52±14.12% in non-DM, 52±14.19% in DM group; p=0.968), left ventricular end systolic volume (LVESV) (54±14.19% in non-DM, 54±14.38% in DM group; p=0.98). The number of all-cause death was 240 at one-year follow-up. The mortality of patients with vascular disease was significantly higher than those without vascular disease (VD) (VD vs. non-VD: 4 patients (2.82%) vs. 35 patients (2.79%); p=0.98). The number of all-cause cardiac events in VD group was significantly higher than those in non-VD group (VD vs. non-VD: 76.8% vs. 56.0% respectively; p=0.008). The total number of MACES was significantly higher in VD group than non-VD group (VD vs. non-VD: 95.0% vs. 76.8% respectively; p=0.008). The Kaplan-Meier analysis showed significant difference between two groups (p=0.002). Independent predictors of two-year MACES were high Killip class (OR 1.833, 95% CI 1.255-2.677, p=0.002), tachycardia (Heart rate > 100 beats per minute, OR 1.954, 95% CI 1.284-2.975, p<0.002), left ventricular systolic dysfunction (ejection fraction < 40%, OR 2.072, 95% CI 1.393-3.028, p<0.002), and performed cardiopulmonary resuscitation during admission (OR 2.531, 95% CI 1.546-4.144, p<0.001).

Conclusion: DM had critical impact on poor outcome in AMI patients combined with AF. In these patients early intensive therapy and rate control should be performed for better outcome.

P800 | BENCH

The effects of diabetes mellitus on long-term prognosis in acute myocardial infarction patients with atrial fibrillation who underwent primary percutaneous coronary intervention

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Background: Impaired insulin sensitivity and decreased insulin secretion are considered a risk factor of stroke in AF patients, and is one of the components of a risk stratification scheme, CHADS2/CHA2DS2-VASC score. However, it is not clear whether vascular disease is an independent risk factor for stroke and thromboembolism in Japanese AF patients.

Methods: The Fushimi AF Registry was designed to enroll all of the AF patients. We have enrolled 3,821 patients and one-year follow-up was completed in 2,966 patients from March 2011 to December 2013. We defined vascular disease as the presence of prior myocardial infarction or peripheral artery disease. We investigated the association between the presence of vascular disease and the incidence of stroke or thromboembolism at one-year follow-up.

Results: At baseline, 298 patients (12.4%) had vascular disease (VD group). CHADS2 score was significantly higher in VD group than non-VD group (VD vs. non-VD: 2.65 vs. 1.99; p<0.01). However, at one-year follow-up, the incidence of stroke or thromboembolism was similar between the two groups (VD vs. non-VD: 10 patients (3.6%) vs. 71 patients (2.66%); p=0.49). Among 1398 patients who had not had any anticoagulants at baseline (142 patients in VD group, and 1256 patients in non-VD), CHADS2 score was significantly higher in VD group than non-VD group (VD vs. non-VD: 2.40 vs. 1.71; p<0.01), but the incidence of stroke or thromboembolism was also similar between the two groups (VD vs. non-VD: 2.65 vs. 2.79%; p=0.98). The number of all-cause death was 240 at one-year follow-up. The mortality of patients with vascular disease was significantly higher than those without vascular disease (VD vs. non-VD: 44 patients (14.77%) vs. 196 patients (7.35%); p<0.01). Multiple logistic regression analysis, including vascular disease plus five factors of CHADS2, revealed that vascular disease was independently associated with all-cause death [odds ratio: 1.63, 95% confidence interval: 1.12-2.34, p=0.01].

Conclusion: In Japanese AF patients, vascular disease may not be a risk factor of stroke or thromboembolism, but rather a risk of all-cause death. Further follow-up is required to determine the importance of vascular disease in Japanese AF patients.
P801 | BEDSIDE
Association of increased serum glycated albumin levels with poor coronary collateralization in diabetic patients with stable angina and chronic total occlusion
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Purpose: We investigated whether serum glycated albumin (GA) levels are related to coronary collateralization in type 2 diabetic patients with chronic total occlusion.
Methods: Blood levels of GA and glycosylated hemoglobin (HbA1c) were determined in 317 diabetic and 117 nondiabetic patients with stable angina and angiographic documentation of at least one major coronary artery. The degree of collaterals supplying the distal aspect of a total occlusion from the contralateral vessel were graded as low (Rentrop score of 0 or 1) or high collateralization (Rentrop score of 2 or 3).
Results: For diabetic patients, GA (21.2±6.5 mg/dl vs. 18.7±5.6 mg/dl, P=0.01) but not HbA1c levels (7.0±1.1% vs. 6.8±1.3%, P=0.27) were significantly elevated in low collateralization than in high collateralization group, and correlated inversely with Rentrop score (Spearman's r = -0.28, P<0.001; Spearman's r = -0.10, P=0.09, respectively).
Conclusions: Increased GA levels in serum are associated with impaired collateral growth in type 2 diabetic patients with stable angina and chronic total occlusion.

P804 | BEDSIDE
Endothelial dysfunction, oxidative stress and inflammation in patients with acute myocardial infarction and abnormal glucose tolerance
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Abnormal glucose tolerance is known to be associated with a poor prognosis in patients (pts) with acute myocardial infarction (AMI). Endothelial dysfunction has a multifactorial mechanism and has been shown to be predictive of cardiovascular events. We aimed to study biomarkers of endothelial function, oxidative stress and inflammation in patients with AMI and abnormal glucose tolerance.
Methods: In 83 patients with AMI (mean age 56.4±1.5 years, 78% men) classified by an oral glucose tolerance test performed before discharge (overall day 10) into normal glucose tolerance (NGT, n=30), impaired glucose tolerance (IGT, n=37) and diabetes (DM, n=25) we determined plasma levels of malondialdehyde-hyde (MDA), a marker of oxidative status, asymmetric dimethylarginine (ADMA), inhibitor of nitric oxide synthase, hs-CRP, indicator of inflammation and evaluated endothelial function with flow-mediated dilatation of the brachial artery (FMD).
Results: No difference between groups in patients' demographic and baseline characteristics as well as in AMI size and location were observed. Plasma levels of MDA (p=0.05, p=0.01), ADMA (p=0.001 for both) and hs-CRP (p=0.001 for both) were significantly higher in pts with IGT and DM compared to those with NGT, respectively. The rate of vasodilatation measured by FMD decreased across the spectrum of glucometabolic disturbances and was significantly lower in subjects with IGT (p=0.001) and DM (p=0.001) compared to NGT.
Conclusion: These data suggest that endothelial dysfunction in AMI patients with abnormal glucose tolerance is related to impaired bioavailability of nitric oxide mediated by oxidative stress and inflammation and is correlated with the degree of glucometabolic disturbances.

P803 | BEDSIDE
Admission hyperglycemia improves the GRACE risk score for prediction of in-hospital mortality. Insights from the Euro Heart Survey ACS III
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Background: Stress hyperglycemia is associated with higher mortality. Using data from Euro Heart Survey Acute Coronary Syndromes (ACS) III, we determined the incremental prognostic value of adding admission hyperglycemia (AH) to the GRACE risk score for Heart Diseases (SCHD), Zabrze, Poland; 7Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Results:
P808 | BEDSIDE
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Results:

Worsening renal failure and chronic kidney disease synergistically deteriorated the long-term clinical outcomes of ACS patients in association with enhanced inflammatory response and LV remodeling.

P806 | BEDSIDE
SYNTAX score in diabetic patients in the acute phase of myocardial infarction

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Introduction: The syntax score (SS) was developed to characterize the complexity of the coronary network by taking into account: 1/ the number of lesions and their impact on function, 2/ the location of the lesions, and 3/ their complexity. However, patients in this study had multivessel disease and stable angina. In patients with acute myocardial infarction (AMI), we aim to study the characteristics of the SS in diabetic patients and to determine the predictive value of the SS as compared with the GRACE score for in-hospital death.

Materials and methods: We studied 1107 consecutive patients, including 873 non-diabetic patients and 234 diabetic patients, hospitalized for AMI in the intensive coronary care unit of Dijon from September 2011 to December 2012 and who had undergone coronary angiography. The SYNTAX and GRACE scores were both calculated for each patient.

Results: Median SS was significantly higher in diabetic patients (11±15 vs. 8±15, p<0.001) than in non-diabetic patients. In multivariable analysis, three predictors for a high SS were found: female OR=0.45; 95%CI = [0.25-0.89], (p=0.005); age (OR=1.03; 95%CI = [1.02-1.04], (p=0.001)) and HDL-C (OR=0.28; 95%CI = [0.11-0.72], (p=0.008)). In-hospital mortality increased significantly with increasing SS score quartiles (Q1: 2.9%, Q2: 2.2%, Q3: 4.0%, and Q4: 9.7%, p<0.001). SS score was associated with in-hospital mortality, even after adjustment for confounding factors (GRACE score and left ventricular ejection fraction).

Conclusion: In acute MI, the SS score is a reliable tool as it provides objective information on the coronary network and is a prognostic factor in the short term. Nonetheless, further studies are needed to understand the influence of risk factors such as diabetes or hyperglycemia on the initial and residual SS, and to assess the impact of SS on pharmacological and other revascularization strategies.

THE CARDIORENA AXIS

P808 | BEDSIDE
Worsening renal failure and chronic kidney disease synergistically deteriorated the long-term clinical outcomes of ACS patients in association with enhanced inflammatory response and LV remodeling

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Purpose: Worsening renal failure (WRF) and chronic kidney disease (CKD) were independently associated with the adverse clinical outcomes of ACS patients after PCI. The synergistical role of WRF and CKD in reperfused ACS patients was not fully understood. In the present study, we aimed to clarify the prognostic impact of WRF and CKD on the long-term outcomes of ACS patients after percutaneous coronary intervention (PCI).

Methods: With a single hospital-based cohort in the Shinken Database 2004-2012, comprising all the new patients (n=19,994) visiting the Cardiovascular Institute, Tokyo, Japan, we followed ACS patients treated with PCI (n=584). We defined WRF as a rise in serum creatinine of ≥0.3mg/dL and CKD as eGFR <60 mL/min/1.73m².

Results: Among 584 ACS patients, WRF was observed in 75 patients (13%), whereas CKD in 159 patients (27%). Complication of WRF and CKD (n=37, 6%) was associated with older age, higher peaked creatinine kinase release, white blood cell counts, c-reactive protein levels, and depressed left ventricular (LV) function. Prevalence of ST-elevation myocardia infarction, hypertension, diabetes mellitus, and dyslipidemia were comparable between 4 groups. Although WRF and CKD respectively deteriorated the long-term outcomes and HF admission, complication of WRF and CKD further deteriorated the long-term outcomes. Multivariable Cox regression analysis showed the complication of WRF and CKD was independently associated with the adverse clinical outcomes of ACS patients after PCI.

Conclusion: WRF and CKD were independently associated with the adverse clinical outcomes of ACS patients after PCI, suggesting that WRF and CKD might synergistically contribute to the adverse clinical outcomes of reperfused ACS patients in association with enhanced inflammatory response and LV remodeling.

P809 | BEDSIDE
High sensitive troponin T and I levels and variation over three months in prevalent hemodialysis patients

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Purpose: Troponin levels are often elevated in patients (pts) on hemodialysis (HD) even without signs of myocardial ischemia. There is lack of data concerning the variability of troponin T and I levels in dialysis pts. We aimed to determine the normal variability of troponins in pts without signs of acute cardiac ischemia undergoing maintenance HD treatment.

Methods: The study is based on a selected cohort of 200 clinically stable prevalent HD pts. High sensitive troponin T (TnT) and I (TnI) were measured at 0, 4, 8 and 12 weeks before HD sessions. Time to average was measured with Roche Diagnostics Cobas E Analyzer (level of detection ≥5ng/L) and TnI with the Abbott Diagnostics Architect i4000SR analyzer (level of detection ≥2ng/L). The clinical decision level for myocardial infarction (MI) in a non-renal population is ≥14 ng/L for TnT and ≥26 ng/L for TnI. Information on comorbidity and clinical characteristics was gathered at baseline.

Results: Clinical characteristics: men; 57%, median age; 51 years, time on dialysis: 24 months, previously known ischemic heart disease (IHD); 31%, previously known left ventricular dysfunction (LVD); 22%. TnTmedian was 24 ng/L (range 2-4057), TnImedian was 73 ng/L (range 7-51962), 99% of the pts had TnT above the clinical decision level (CDL) for MI at nearly all time points whereas 48% of TnI values were above the CDL. There was a large variability in TnT and TnI values. TnI varied over 1.5 times above the lowest measurement in 63% and TnT in 30% of the pts. The total coefficient of variation (CVI) and reference change value (RCV) was 828%/2296% for TnI and 130%/361% for TnT. The absolute change in the median value over 3 months was 18.5 ng/L for TnT and 10 ng/L for TnI (range 1414, vs 4047).

Conclusion: Nearly all TnT and about half TnI assessments of randomly taken samples are above the decision limit for MI in HD pts. The variability of high sensitive troponin levels in HD pts is also much higher than in a healthy population, which limits the use of single troponin levels as markers of acute myocardial ischemic events.

P810 | BEDSIDE
Acute kidney injury and uric acid in-hospital changes synergistically predict early mortality in patients with acute myocardial infarction


Purpose: We investigated the incidence and the prognostic value of acute kidney injury (AKI) and uric acid (UA) in-hospital changes regarding 30-day mortality in acute myocardial infarction (AMI) patients.

Methods: We studied 375 consecutive patients admitted with the diagnosis of acute myocardial infarction who had at least one AKI diagnosis during hospitalisation. AKI was defined according to KDIGO 2012 criteria. AKI incidence, severity and the presence of AKI in the intensive coronary care unit (ICU) were recorded. Uric acid levels were measured at admission, ICU discharge and after 24 hours. Multivariate Cox regression analysis was used to test the association of AKI, uric acid and their combination with in-hospital mortality. Results: AKI was identified in 115 patients (30.9%). The ICU admission AKI rate was 45.4%. Uric acid levels were higher in patients who died compared to survivors (106 vs 28, p<0.001). The combined AKI and uric acid group had a higher mortality rate (55.7%) compared to the other three groups (p<0.001). Multivariate Cox regression analysis showed that AKI and uric acid level were independent predictors of early mortality. The combination of AKI and uric acid was an even stronger predictor of early mortality (HR 3.1; 95% CI: 2.2-4.6; p<0.001). Conclusion: Acute kidney injury and uric acid levels are independent predictors of early mortality in ACS patients. The combination of AKI and uric acid further increases the risk of early mortality.
Conclusions: Odds ratios of 1.65 (95% confidence interval 1.16 to 2.36) for an eGFR of 60 to served between reduced eGFR and presentation with painless AMI, with adjusted In conclusion, lower eGFR was a strong, independent predictor of Conclusions: odds ratios of 1.65 (95% confidence interval 1.16 to 2.36) for an eGFR of 60 to served between reduced eGFR and presentation with painless AMI, with adjusted In conclusion, lower eGFR was a strong, independent predictor of
Results: Some degree of RI was present in 62% of patients (eGFR<30 in 2%,eGFR 30-59 in 15.3% and eGFR 60-89 in 45%). Patients with eGFR<90 had higher mortality rates at 30 days (7.3% vs. 1.3%, p<0.001) and at one-year (12.5% vs 4.2%, p<0.001). Mortality rates were gradually increasing with the degree of RI at both short- and long-term follow-up (Figure, left and right). At 30-days, patients with mild RI had higher mortality hazard, compared to patients with normal eGFR (HR 1.84, CI95% 1.2-2.9, p<0.009). At 1-year, mild RI was also associated with higher mortality (HR 1.9, CI95% 1.4-2.6, p<0.001). As expected, severe (eGFR<30) and moderate (eGFR 30-59) RI were associated with very high mortality (30-day: HR 27.7 and 7.3 respectively; 1-year: HR 17.2 and 5.7 respectively).

Conclusions: Short- and long-term mortality rates increase proportionally with the degree of renal impairment. Compared with patients with intact renal function, even mild RI with eGFR 60-89/mn/1.73m² is associated with higher mortality hazard at 30-days and one year.

P615 | SPOTLIGHT
Elevated plasma thrombomodulin is associated with the development of acute kidney injury in patients with acute myocardial infarction
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Objectives: Acute kidney injury (AKI) following acute myocardial infarction (AMI) is associated with unfavorable prognosis. Endothelial activation and injury in plasma are independent predictors for AKI in patients with AMI.

Methods: This prospective study was conducted from March 2010 to July 2012 and enrolled consecutive 80 patients with catheter-proven AMI. Plasma levels of thrombomodulin (TM) and other biochemistry tests were measured on day 1 of AMI. AKI was defined as elevation of serum creatinine of more than 0.3 mg/dl within 48 hours.

Results: Eleven of 80 (13.3%) patients with AMI developed AKI within 48 hours. TM was a significant predictor of AKI (AUC=0.853, 95% CI 0.75-0.97, p=0.004) as independent protective factor. Furthermore, the areas under the receiver operating curves demonstrated that plasma TM levels on day 1 of AMI had good discriminative powers for predicting AKI development following AMI (AUC=0.735, p<0.01).

Conclusion: Plasma levels of TM were independent predictors of AKI in patients with catheter-proven AMI.

P616 | BEDSIDE
Incidence and prognosis for acute kidney injury undergoing primary percutaneous coronary intervention
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Incidence and prognosis for acute kidney injury among coronary stenting patients with diabetic renal disease
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Objective: To determine the incidence of acute kidney injury (AKI) following percutaneous coronary interventions (PCI) in patients with diabetes and chronic kidney disease (CKD), and to evaluate the impact of medical therapy on AKI incidence and patient prognosis.

Methods: We conducted a retrospective study of all patients undergoing PCI procedures in a tertiary care center from January 2010 to December 2015. AKI was defined as an increase in serum creatinine of ≥0.3 mg/dl within 48 hours of PCI. Patients with pre-existing AKI, those with pregnancy, and those with AKI secondary to non-PCI-related causes were excluded.

Results: A total of 1016 patients underwent PCI during the study period. The incidence of AKI was 26 (7.8%). AKI group was significantly higher compared with non-AKI group. Serum cardiac troponin I (cTnI) at admission (7.4 vs 6.8, p<0.001) and peak CKP (387 vs 334 (1747) vs 2026±106 (1476) UI, p<0.0004) were significantly higher in AKI group than those in non-AKI group. In Kaplan-Meier analysis, AKI group had more all-cause death (HR: 4.05, logrank p<0.0001) and cardiac events (HR: 3.50, logrank p=0.007) comparison with non-AKI group. On multivariate logistic analyses, female gender (HR: 6.02, p=0.003), prevalence of CKD (HR: 3.87, p=0.03) and DM (HR: 3.14, p=0.03), lower EF (HR: 0.95, p=0.01) and higher cTnI at admission (HR: 1.02, p<0.049) were independent predictors of AKI.

Conclusions: These findings indicated that the incidence of AKI after primary PCI in AMI patients was related to worse prognosis, and gender, prevalence of DM and CKD and larger cardiac injury at admission were important risk predictors of AKI.

P817 | BEDSIDE
Long-term outcomes of patients with coronary artery disease and type 2 diabetes mellitus with chronic kidney disease undergoing surgery, angioplasty, or medical treatment
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Acute Kidney Injury (AKI) is a commonly complicated with percutaneous coronary intervention (PCI) and is associated with adverse outcomes. The aim of this study is to investigate the prognosis of AKI with acute myocardial infarction (AMI) and the potential role of risk predictor for AKI.

Methods: The study subjects were 335 patients with AMI who underwent primary PCI between 2006 and 2013. We compared clinical characteristics, hemodynamic parameter, laboratory data and prognosis between patients with AKI (AKI group) and without AKI (non-AKI group), and evaluated with predictor of AKI.

Results: The incidence of AKI was 26 (7.8%). AKI group was significantly higher age (76.5±2.2 vs 67.9±1.7, p=0.0005), more female gender (57.7% vs 22.0%, p<0.0001) and more prevalence of diabetes mellitus (DM) (50.0 vs 27.8%, p=0.02) and chronic kidney disease (CKD) (80.8 vs 43.0%, p=0.0002) compared with non-AKI group. Serum cardiac troponin I (cTnI) at admission (25.0±7.4 (6.8 vs 12.5±4.1, p=0.03) and peak CKP (387±334 (1747) vs 2026±106 (1476) UI, p=0.0004) were significantly higher in AKI group than those in non-AKI group. In Kaplan-Meier analysis, AKI group had more all-cause death (HR: 4.05, logrank p<0.0001) and cardiac events (HR: 3.50, logrank p=0.007) comparison with non-AKI group. On multivariate logistic analyses, female gender (HR: 6.02, p=0.003), prevalence of CKD (HR: 3.87, p=0.03) and DM (HR: 3.14, p=0.03), lower EF (HR: 0.95, p=0.01) and higher cTnI at admission (HR: 1.02, p<0.049) were independent predictors of AKI.

Conclusions: These findings indicated that the incidence of AKI after primary PCI in AMI patients was related to worse prognosis, and gender, prevalence of DM and CKD and larger cardiac injury at admission were important risk predictors of AKI.

P819 | BEDSIDE
Early advantages of ivabradine-b-blocker combination, as compared to b-blocker uptitration, in exercise capacity, chronotropic reserve and resting myocardial longitudinal function amelioration in CAD
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Purpose: To compare the early effects of equivalent heart rate (HR) control with ivabradine (Iva) plus bisoprolol (Bs) and Bs uptitration on exercise performance and resting longitudinal LV systolic and diastolic function in CAD pts with moderate to severe LV dysfunction.

Methods: In this single-blind, parallel-group study 78 pts aged ~60 years (54±2.3) in sinus rhythm ~70 bpm with CAD (stable angina CCS class I-II), documented MI ~3 months, mild hypertension and mean EF of 38-45%, treated with ACE inhibitors and Bs 2.5 mg od or BB naive, were randomized into 2 groups. In Group 1 (n=39) Iva (5 mg pd) was uptitrated to 5mg pd and iv was added (5mg bid uptitrated to 7.5 mg bd, 12±0.49mg pd), in Group 2 (n=38) Bs was uptitrated to 5 mg od (9±1.35 mg pd). At baseline (M0) and 2 months (M2), symptom-limited treadmill test - TT (Bruce protocol) was performed and EF, peak systolic velocity, sepal mitral annulus site (Slat) and ratio of early mitral flow velocity to annulus velocity (E/E') by TDI and plasma NT proBNP by ELISA was assessed.

Results: Resting HR and systolic BP were similar in both groups at M0 (76.8±3.5 vs 81.4±3.7 bpm and 135.4±5.8 vs 132.4±5.8 mmHg), and at M2 (66.4±2.93 vs 64.5±2.91 bpm and 124.2±5.4 vs 125.2±5.7 mmHg, p<0.05). TT, EF, Slat, E/E’ and NTproBNP results (M±m) see in table. Fatigue and/or dyspnea were predominant reason for TT termination in both groups at M0 (55% vs 47.5%) and at M2 (68.6% vs 60%).
**Conclusion:** In pts with CAD and moderately lowered EF, Iva-Bs combination, but not Bs uptitration with similar HR control at rest, was associated by M2 with exercise capacity improvement accompanied with major increase of chronotropic reserve as well as moderate amelioration of resting myocardial longitudinal systolic and diastolic functions.

**Methods:** Thirty consecutive patients with cardiac sarcoidosis who had positive myocardial uptake of 67Ga or 18F-FDG at baseline were enrolled. The response to steroid treatment for the resolution of myocardial inflammation was defined as the disappearance of positive myocardial uptake of 67Ga or 18F-FDG at follow-up study. The functional responder to steroid treatment was defined as a patient who had ≥15% decrease in LV end-systolic volume at 12 months after the initiation of steroid treatment.

**Results:** All patients were treated with a steroid. At a mean of 2 months after the initiation of steroid treatment, positive myocardial uptake of 67Ga or 18F-FDG disappeared in all patients. However, LV function had not improved at 12 months after the initiation of steroid treatment in the whole study population (baseline vs. 12 months: 83±19 mm²/m² vs. 78±23 mm²/m²; p=0.280 for LV end-diastolic volume, 49±23 mm²/m² vs. 43±24 mm²/m²; p=0.327 for LV end-systolic volume, 43±15% vs. 47±16%; p=0.367 for LV ejection fraction). Fourteen (47%) of the 30 patients showed a >15% decrease in LV end-systolic volume as the functional responders after the initiation of steroid treatment and were regarded as the functional responders to steroid treatment. Multivariate analysis demonstrated that the high-degree heart block (OR, 13.5; 95% CI, 1.92-279: p=0.007) and female gender (OR, 16.0; 95% CI, 1.39-395; p=0.05) were independent predictors of the functional responder to steroid treatment.

**Conclusion:** Steroid treatment is highly effective for resolving active myocardial inflammation in patients with cardiac sarcoidosis, but only about half of them are the functional responders to steroid treatment. The functional responder may be linked to the high-degree heart block and female gender but not to the resolution of active myocardial inflammation.

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**P820 | BENCH**

The mitochondria-targeting peptide Bendavia restores mitochondrial function in diabetic hearts by normalizing cardiolipin content

**Purpose:** Bioenergetic inefficiency is a hallmark of diabetic cardiomyopathy, yet there are currently no therapies that can improve cardiac mitochondrial function in diabetic patients. Bendavia is a cell-permeable peptide currently being tested in diabetic patients. Bendavia targets cardiolipin, a mitochondrial phospholipid that influences respiratory chain activity.

**Methods:** Diabetic or healthy rats were treated daily with vehicle or Bendavia (1 nmol/kg). Mitochondrial oxygen consumption (MVO2) and electromechanical function were evaluated in hearts paced at different workloads. High-resolution respirometry was assessed in permeabilized ventricular fibers. Total cardiolipin and cardiolipin acyl side chain composition were determined with chromatography.

**Results:** Diabetic hearts showed attenuated MVO2 responses following workload transitions (64±10 vs. 40±6 μmol/min/g in healthy vs. diabetic, respectively; P<0.05), and improved with Bendavia treatment (64±8 μmol/min/g, P<0.05). Complex I-dependent respiration in fibers decreased from 965±68 μmol/min/g in non-diabetic hearts to 770±51 (P<0.05), and was normalized with Bendavia (1225±143 μmol/min/g). Complex I protein expression decreased by 53% in diabetic mitochondria, and was restored after treatment. Total cardiolipin and linoleic acid (18:2)-enriched cardiolipin were replenished with Bendavia (Figure). Bendavia did not influence energetics or cardiolipin in healthy mitochondria.

**Conclusion:** Bendavia augmented mitochondrial function in diabetic hearts by restoring cardiolipin. As respiratory proteins are critically dependent on cardiolipin, these data illustrate the promise of targeting mitochondrial lipids to improve cardiac function in diabetic patients.
P823 | BEDSIDE
Hemodynamic effects of ivabradine in addition to dobutamine in cardiac shock patients with severe systolic dysfunction
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Background: Dobutamine therapeutic effect is limited by tachycardia. We assessed the effects of ivabradine in addition to dobutamine in stable heart failure (HF) patients with reduced left ventricular ejection fraction (LVEF<35%, n=22, mean age 76±14 years, 781 patients in sinus rhythm were included in this analysis. Resting heart rate (HR) was found to be 76.7±14 bpm (78.4±14 bpm in females and 76.2±14 bpm in males) and 68% of the patients had a resting HR >70 bpm. Out of 781 patients in sinus rhythm, 633 (81%) were receiving BB treatment at recommended doses by their own physicians. Mean HR was significantly lower in patients who were already receiving BB therapy than those not receiving BB (75.8±13 bpm vs 80.4±16 bpm respectively, p<0.001). Although patients receiving BB therapy had lower resting HR, 419 (66%) patients using BB therapy and 112 (75%) patients not receiving BB therapy had a resting heart rate >70 bpm (p=0.026), suggesting that almost two-thirds of patients HF receiving basic therapy even in the presence of BB therapy. The use of ivabradine in addition to basic therapy may significantly reduce heart rate and improve cardiac function in patients with severe systolic dysfunction.

Conclusions: These results showed that despite the high prevalence of BB therapy in patients with systolic HF in real life clinical practice and despite the significant reduction in resting HR by BB, most patients still have a resting HR >70 bpm.

P825 | BENCH
The early mineralocorticoid receptor antagonist mitigates the metabolic syndrome symptoms and transition to chronic heart failure in the SHHF rat model
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Purpose: Mineralocorticoid Receptor Antagonists (MRA) are clinically beneficial in individuals with chronic heart failure (HF). One of the major risk factors for HF, the metabolic syndrome (MetS), has been reported to be associated with increased aldosterone production and excessive MR activation. In this context, we hypothesized that the use of MRA could be applied to target the MetS symptoms and mitigate the subsequent development of HF. We aimed to prevent the faster progression of Spontaneously Hypertensive Heart Failure rats exhibiting MetS features (SHHFcp/cp) towards fully developed HF as compared to their SHHF+/+ counterparts.

Methods: 15 month-old male SHHF+/+ and SHHFcp/cp rats were given either the MRA Eplerenone (Eple, 100 mg/kg/day) or placebo (n=8 to 10 group) for a period of 11 months. Metabolic parameters (metabolic cages, serum biochemical assays) as well as cardiovascular phenotypes (blood pressure and echocardiography) were monitored at regular intervals.

Results: SHHFcp/cp rats developed eccentric cardiac hypertrophy, left ventricular (LV) dilatation and reduced ejection fraction (EF) by 12.5 month-old as compared to SHHF+/+ . While Eple did not induce differences in metabolic and cardiovascular phenotypes in SHHF+/+ rats, Eple-SHHFcp/cp had less body weight gain (Eple-SHHFcp/cp:787±19 g, p<0.001), reduced rise in triglycerides (Eple-SHHFcp/cp:20.5±6.1 vs SHHFcp/cp:8.3±1.1 g, p<0.001), total cholesterol (Eple-SHHFcp/cp:2.7±1.0 vs SHHFcp/cp:4.2±0.7 mmol/L, p<0.001) and an increased adiponectin blood levels (Eple-SHHFcp/cp:23±3 vs SHHFcp/cp:12±1 μg/ml, p<0.001). Albeit blood pressure did not vary significantly, Eple-SHHFcp/cp rats had lower LV end diastole diameter (Eple-SHHFcp/cp:9.9±1.4 vs SHHFcp/cp:11.4±4.0 mm, p<0.001) and LV mass (Eple-SHHFcp/cp:1760±72 g vs SHHFcp/cp:2195±73 g p<0.001), improved ejection fraction (Eple-SHHFcp/cp:68±8 vs SHHFcp/cp:59±1%, p<0.001), isovolumic relaxation time (Eple-SHHFcp/cp:30±1 vs SHHFcp/cp:22±1 ms, p<0.001) and E/A ratio (Eple-SHHFcp/cp:1.7±0.1 vs SHHFcp/cp:3.0±0.3, p<0.002). Death rate was 30% lower in Eple-SHHFcp/cp as compared to SHHFcp/cp.

Conclusions: Altogether, our data demonstrated that treatment with Eple during MetS protection from sudden death and prevention of the main MetS features, namely weight gain and dyslipidemia, and this was associated with a delayed onset of HF in Eple-SHHFcp/cp rats. Interestingly, those beneficial cardioprotective effects were obtained via mechanisms independent of blood pressure lowering and hemodynamic effects.

P826 | BEDSIDE
Eplerenone reduces cardiovascular death and heart failure hospitalisation in mild systolic heart failure patients irrespective of baseline heart rate
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The mineralocorticoid receptor antagonist (MRA), eplerenone (EPL), reduced cardiovascular (CV) death & heart failure (HF) hospitalisation (hosp) vs placebo in mild systolic HF patients in EMPHASIS-HF. Heart rate (HR) is an established driver of CV events; the impact of MRA on outcomes according to baseline HR has not been previously studied in this setting. Accordingly, we undertook an analysis of baseline HR and major outcomes in EMPHASIS-HF (n=2713). We looked at the association between baseline HR and other baseline variables, as a risk factor for CV events (independent of treatment allocation) and potential interaction with treatment on major outcomes. Patients with high baseline HR had lower left ventricular ejection fraction, greater previous hosp for HF, more diabetes, and less hypertension, previous MI, ICD placements and beta-blocker use. Baseline HR was significantly and positively correlated with all major outcomes (CV death/hosp [EMPHASIS-HF primary endpoint], CV death; HF hosp and all-cause death, all P<0.05) with HR 60-69 bpm having the lowest event rate. This relationship was preserved after baseline covariate adjustment. Figure 1 shows the similar-
ous association of baseline HR and treatment (epilone vs placebo) on CV death/HF hosp. There was no heterogeneity in the benefit of EPL according to baseline HR on this (interaction P=0.77) or other endpoints evaluated (P=0.42, 0.66, 0.43, respectively).

Thus, baseline HR appears to be an important predictor of major outcomes in patients with systolic HF, as previously reported. The benefits of EPL, as observed in the EMPHASIS-HF study, were evident across the entire range of baseline HR. Thus, an MRA should be given to mild systolic CHF patients, irrespective of baseline HR, to reduce major CV events.

P827 | BENCH
Biphasic effect of cyclic AMP on cardiomyocyte survival: Distinct role of protein kinase A and EPAC
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Purpose: Clinical evidence revealed that one of the beneficial medications for targeting pathologic myocardial hypertrophy is β1-adrenergic receptor (β1R) blockers. The molecular pathway of β1R is mediated by the second messenger cyclic AMP (cAMP). However, there are debates regarding the role of cAMP in myocardial survival because β1R stimulation promotes mitochondrial ROS or impaired Ca2+–transient balance. Glucagon-like peptide-1 (GLP-1) exhibits inotropic action via cAMP; however, its impact on myocardial apoptosis remains uncertain. We hypothesized whether there may be cAMP-dependent threshold of cell susceptibility to cardiomyocyte death and tested the impact of GLP-1/GLP-1R axis on myocardial apoptosis in cardiac hypertrophy and cAMP dependency.

Methods: Pressure-overloaded (TAC) mice were subjected to endogenous GLP-1 stimulation for 4 weeks by DPP4-inhibitor (alogliptin 10mg/kg/d, TAC-DP4i) or GLP-1R agonist (TAC-Ex4: 24 nmol/kg/day). Mitochondrial injury was assessed by changes in mitochondrial-specific autophagy markers mitofusion1/2 ratio and PINK/PARKIN content. The concentration-dependency of cAMP was evaluated by comparing the cell-permeable cAMP (8-br-cAMP) at 60μ M (low-cAMP; the relevant level obtained by endogenous GLP-1 stimulation) and at 6 mM (high-cAMP).

Results: TAC promoted impaired cardiac function (systolic and diastolic) and remodeling (hypertrophy and fibrosis), and cell death (TUNEL-positive cell number and increased Mfn1/Mfn2 ratio and PINK/PARKIN content), which were reversed by both of ALO and Ex4. TAC-CON exhibited about 1.66-fold decrease in cardiac cAMP compared to sham-CON, which was normalized by ALO and Ex4. In vitro analysis revealed that serum depletion induced a decrease in cardiac cAMP; however, this decrease was reversed by both of ALO and Ex4. In vitro analysis revealed that serum depletion induced a decrease in cardiac cAMP compared to sham-CON, which was normalized by ALO and Ex4. In vitro analysis revealed that serum depletion induced a decrease in cardiac cAMP; however, this decrease was reversed by both of ALO and Ex4.

Conclusions: The impact of cAMP on myocardial apoptosis is concentration-dependent. Activation of GLP-1/GLP-1R-1R axis protects heart from cell death in TAC by reduction of mitochondrial injury in a cAMP-dependent, but PKA-independent manner. The cAMP-related apoptosis was mediated by PKA activation, which was reversed by Exac activation.

P828 | BEDSIDE
Super-response to guideline-directed medical therapy in patients with new-onset heart failure and reduced left ventricular ejection fraction

Purpose: To determine the proportion of patients with new-onset heart failure and reduced left ventricular ejection fraction (HF-REF) that experience a ‘super-response’ (SR) to guideline-directed medical therapy, to identify predictors of this condition, and to study its prognostic significance.

Methods: We conducted an observational study of 133 consecutive patients who developed new-onset HF-REF between January-2010 and March-2013 and who were followed at an especially dedicated clinic. Upon diagnosis, all presented an LVEF <55% as assessed by transthoracic echocardiography (TTE). Pharmacological therapy was up-titrated to maximum tolerated doses before a second TTE was performed. Super-response to medical therapy was defined by the presence of a final LVEF <45% or a >2-fold increase of LVEF with regard to baseline together with a super response to guideline-directed medical therapy until July-2013.

Results: We studied 27 (20%) women and 106 (80%) men with a mean age of 59±11 years. Forty-five (33%) patients had ischemic heart disease. Upon diagnosis, NYHA class III-IV symptoms were present in 91 (68%) patients, and 84 (63%) required admission. Mean NT-proBNP was 3031 (pg/mL) for patients who received ACE inhibitors/ARBs, beta-blockers, mineralocorticoid receptor antagonists, diuretics, digoxin and ivabradine were 94%, 98%, 73%, 92%, 8% and 10%, respectively. Mean daily doses achieved were 34±10mg of carvedilol equivalents and 12.8±4mg of enalapril equivalents. Mean changes from baseline and follow-up TTE were 216 days. Mean LVEF increased from 26%±6 to 37%±12, while mean LVEFD decreased from 61±6 mm to 52±9 mm to 58±9 mm and 47±11 mm, respectively (p<0.001 for all comparisons). Thirty-seven (28%) patients met the definition criteria for SR. By means of multivariable logistic regression, a non-ischemic etiology of HF, a history of excessive alcohol intake, the absence of significant (grade >2) mitral regurgitation and the achievement of guideline-recommended beta-blocker target doses were independently associated with a higher probability of SR (p=0.05 for all predictors).

Conclusions: In our series, 28% patients with new-onset HF-REF experienced SR to guideline-directed medical therapy. This phenomenon carried a favorable prognostic impact.

P829 | BEDSIDE
A randomized controlled trial of aspirin compared to clopidogrel in patients with heart failure
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Background: Previous studies suggest that relatively high doses of aspirin (150mg/d) may impair renal function, increase blood pressure (BP) and plasma concentrations of amino-terminal pro-brain natriuretic peptide (NT-proBNP) and be associated with worse outcomes in patients with heart failure.

Methods: Patients with a clinical diagnosis of heart failure, in sinus rhythm with an NT-proBNP - 400 ng/L receiving diuretic therapy were randomised, open-label, to either aspirin (75mg/day) or clopidogrel (75mg/day). Patients were assessed at baseline and at 6 months.

Results: The median (IQR) age of the 87 patients randomised was 75 (62.69) years. 22 were women. 15 were in New York Heart Association (NYHA) class III or IV and 67 had been treated with aspirin prior to study. By 6 months, of 38 patients assigned to aspirin, five had died and six withdrew from treatment and of 49 assigned to clopidogrel, three had died and three withdrew. At 6 months, serum creatinine increased more in those assigned to aspirin rather than clopidogrel (11±17 vs 0.04 μmol/L; p=0.04) with a similar trend for serum urea (2.7±2.2 vs 2.4±2.5 mmol/L; p=0.60). Systolic BP declined to a similar extent in patients assigned to aspirin and clopidogrel (-7±27 vs -11±27mg/mg respectively; p=0.61) but diastolic BP declined more with clopidogrel (+1±4 vs +6±10mmHg; p=0.023). The median change in NT-proBNP was similar on clopidogrel and aspirin (Clopidogrel -78 (-452, 201)ng/L vs Aspirin -88 (-341, 167)ng/L; p=0.91) and NYHA class was independently associated with a higher probability of SR (p=0.05 for all predictors). In our series, 28% patients with new-onset HF-REF experienced SR to guideline-directed medical therapy. This phenomenon carried a favorable prognostic impact.

P830 | BEDSIDE
Diuretic strategies in patients with acute decompensated heart failure and preserved left ventricular ejection fraction
C.W. Ho, M.H. Ho, H.L. Cheung, T.M. Chan, H.F. Tse, C.W. Shu. The University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong SAR, People’s Republic of China

Background: Heart failure with preserved ejection fraction (HFpEF) lacks evidence-based management, both in chronic and acute stage. Whilst intravenous frusemide is the central therapy for acute decompensated heart failure (ADHF), the optimal regimen remains uncertain.

Methods: This is a randomized, double-blind, head-to-head trial to compare continuous infusion of frusemide (8mg/hr for 48 hours) with intermittent bolus (80mg every 12hr for 4 doses) in patients admitted for ADHF –24hr with LVEF ≥50%. Primary endpoints were changes in brain-type natriuretic peptide (BNP) and neutrophil gelatinase...
associated lipocalin (NGAL) in 48hr. Secondary endpoints were: worsening of renal function (WRF) defined by a rise in serum creatinine by ≥26.5 μmol/L or 50%, haemodynamic status assessed by serial quantitative echocardiography and body fluid status by biop impedance vector analysis.

**Results:** 54 patients were randomized (age 79 years; 67% female) in 1:1 ratio. Baseline BP and NGAL were similar in both groups (p=0.596 and p=0.074). After 48 hours, both groups showed significant BNP reduction. 19 patients (38%) developed WRF (40% vs. 36%; p=0.771). Unexpectedly, cardiac output decreased in both groups. Furthermore, infusion group had a greater reduction in cardiac output and weight loss compared to bolus group, together with an elevation of NGAL indicating possible acute kidney injury.

**Conclusion:** Frusmide infusion is superior to bolus in achieving diuresis, but is associated with subclinical acute kidney injury.

**HEART FAILURE MANAGEMENT**

**P833 | BEDSIDE**

**Effects of triiodothyronine (T3) replacement therapy in patients with chronic heart failure and low-T3 syndrome: a randomized placebo-controlled Study**

A. Amin, M. Chitsazan, N. Babaali.

**University of Indiana School of Medicine & Health Services, Tehran, Iran (Islamic Republic of)**

**Objectives:** The present study assessed the changes in functional, biochemical and echocardiographic measures following long-term liothyronin therapy in heart failure (HF) patients with low-triiodothyronine (T3) syndrome.

**Methods:** In the present placebo-controlled, double-blind study adult patients with clinically stable NYHA functional class III-IV systolic heart failure and low T3 syndrome receiving standard HF therapy were randomly assigned 1:1 to receive oral liothyronin or placebo for 6 weeks. Low T3 syndrome was defined as a low serum level of T3 with normal TSH and free T4 values. Fifty patients, including 39 (78%) male with a mean age of 60.15 years were included. The 6-minute walk distance increased in the liothyronin group by 93.16 m and in the placebo group by 67.28 m, resulting in a treatment effect of 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003).

**Results:** Fifty patients, including 39 (78%) male with a mean age of 60.15 years were included. The 6-minute walk distance increased in the liothyronin group by 93.16 m and in the placebo group by 67.28 m, resulting in a treatment effect of 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003). A higher decrease of high-sensitivity CRP level was developed in the placebo group by 67 m and in the placebo group by 26 m (p=0.003).

**Conclusion:** T3 replacement by liothyronin therapy seems to benefit HF patients with the low T3 syndrome.

**P833 | BEDSIDE**

**Importance of beta-blocker therapy optimization in elderly patients with left ventricular systolic dysfunction**


**Introduction:** The elderly population with left ventricle systolic dysfunction (LVDs) has been underrepresented in clinical trials of beta-blockers (BB) and maybe this is the reason why these drugs are used less commonly and in lower doses in this group of population. The objective of this study is to evaluate the importance of the optimization of the medical treatment with BB in elderly population with LVDs.

**Methods:** We included all patients (pts) ≥75 years old, with LVEF <35%, studied in our center between January 2008 and April 2012. Clinical variables of interest were collected and clinical follow-up was performed. In each pt we collected information about treatment with BB and the dose reached. With this data we created a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%). With this data we created a variable that determined the percent dose of BB (BB%) compared to the estimated a variable that determined the percent dose of BB (BB%). With this data we created a variable that determined the percent dose of BB (BB%). With this data we created a variable that determined the percent dose of BB (BB%). With this data we created a variable that determined the percent dose of BB (BB%).

**Results:** We enrolled consecutive 96 heart failure patients (59 male; mean age, 77±11.2 years) who were given liothyronin of 3.75±15 mg/day after admission in our hospital. NYHA classes of almost all patients were III (54.2%) or IV (43.8%) on admission and their body weight decreased significantly (3.8±3.6 kg) after in-hospital treatment. At the time of discharge, they were divided into 2 groups according to continuation of tolvaptan; half of them continued it (Group A) and the others discontinued it (Group B). Baseline characteristics were similar and there wasn't significant difference in rehospitalization-free rates between both groups (38.2% vs. 55.7%, P=n.s.) during one year follow-up period after discharge. Then, patients with preserved renal function (eGFR≥30 ml/minute/1.73m2) were selected from each group; 29 patients from Group A (Group A') and 37 from Group B (Group B'). Though baseline characteristics were similar, rehospitalization-free rate of Group A tended to be lower than that of Group B (40.2% vs. 64.1%, P=0.05; Figure) during the follow-up period.

**Conclusions:** Continuous use of tolvaptan isn’t recommended for the heart failure patients with preserved renal function in terms of increasing rehospitalization.

**P835 | BEDSIDE**

**Vasopressin V2 receptor antagonist tolvaptan is effective in heart failure patients with reduced left ventricular systolic function and low blood pressure**

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**Background:** Though tolvaptan can increase urinary volume and reduce body weight of the heart failure patients, especially with preserved renal function, whether continuous use of it has benefit for them is uncertain.

**Methods and results:** We enrolled consecutive 96 heart failure patients (59 male; mean age, 77±11.2 years) who were given liothyronin of 3.75±15 mg/day after admission in our hospital. NYHA classes of almost all patients were III (54.2%) or IV (43.8%) on admission and their body weight decreased significantly (3.8±3.6 kg) after in-hospital treatment. At the time of discharge, they were divided into 2 groups according to continuation of tolvaptan; half of them continued it (Group A) and the others discontinued it (Group B). Baseline characteristics were similar and there wasn't significant difference in rehospitalization-free rates between both groups (38.2% vs. 55.7%, P=n.s.) during one year follow-up period after discharge. Then, patients with preserved renal function (eGFR≥30 ml/minute/1.73m2) were selected from each group; 29 patients from Group A (Group A') and 37 from Group B (Group B'). Though baseline characteristics were similar, rehospitalization-free rate of Group A tended to be lower than that of Group B (40.2% vs. 64.1%, P=0.05; Figure) during the follow-up period.

**Conclusions:** Continuous use of tolvaptan isn’t recommended for the heart failure patients with preserved renal function in terms of increasing rehospitalization.
Results: TAC-CON exhibited marked increase in casual blood glucose level compared to sham-CON (in mg/dL; 214.0±14.6 vs TAC-CON versus 152.8±8.1) and concomitant decrease in circulating GLP-1 (in pM; 0.86±0.10 for TAC-CON versus 2.13±0.54) without affecting body weight. ALO normalized the hyperglycemia in TAC with simultaneous increase in GLP-1 (in pM; 3.78±0.56). Echocardiographic analysis revealed that TAC-ALO tolerated ALO (65 pmoles/mg protein). We next examined changes in signaling related to myocadiac remodeling: Akt, AMPK, ERK, and mTOR/S6K and contractility (SERCA, phospholamban (PL), troponin T/C and I (TnT/C, TnI), cardiac myosin heavy chain (MYH7)). There was no changes in the remodeling-related signaling. MYH7, the PKA-dependent Ca2+ sensitizing myofilament proteins, was increased and the PKA-dependent phosphorylation of PL was decreased in TAC-CON. Myocardial PKA activity was reduced in TAC-CON, all which were reversed by ALO. Conclusions: TAC-induced HF as induced by TAC exhibits decline in the inotropic peptide GLP-1. ALO reverses cardiac remodeling and dysfunction in TAC by modulating myofilament Ca2+ sensitivity-related proteins [PL & MYH7] via GLP1/GLP1-R-mediated cAMP/PKA activation.

P838 | BESIDSE
Time of enrollment impacts time to randomized treatment in clinical trials of acute heart failure: findings from the RELAX-AHF study

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Background: Amongst patients with heart failure (HF) due to left ventricular systolic dysfunction (L VSD) in sinus rhythm, those with higher resting heart rate (HR) have a worse prognosis. Reducing sinus rate to 50-60 bpm might improve outcomes. If beta blockers (BB) are not tolerated or HR remains >70 bpm despite BB, ivabradine may reduce HR and improve outcome.

Aims: To characterize patients attending a HF clinic and identify the proportion eligible for optimization of BB or ivabradine treatment. The clinic accepts referrals from primary and secondary care and offers long term follow-up to patients regardless of LVEF.

Methods and results: Between January 2013 and July 2013, 1000 consecutive HF clinic follow-up appointments were reviewed and demographic, clinical and echocardiographic data were collected in patients who attended (n=959, 644 patients were already treated with target doses of BB, 24 had BB dose increased, 19 were started on BB and 5 who were already taking BB were retreated). The clinic accepts referrals from primary and secondary care and offers long term follow-up to patients regardless of left ventricular ejection fraction (EF).

Conclusions: The proportion of patients eligible for optimization of BB or ivabradine treatment is lower than expected.

P839 | BESIDSE
Wireless left ventricular endocardial cardiac resynchronisation in heart failure patients: 12 months follow-up

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Purpose: HF pts remain untreated due to peri-operative and long-term compli-
cations or lack of response to CRT in ~40% of cases. These issues have been addressed through alternative approaches including the Wireless Cardiac Stimulation System, WiCS-LV, a novel system which provides ultrasonic based wire-
less endocardial LV pacing synchronously with RV pacing via a co-implanted PM or ICD. The WiCS-LV comprises a substratue battery-powered transmitter, implanted in an appropriate acoustic window identified during mandatory pre-
implant TTE, and a leadless, passive electrode anchored to LV endocardium during retrograde aortic approach using a steerable delivery system. Sensing of RV pac-
ing output from co-implanted device synchronously triggered, within 3ms, ultra-
sonic energy transmission to the 3mm x 3mm passive electrode, which converts this energy into electrical energy with consequent stimulation of the LV.

Methods: 13 (76.4%) of 17 pts enrolled in this first in man study, WISE-CRT, were implanted. Pre-operative TTE screening identified adequate acoustic window in all patients between 4-7th intercostal spaces. The leadless, passive electrode was placed in the LV mid-lateral wall. Study duration was 6 months but pts continue in a registry. We report 12 month results on 10 pts with mean ± SD follow-up of 37±15 days. 3pts were not evaluable, x2 high threshold and x1 death.

Results: Baseline characteristics for this group, all NYHA III, were: mean ± SD age = 66±7.8 yrs, LVFVE=24±6.4, 7%, intrinsic QRS duration 188±32 msec. Implantation was uneventful. At 12 month follow-up, mean ± SD LVFVE had in-
creased to 33±2.8%, with only 1 (10%) pts showing a reduction, and NYHA was 2 ±1.0 ± 0.6, with 8 (80%) pts showing a reduction of at least one functional class.

Conclusion: The use of leadless LV pacing systems may be a promising approach for CRT.

P640 | BENCHDI 
Diastolic Ca2+ leak and the role of the Na+/Ca2+ exchanger (NCX) in a model of heart failure with preserved ejection fraction

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Background: Heart failure with preserved ejection fraction (HFPEF) is increas-
ingly common but the established HF drugs are not effective. The underlying cel-
ular mechanisms are incompletely understood. Therefore we investigated car-
diomyocyte function and intracellular Ca2+ homeostasis in a model of HFPEF.

Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP). Serial blood/urine samples, echocardiography and pressure-volume-loop measurements were performed at baseline (BL), 8, 24 and 48 weeks. LV diastolic pressure (EDP) volume relation-
ship was markedly shifted left- and upwards and lung weight was significantly in-
creased, indicating HFPEF with pulmonary congestion. LV cardiomyocytes from
NXT showed no significant differences in amplitudes of Ca2+ transients. However, time for early (50%) decay of the Ca2+ transients at 8 weeks was significantly pro-
longed with a further increase after 24 weeks (RT50 17±2.2±9.2 and 30.8±2.7 vs.
27.6±1.8 and 41.8±2.6 ms; n=20; p<0.05); this was significantly correlated with
diastolic dysfunction in vivo. TAU was significantly prolonged at 8 and 24 weeks indicating reduced NCX forward mode activity, while NCX protein expression was
not altered. At 8 weeks Ta2+ spark frequency tended to be increased (p=0.07) while
SR Ca2+ content was unchanged. SEAO400 accelerated Ca2+ transient decay but did not affect Ca2+ spark frequency. At 24 weeks, Ca2+ spark fre-
quency was increased (4.3±0.7 vs. 11.5±1.8 sparks/s/m2; n=20; p<0.05) and
diastolic dysfunction significantly deteriorated at 24 weeks. Moreover, the significant acceleration of Ca2+ transient decay and reduced Ca2+ spark frequency in N xt.

Conclusion: In this model of HFPEF, cystolic Ca2+ leak of the LV cardiomy-
cytes was slower. Diastolic Ca2+ leak increased significantly during diseases processes. Whereas NCX expression was not altered, we showed marked increased NCX protein expression. Acute treatment with NCX inhibitor SEAO400 normalized cystolic Ca2+ transients in young N xt rats, suggesting a role of reverse mode NCX activity and decreased Ca2+ leak at later time points.
P845 | BEDSIDE
Efficacy and safety of Tolvaptan for pediatric patients with congestive heart failure. Multicenter survey in the working group of Japanese Society of Pediatric Circulation and Hemodynamics (J-SPECH)

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**Background:** Tolvaptan, a vasopressin V2-receptor antagonist, has been reported to improve congestion in adult patients with heart failure. However, it is unknown whether tolvaptan may be also effective for pediatric patients as well as adult patients. This study aimed to evaluate the clinical efficacy and safety of tolvaptan for pediatric patients with congestive heart failure.

**Methods:** Seven pediatric cardiology centers belonging to Japanese Society of Pediatric Circulation and Hemodynamics (J-SPECH) participated in this study. Clinical status and laboratory parameters of patients aged <18 years old who received tolvaptan during the period from November 2010 through January 2013 were analysed at baseline and at specified intervals (day 1, day 3, day 7 and month 1 after tolvaptan administration).

**Results:** The 32 patients in this study had a median age of 6 years (range 4 month-18 years). The initial dose of tolvaptan was 0.22±0.16 mg/kg/day and the maximum dose (MOE) was 0.42 mg/kg/day. Urine output was significantly increased at all intervals after tolvaptan administration compared with baseline. On the other hand, both urine osmolality and urine specific gravity were significantly decreased at day 1, day 3 and day 7 compared with baseline. Serum sodium concentration was 131.3±8.6 mmol/L at baseline, and was significantly increased to 135.7±5.9 mmol/L at month 1 after tolvaptan administration. The changes serum sodium and potassium were significant and independent on all intervals. None of the patients experienced hypernatremia. The adverse effects attributed to tolvaptan were mild increases of AST and ALT, thirst and dry mouth.

**Conclusion:** It is suggested that tolvaptan can be effectively and safety administered to pediatric patients with congestive heart failure.

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P846 | BEDSIDE
Contrast-induced acute kidney injury in patients undergoing cardiac resynchronization therapy - incidence and prognostic importance. Sub-analysis of data from randomized TRUST CRT trial

J. Kowalczyk, R. Lenarczyk, O. Kowalski, T. Podolec, P. Francuz, P. Pruszkowska-Skrepz, M. Szulik, M. Mazurek, B. Sredniawa, Z. Kalarus. *Dept of Cardiology, Congenital Heart Diseases & Electrotherapy, SCHD, Medical University of Silesia, Zabrze, Poland*

**Purpose:** Because data on contrast-induced acute kidney injury (CI-AKI) in patients undergoing cardiac resynchronization therapy (CRT-D) are scarce, we aimed to assess the incidence, natural course and prognostic importance of this syndrome in CRT recipients.

**Methods:** Study population consisted of 100 consecutive patients enrolled into the Triple Site Versus Standard Cardiac Resynchronization (TRUST CRT) trial, who were treated with CRT-D. Two patients were excluded up to 3 months after randomization and not analysed further. CI-AKI was defined as a rise in serum creatinine of at least 26.5 μmol/L (0.3 mg/dL) within 48 hours after contrast exposure, or at least 50% increase from the baseline value during index hospital stay with CRT-D implantation according to KDIGO Clinical Practice Guideline for Acute Kidney Injury.

**Results:** Among 98 subjects of TRUST CRT Trial 10 patients (10.2%) developed CI-AKI after CRT-D implantation. In patients with glomerular filtration rate (GFR) <60 ml/min/1.73 m² on admission the incidence of CI-AKI was almost 2-fold (15.4%) higher than in subjects with GFR >60 (8.3%). CRT-D recipients with CI-AKI had significantly higher mortality rate (50.0%) compared to those without CI-AKI (17.0%). During 36-months of follow-up (log-rank p=0.012; Figure 1). Multivariate Cox-regression analysis showed CI-AKI as significant and independent risk factor for death in CRT-D recipients (hazard ratio 5.71; 95%CI 5.16–6.26; p=0.001).

**Conclusions:** Contrast-induced acute kidney injury is a serious and frequent procedural complication of CRT-D implantation with a significant negative influence on long-term survival. The results suggest that clinical evaluation regarding renal function should be considered in CRT-D recipients, both before and after device implantation.

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P847 | BEDSIDE
Haemodynamically-controlled mechanical fluid removal is safe and effective in critical heart failure - a pilot study

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**Background:** Cardiorenal syndrome in CRT recipients. Contrast-induced acute kidney injury is a serious and frequent procedural complication of CRT-D implantation with a significant negative influence on long-term survival. The results suggest that clinical evaluation regarding renal function should be considered in CRT-D recipients, both before and after device implantation.

**Methods:** Study population consisted of 100 consecutive patients enrolled into the Triple Site Versus Standard Cardiac Resynchronization (TRUST CRT) trial, who were treated with CRT-D. Two patients were excluded up to 3 months after randomization and not analysed further. CI-AKI was defined as a rise in serum creatinine of at least 26.5 μmol/L (0.3 mg/dL) within 48 hours after contrast exposure, or at least 50% increase from the baseline value during index hospital stay with CRT-D implantation according to KDIGO Clinical Practice Guideline for Acute Kidney Injury.

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**Renal Function**

P846 | BEDSIDE
Contrast-induced acute kidney injury in patients undergoing cardiac resynchronization therapy - incidence and prognostic importance. Sub-analysis of data from randomized TRUST CRT trial

J. Kowalczyk, R. Lenarczyk, O. Kowalski, T. Podolec, P. Francuz, P. Pruszkowska-Skrepz, M. Szulik, M. Mazurek, B. Sredniawa, Z. Kalarus. *Dept of Cardiology, Congenital Heart Diseases & Electrotherapy, SCHD, Medical University of Silesia, Zabrze, Poland*

**Purpose:** Because data on contrast-induced acute kidney injury (CI-AKI) in patients undergoing cardiac resynchronization therapy (CRT-D) are scarce, we aimed to assess the incidence, natural course and prognostic importance of this syndrome in CRT recipients.

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**Conclusions:** Contrast-induced acute kidney injury is a serious and frequent procedural complication of CRT-D implantation with a significant negative influence on long-term survival. The results suggest that clinical evaluation regarding renal function should be considered in CRT-D recipients, both before and after device implantation.
P648 | BEDSIDE
The evidence between minor degree renal functional impairment, sub-clinical cardiac systolic dysfunction and impaired diastology
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Purpose: Define of renal function correlated linearly with cardiac dysfunction. To what extent of such relation may happen in a cohort with minor degree renal dysfunction and preserved global systolic performance remains controversial Methods: 6201 (mean age: 49.1 years, 3925 females) participants underwent cardiovascular health survey in a tertiary medical center with echocardiography and Tissue Doppler imaging (TDI), Mitral inflow E divided by TDI derived myocardial relaxation E' (E/E') estimated LV filling pressure, with eGFR assessed by using MDRD method, and categorized into three stages. Results: Reduced eGFR was associated with larger LA/LV diameter, greater LV mass index, and evidences of diastolic dysfunction (all trend p < 0.05) though unchanged LVFE. Most of these parameters in conjugate with elevated Pro-BNP did not change significantly after adjusting for clinical variables (adjusted p for trend < 0.05). Lower eGFR had effect modification by TDI on Pro-BNP level (interaction p < 0.05).

Echocardiographic parameters

<table>
<thead>
<tr>
<th>eGFR categories</th>
<th>LV mass index (g/m²)</th>
<th>LV ejection fraction (%)</th>
<th>LVEF (50-60)</th>
<th>LVEF (&gt;60)</th>
<th>Adjusted trend p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1: eGFR &lt; 60 (n=2700)</td>
<td>75.3 ± 14.4</td>
<td>46.4 ± 3.7</td>
<td>0.001</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Stage 2: eGFR 60-90 (n=3109)</td>
<td>77.2 ± 14.4</td>
<td>47.3 ± 3.5</td>
<td>0.001</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Stage 3: eGFR &gt; 90 (n=180)</td>
<td>86.5 ± 17.4</td>
<td>47.3 ± 3.5</td>
<td>0.127</td>
<td>0.9</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Worsened renal function parallel changes of cardiac geometries and accompanied both impaired systolic and diastolic function, even with unchanged global ejection fraction. Thus, minor renal functional decline manifested with co-existence of cardiac anomaly to a certain level.

P649 | SPOTLIGHT
The impact of age among patients with impaired renal function and left ventricular diastolic dysfunction
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Background: Evidence regarding impaired renal function (RI) as a major determinant of left ventricular diastolic dysfunction (LVDD) is emerging. Studies show in an impact of age on this interaction are lacking.
Methods: In this cross-sectional study, we reviewed the electronic medical records of patients who presented to the echocardiographic lab in a tertiary care academic center between 2008 and 2011. CKD staging was categorized based on the estimated glomerular filtration rate (eGFR). Diastolic function was evaluated based on echocardiographic characteristics. Using logistic regression analysis, the association between CKD severity and LVDD was examined after adjusting for potential demographic and clinical confounders. Analysis was re-determined to assess the impact of age on this interaction.
Results: Among 2443 patients, 1018 (41.7%) had normal eGFR, 757 (31%) had stage II, 443 (18.1%) stage III, 106 (4.3%) stage IV, and 119 (4.9%) stage V. LVDD was found in 1697 patients. Our data suggested that patients with CKD stage V have higher likelihood of developing LVDD (OR: 2.62, 95% CI: 1.53-4.47, p < 0.0006) when compared to patients with normal eGFR. Also Patients with CKD stage V were more likely to develop LVDD II/III (OR: 4.12, 95% CI: 2.30-7.40) than LVDD I (OR: 1.99, 95% CI: 1.27-3.13). Besides 6.5%, 12.3%, 13.8%, 17.0% and 20.2% patients with normal eGFR, CKD stage II, stage III, IV and V had LVDD stages II or higher respectively. Patients aged less than 65 years with CKD stage V were 3.9 times (OR: 3.9, 95% CI: 2.08-7.32) more likely to develop LVDD II/III and 2.5 times (OR: 2.5, 95% CI: 1.46-4.29) more likely to develop LVDD I compared to patients with normal eGFR. Among patients with CKD5 who were older than 65 years, there was no significant difference in the likelihood of developing LVDD (OR: 0.87, 95%CI: 0.34 – 2.26) or LVDDII/III (OR: 1.01, 95% CI: 0.31-3.39) when compared to those with normal eGFR.
Conclusion: Our study indicates a clear association between RI and DD. The likelihood of CKD tends to correlate with the severity of DD. Also younger patients with CKD5 were more likely to develop LVDD and in more severe stages.

P650 | BEDSIDE
High renal arterial resistance index is independently associated to worsening of renal function in heart failure outpatients
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The aim of this study was to evaluate in a group of chronic heart failure (CHF) outpatients whether a parameter reflecting renal perfusion (Renal Resistance Index, RRI) is associated to the worsening of renal function (WRF). We enrolled 168 outpatients (79% males, 64 ± 14 years, NYHA class 2.2 ± 0.6, left ventricular ejection fraction, LVEF, 34 ± 9% with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (±1 month) and in conventional therapy. Peak systolic velocity and end diastolic velocity of segmental renal artery was obtained by pulsed Doppler flow and RRI was then calculated. Standard renal function assessment was obtained by measurement of creatinine serum levels and the calculation of glomerular filtration rate by MDRD formula. The evaluation of renal function was repeated after 1 year and WRF was defined as an increase of creatinine > 0.3 mg/dl. During follow-up 23 patients (14%) showed WRF. Patients with WRF were characterised by higher RRI when compared with those without WRF (76.8 ± 8.8 vs. 88.9 ± 0.001). At multivariate Cox regression analysis baseline RRI > 72% was significantly associated to WRF (p: 0.04) in a model including hospitalizations due to acute decompensated heart failure within first year (p: 0.036), high loop diuretic dose (p: 0.004), presence of high central venous pressure (p: 0.004) and GFR-MDRD (p: 0.63). Figure 1 shows the absolute and percentage changes of creatinine serum levels and the WRF range according to RRI cut-off of 72.

P651 | BEDSIDE
Acute renal function worsening in therapeutic patients, hospitalized with acute decompensated heart failure and hypertensive urgency
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Purpose: To assess the prevalence and predictors of acute worsening of renal function (WRF) in patients admitted to therapeutic departments of city clinical hospital.
Methods: 655 consecutive therapeutic in-patients (female 60%, 64 ± 18 years (MDS), arterial hypertension 71%, myocardial infarction (MI) 16%, chronic heart failure (CHF) 59%, atrial fibrillation 21%, diabetes mellitus (DM) 16%, chronic kidney disease 17%, serum creatinine (SCr) 9546 mol/l) were included in the study. Acute WRF was diagnosed by SCR change > 30% during hospitalization. Early WRF was diagnosed by SCR decrease during hospitalization compared with SCR on admission. Late WRF was diagnosed by SCR increase during hospitalization. Acute kidney injury (AKI) was assessed according 2012 KDIGO Guidelines. Mann-Whitney test and multivariate analysis were performed. P < 0.05 was considered significant.
Results: Acute WRF was revealed in 19.4% of patients, 67.6% of them had late WRF. 42.5% of patients with late WRF met AKI criteria, 57.5% had 30-50% in-
crease of SCR. Patients with late WRF compared with patients without WRF had higher rate of hypertension (91 vs 69%), MI (40 vs 13%), CHF (79 vs 56%), DM (37 vs 13%), first hospital prescription of ACE inhibitors (45 vs 30%), beta-blockers (70 vs 36%) and loop diuretics (43 vs 20%), (p<0.01 for all comparisons). Patients with AKI compared with patients with 30-50% increase of SCR had no differences except higher rate of loop diuretic therapy in hospital (2=5.9, p<0.01). Acute decompensation of HF (33%) and hypertensive urgency with decrease of systolic blood pressure <60 mmHg for 24 hours (37%) were the main causes of late WRF. The following predictors of WRF were determined: arterial hypertension (OR 4.3, 95% confidence interval (CI) 1.9-9.5), MI (OR 4.2, 95% CI 2.49-7.34), DM (OR 3.9, 95% CI 2.28-6.85), CHF (OR 3.0, 95% CI 1.67-5.51), first prescription of beta-blockers (OR 3.8, 95% CI 2.26-6.53), loop diuretics (OR 2.9, 95% CI 1.72-4.84), ACE inhibitors (OR 1.97, 95% CI 1.19-3.25). Cardiac amyloido
dystrophy type 2

Conclusion: was diagnosed in 12.4% of admitted treated patients, 42.5% of them met AKI criteria. Patients with AKI and 30-50% of increase SCR had comparable basic characteristics. Acute decompensation of HF and hypertensive urgency with decrease of systolic blood pressure <60 mmHg for 24 hours were the main causes of late WRF. First prescription of beta-blockers, ACE inhibitors and loop diuretics in hospital was associated with late WRF. These data emphasize the need to follow the algorithms of initiation and titration of drugs in HF.

P852 | BEDSIDE
Long-term mortality and cardiac morbidity and progression rate in patients with Becker muscular dystrophy and limb-girdle muscular dystrophy type 2

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Purpose: To assess long-term mortality and progression of cardiac involvement in patients with limb-girdle muscular dystrophy type 2 (LGMD2A–L) and Becker muscular dystrophy (BMD).

Methods: A follow-up study of 130 patients assessed by electrocardiogram (ECG), echocardiography, vital status and biochemistry (NT-proBNP). Additionally, Holter-monitoring was performed at follow-up.

Results: After a median (range) of 8.9 (0.4–13.7) years, 12 patients had died (100% follow-up): BMD (n=2, age 43 and 45 years), LGMD2 (n=10, age 61 (11) years). Of the remaining 118, a total of 89 patients completed follow-up: BMD (n=2, age 43 and 45 years), LGMD2 (n=10, age 61 (11) years). Of the remaining 28 patients, 10 had LGMD2I (10 men, age 44 (13) years), 16/51 (31%) in LGMD2. Non-sustained ventricular tachycardia was found in 26 patients (average 1.5 treatment/patient). The mean duration of the treatment was 7.5 ± 12 for ID patients versus (vs) 67 ± 13 for non-ID patients (p = 0.002). A worse KCCQ score was also related to a more advanced NYHA functional class, classified as II (48 ± 66.1, p < 0.001) higher BNP levels (55 ± 15 vs 66 ± 12, p < 0.001) and a higher rate of subsequent mortality or cardiovascular events (40 ± 2 vs 68 ± 10, p < 0.001) in a follow-up of 20 months. For other factors associated with HRQoL, ID (OR 3.167, p < 0.047) independently predicted worse AKI overall summary (classification ≤ 50), whereas anemia did not (OR 2.565, p > 0.120).

Conclusion: In a CHF outpatient population, ID was related to a worse HRQoL, irrespectively of the presence of anemia.

P854 | BEDSIDE
Multi-center feasibility study on a single peripheral venous access approach for ultrafiltration in the treatment of congestive heart failure

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Purpose: Fluid overload is a major characteristic of congestive heart failure (CHF) and is among the most important targets of treatment. Several studies have shown that ultrafiltration (UF), by improving hemodynamic abnormalities causing diuretic hyporesponsiveness, is able to improve signs and symptoms of congestion and to reduce re-hospitalizations rate. However, the need for a central venous catheter has always limited the widespread use of UF in daily clinical practice. CHIARA (Congestive Heart Impairment Advanced Removal Approach) is a new device for UF using a single-lumen cannula (17G multi-hole) inserted in a peripheral vein. The CHIARA system is based on a syringe-pump acting on a silicone membrane that draws the blood from the vein and re-jects it back, thanks to dedicated check valves. This kind of device has never been used in clinical practice, and we have no information about its efficiency. The aim of this study was to evaluate the feasibility of this innovative “mini-invasive” approach for the treatment of CHF patients.

Methods: We planned to perform 100 UF treatments lasting ~6 hours and with an UF rate ~100 ml/h. The required condition to start UF treatment was a withdrawal flow from the peripheral vein ~60 ml/min, verified by a dedicated tool (Haemocatch). For each session, we evaluated the performance of the venous access, the ultrafiltrate volume removed, the length of UF treatment, and the cause for its interruption.

Results: This initial analysis regards the first 40 treatments (out of 100), performed in 26 patients (average 1.5 treatment/patient). The mean duration of the treatment was 7.5 ± 8 hours (range 6–14 hours) with removal of 1417 ± 433 ml of fluid (88 ± 31 mI/hour). The treatment was successfully completed in 38 cases (out of 40 (95%)). The mean suction flow rate from the vein was 72 ± 17 ml/hour. Most patients were in NYHA class II (67%±13±14%)

For each session, we evaluated the performance of the venous access, the ultrafiltrate volume removed, the length of UF treatment, and the cause for its interruption.

Conclusion: This preliminary results of our study seem to confirm the clinical applicability and efficacy of the CHIARA system in the treatment of CHF, in terms of adequate fluid removal through a single peripheral venous access.
The interaction between worsening renal function and persistent congestion in acute decompensated heart failure


Background: Worsening of renal function (WRF) is common in hospitalized patients with acute decompensated heart failure (ADHF) and is associated with increased mortality. WRF may occur in the context of successful decongestion or when congestion has not been satisfactorily alleviated. These 2 clinical scenarios likely differ with respect to the risk of mortality.

Methods: We studied 566 patients with ADHF with at least 1 sign of congestion at admission. Congestion status was reevaluated at the time of WRF (≥0.3 mg/dL increase in serum creatinine) and at discharge in patients without WRF. Persistent congestion at the time of WRF was defined as ≥1 sign of congestion (peripheral edema >1, third heart sound, pulmonary rales, increased jugular venous pressure or hepatomegaly). Patients were subdivided into 4 groups according to the development or not of WRF and the persistence of congestion. The study endpoint was all-cause mortality at 2 years.

Results: The figure shows the Kaplan-Meier curves of the 4 groups. Compared with patients without WRF or congestion (lowest mortality group), the adjusted hazard ratio for mortality was 1.75 (95% CI 1.20–2.54) in patients with persistent congestion and without WRF; 1.66 (95% CI 1.28–3.14) in patients with WRF and without congestion and 2.98 (95% CI 2.03–4.42) in patients with WRF and persistent congestion.

Conclusion: Both WRF and persistent congestion are independent predictors of mortality in ADHF. Patients who develop WRF while remaining congested have the worst outcome.

Variations of hemoglobin and of iron metabolism in long-term survivors of cardiac decompensation for systolic heart failure

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Purpose: Anemia (A) and iron deficiency (ID) are common in heart failure (HF). Limited is known about spontaneous remission or frequency of new onset of AID. We performed repeat assessment of hemoglobin (Hb) and iron metabolism in participants of the extended INH Study.

Methods: Patients were eligible, if left ventricular ejection fraction was <40% prior to discharge after hospitalization for decompensated HF and if 6, 12 and 18 month follow-ups (FUP) were performed. Neither treatment with iron or agents stimulating erythropoiesis, nor transfusion of red blood cells were allowed during this period. A was defined as Hb <13/12 g/dL in men/women, ID as ferritin <100 ng/ml or ferritin ≥400 ng/ml plus transferrin saturation <20%. ID was defined as ferritin ≥400 ng/ml plus transferrin saturation <20%.

Results: 495 patients qualified for this analysis (median age 67 [58-74] years, 22.2% female, 34% NYHA class III/IV). From baseline to FUP 6 (6-12,12-18) A resolved in 45.3% (27%, 38%) of anemic patients and ID in 33.8% (22.8%, 24.9%) of patients with ID at prior assessments. New A developed between baseline and FUP 6 (6-12, 12-18) in 8.3% (11.0%, 6.8%) and new ID in 28.5% (18.7%, 20.0%) of patients without A or ID at prior assessment. During the 3 FUP periods, 106/117 episodes of onset/resolution of A, and 180/185 of onset/resolution of ID occurred. Changes in A/ID were independent of each other (P=0.99). Resolution of A and ID were independently associated with an increase in the onset of each with a decrease in total cholesterol [mg/dL]: resolved A +8 (95% CI 1 to +30, P<0.001), A onset -16 (23 to -8, P<0.001), resolved ID +9 (3 to +15, P=0.003), ID onset -8 (-14 to -2, P=0.009). Resolution of ID was also associated with improvement in self-rated health (scale 1-5) by 0.17 points (0.05 to 0.29, P=0.003).

Conclusions: Repeat follow-up examinations of long-term survivors after cardiac decompensation showed that prevalence rates of both A and ID fluctuate over time and independently of each other, even without therapeutic interventions to stimulate erythropoiesis or to replace ID.
Purpose: The identification of patients with non-ischaemic dilated cardiomyopathy (NIDC) who are at risk for sudden cardiac death (SCD), and could subse-
quently benefit from an implantable cardioverter-defibrillator (ICD) implantation, is sub-
stantial. The role of programmed ventricular stimulation (PVS) in the risk strat-
ification of these patients remains controversial.
Methods: The study population consisted of 187 patients with NIDC who had
NYHA functional class II-III heart failure, a left ventricular ejection fraction (LVEF)
<35%, and were candidates for ICD implantation for primary prevention of SCD.
All patients underwent PVS before the procedure of implantation.
Results: Ventricular tachycardia/ventricular fibrillation was triggered in 39 pa-
tients (group I, 20.8%) versus 148 patients (group II, 79.2%), where ventricular
tachycardia/ventricular fibrillation was not induced. The major end point of the
study was appropriate ICD activation.
Appropriate ICD activation rate was higher in group I compared with group II, ei-
ther as antitachycardia pacing or as shock delivery. Induction of ventricular tachy-
cardia/ventricular fibrillation during PVS was an independent prognostic factor for
future ICD activation.
Conclusion: In contrast to the prevailing view, we conclude that induction of ven-
tricular tachycardia/ventricular fibrillation during PVS in patients with NIDC is as-
associated with subsequent serious arrhythmic events in this patient population.

P661 | BEDSIDE
Coronary flow reserve is reduced during dobutamine stress for
takotsubo stress cardiomyopathy
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Objectives: Takotsubo stress cardiomyopathy (TSC) is an increasingly recog-
nized and diagnosed disease in recent years although the underlying pathophys-
iology is still not known. Our objective was to investigate the effect of dobutamine stress
echocardiography (DSE) and mental stress on non-invasive coronary flow
reserve (CFR) in TSC patients and controls.
Design: This study is a case-control study and a sub-study of the Stockholm
Myocardial Infarction with Normal Coronaries (SMINC) study.
Setting: An elective DSE and mental stress investigation was performed focusing
on non-invasive measurements of CFR. Mental stress was performed using an
adapted short interview and mental arithmetics tests. Both investigations were
performed more than 6 months after the acute event.
Subjects: Twenty-two patients with a previous episode of TSC and 22 controls
were recruited from the SMINC study. All TSC patients had a previous normal
cardiovascular magnetic resonance (CMR) investigation.
Results: CFR at low-dose DSE was significantly lower in the TSC group com-
pared to controls, 1.51 and 1.72, respectively (p=0.017). At high-dose DSE CFR
was 1.95 and 2.21 in the TSC group and controls, respectively (p=0.098).
During both anger recall interview and mental arithmetics there were no significant
differences between the groups.
Conclusion: In this study we found a significant difference in non-invasive CFR
at low-dose and as a trend at high-dose DSE but not during mental stress.
These findings support the evidence that TSC is at least in part caused by a
catecholamine- or innervation-mediated microvascular dysfunction.

P662 | BEDSIDE
Meta-analysis identifying the source of conflict of differing reports of
CRT patients with narrow QRS heart failure
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United Kingdom
Background: Biventricular pacing (CRT) shows clear benefits in heart failure with
wide QRS, but results in patients with narrow QRS have been conflicting. In this
meta-analysis we tested the hypothesis that trial design might have influenced
findings.
Method and results: We identified all reports of CRT-P/D therapy in subjects with
narrow QRS. 12 studies (2974 patients) met the inclusion criteria. Studies were
assessed for the presence of bias resistance steps, i.e. a randomized control
and blinded outcome measurement. The effect on each endpoint was quantified
using a standardised z score. The weight-number effect size for CRT studies with
no bias resistance features was 0.75 (95% CI 0.45 to 1.05). For those with one
feature, randomization but not blinding, it was 0.84 (95% CI -0.14 to 1.81). For
those with two features (i.e. blinded, randomized controlled trials), it was
0.02 (95% CI -0.10 to 0.06). Study design had a strong effect on results (p=0.0007 for
contrast between the three groups; See Figure).
Conclusions: Only in studies which do not have randomization and full blinding
is CRT found to be effective in patients with narrow-QRS heart failure. When ran-
donization and full blinding are implemented, there appears to be no benefit. This
is driven by study design, not choice of endpoint. This means that either random-
ization or blinding inhibit positive physiological effects or that lack of blinding and
randomisation introduce positive bias unintentionally.

P663 | BEDSIDE
New pretherapeutic diagnostic criteria to predict non-responder to
adaptive servo ventilation in patient with heart failure
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Cardiovascular Medicine, Maebashi, Japan
Purpose: Adaptive servo-ventilation (ASV) was originally developed as a treat-
ment modality for patients with central sleep apnea (CSA) and complex sleep
apnea syndrome. Recently, it has also been used for heart failure (HF). However,
it is unclear how ASV non-responder could be diagnosed before ASV therapy.
We aim to estimate the new pretherapeutic diagnostic criteria to distinguish ASV
non-responder from ASV responder.
Methods: The study group consisted of 75 HF patients. The diagnostic criteria
for ASV non-responder was categorized according to fatal cardiovascular events
and/or worsening brain natriuretic peptide and/or left ventricular ejection fraction
after using ASV for ≥4 h/night. We estimate several parameters to diagnose
pretherapeutic factors using several polysomnographic parameters including inte-
grated area of desaturation (IAD) index, which is new measurement for assessing

Figure 1

Figure 1
the severity of sleep apnea, which is obtained by integrating nocturnal desaturation area.

**Results:** There were no significant differences with regard to polysomnographic parameters including apnea hypopnea index, central apnea index, obstructive apnea index, hypopnea index, and IAD index. New calculation formula (Hypopnea index+IAD index) and the median difference was significantly higher in the patients with sleep apnea compared to non-sleep apnea patients. In the patients without sleep apnea, independent variables associated with the presence of sleep apnea were age, BMI, and FVC. While in the patients with sleep apnea, independent variables associated with sleep apnea were age, BMI, and FVC.

**Conclusions:** Hypopnea index/IAD index is important factor to predict the presence of sleep apnea.

### P863 BEDSIDE

**Conclusions:** CHF may worsen overall survival and freedom from MACe after revascularization for intracoronary artery disease in critical limb ischemia patients. CHF may be a risk factor for patients with critical limb ischemia.

#### P864 | BEDSIDE

**Conclusions:** CHF may worsen overall survival and freedom from MACe after revascularization for intracoronary artery disease in critical limb ischemia patients. CHF may be a risk factor for patients with critical limb ischemia.

#### P865 | BEDSIDE

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#### P866 | BEDSIDE

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#### P867 | BEDSIDE

**Conclusions:** CHF may worsen overall survival and freedom from MACe after revascularization for intracoronary artery disease in critical limb ischemia patients. CHF may be a risk factor for patients with critical limb ischemia.
group was treated with CMF (OMT group; n=212). Major clinical outcomes were compared between the two groups up to 12 months.

Results: At baseline, the OMT group had a higher prevalence of elderly, cerebrovascular accidents, de novo lesion, left main disease, multivessel disease, multivessel CTO, RCA-CTO, and abundant collaterals (≥ grade 2), whereas the PCI group had a higher prevalence of male gender, prior MI, prior PTCA and LAD-CTO lesions. Clinical outcomes at 12 months were similar between the 2 groups except lower mortality in the PCI group (Table). After baseline adjustment by multivariate analysis, however, there was no difference between the Z groups.

Conclusions: In our study, mechanical revascularization by PCI for CTO lesions in pts with new onset heart failure as compared with OMT seems to have no benefit in reducing 12-month mortality. Long-term follow up with a larger study population will be necessary for further determination.

P866 | BEDSIDE
Lower average intrathoracic impedance in ICD and CRT-D patients is associated with higher mortality
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Purpose: Several ICD and CRT-D devices measure intrathoracic impedance (Z) across RV coil to can vector. Fluid index derived as cumulative sum of difference between raw and expected Z has utility in predicting HF events and long term mortality. However, the prognostic value of Z alone has not been well studied. We show that average long-term Z can be used to stratify patients (pts) at varying risk of mortality.

Methods: We analyzed data from 146,238 ICD and CRT-D pts implanted over ~8 years duration. The dataset contained pt age, sex, and date of death. Excluding first 9 months (mos), average follow-up (FU) was 29 ± 19 mos. 85% pts were alive at the time of last device transmission. Average intrathoracic Z for a pt was computed using Z from 6 to 9 mos post implant. First 6-mos Z was excluded because of its tendency to increase with device pocket maturation. The average 3-mo Z was divided into tertiles (Z1: 27–65 Ω, Z2: 66–72 Ω, Z3: 73–170 Ω) and relationship between Z and mortality studied using Cox-regression method. Analysis was repeated by adjusting for age, sex and device type.

Results: Lower average 3-mo Z was associated with higher mortality. After a mean follow-up of 28±18 mos, 82% of pts in Z1 were alive. The percentage of pts alive in Z2 and Z3 were 86% (FU: 29±19 mos) and 87% (FU: 32±20 mos), respectively. Pts in Z1 were at a higher mortality risk compared to those in Z2 and Z3 (Z1 vs Z2 HR, 95% CI: 1.54 [1.50-1.60], Z1 vs Z3: 1.83 [1.77-1.89], both p <0.001). After adjusting for age, gender, and device type, the corresponding HRs and 95% CIs were 1.38 [1.33-1.42] and 1.39 [1.34, 1.44] (both p <0.001).

Conclusion: Lower intrathoracic Z pts are at higher mortality risk vs. higher Z pts. Long-term average intrathoracic Z may be useful in stratifying HF pts at mortality risk.

P869 | BEDSIDE
Modulation of the inflammatory response and apoptosis by cardiac resynchronization in heart failure
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Purpose: Several ICD and CRT-D devices measure intrathoracic impedance (Z) across RV coil to can vector. Fluid index derived as cumulative sum of difference between raw and expected Z has utility in predicting HF events and long term mortality. However, the prognostic value of Z alone has not been well studied. We show that average long-term Z can be used to stratify patients (pts) at varying risk of mortality.

Methods: We analyzed data from 146,238 ICD and CRT-D pts implanted over ~8 years duration. The dataset contained pt age, sex, and date of death. Excluding first 9 months (mos), average follow-up (FU) was 29 ± 19 mos. 85% pts were alive at the time of last device transmission. Average intrathoracic Z for a pt was computed using Z from 6 to 9 mos post implant. First 6-mos Z was excluded because of its tendency to increase with device pocket maturation. The average 3-mo Z was divided into tertiles (Z1: 27–65 Ω, Z2: 66–72 Ω, Z3: 73–170 Ω) and relationship between Z and mortality studied using Cox-regression method. Analysis was repeated by adjusting for age, sex and device type.

Results: Lower average 3-mo Z was associated with higher mortality. After a mean follow-up of 28±18 mos, 82% of pts in Z1 were alive. The percentage of pts alive in Z2 and Z3 were 86% (FU: 29±19 mos) and 87% (FU: 32±20 mos), respectively. Pts in Z1 were at a higher mortality risk compared to those in Z2 and Z3 (Z1 vs Z2 HR, 95% CI: 1.54 [1.50-1.60], Z1 vs Z3: 1.83 [1.77-1.89], both p <0.001). After adjusting for age, gender, and device type, the corresponding HRs and 95% CIs were 1.38 [1.33-1.42] and 1.39 [1.34, 1.44] (both p <0.001).

Conclusion: Lower intrathoracic Z pts are at higher mortality risk vs. higher Z pts. Long-term average intrathoracic Z may be useful in stratifying HF pts at mortality risk.

P871 | BEDSIDE
The ratio of the bilateral-filling pressure is superior to the right atrial pressure alone for predicting right ventricular dysfunction in patients with post-capillary pulmonary hypertension

Purpose: The right ventricular (RV) filling pressure (i.e. the right atrium pressure (RAP)) correlates with the left ventricular filling pressure (i.e. pulmonary capillary wedge pressure (PCWP)). However, the ratio of the bilateral filling pressure (RAP/PCWP) is subject to the influence of the right ventricular function. The aim of this study was to elucidate the clinical significance of using the RAP/PCWP compared to the RAP alone to predict right ventricular dysfunction.

Methods: There were 542 patients who underwent right heart catheterization in our hospital from January 2009 to July 2013. We investigated 119 patients who had post-capillary pulmonary hypertension (PH).

Results: The RAP/PCWP provided a better prediction of RV dysfunction, as defined by the RV stroke work index, than did the RAP alone (r=-0.38, -0.31). Although this superiority of the RAP/PCWP compared to the RAP alone was in- creased in the subgroup of patients with an ejection fraction (EF) ≥ 40% (r=-0.50, -0.32), this superiority disappeared in those with an EF <40% (r=-0.35, -0.37). Neither the RAP/PCWP nor the RAP alone correlated with the renal function, brain natriuretic peptide level, PCWP, degree of mitral regurgitation, cardiac output or the prognosis.

Conclusions: These data suggest that, in cases with post-capillary PH, the RAP alone can reflect the pathophysiology of right heart failure, but the RAP/PCWP has an advantage over the RAP alone for predicting RV dysfunction, especially in the patients of the HF with preserved EF.

Correlation (RVSWI-RAP, RVSWI-RAP/PCWP).

P872 | BEDSIDE
Echocardiographic and cardiopulmonary phenotypes related to the severity of functional mitral regurgitation during maximal exercise testing in heart failure
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Background: In heart failure (HF) patients the severity of mitral regurgitation (MR) at rest has well established prognostic value and its increase during exercise further adds to an increased risk. Our goal was to define the relationship between the degree of exercise MR severity with cardiopulmonary and echocardiographic related phenotypes in a cohort of HF patients.

Methods: 511 HF reduced ejection fraction patients (mean age 67±11; male 72%; ischemic etiology 61%; NYHA class I, II, III and IV 13%, 36%, 39% and 12%, mean ejection fraction 33±9%) underwent cardiopulmonary exercise test (CPET) on tilttable cycle-ergometer combined with echocardiography at rest and during

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 fraction (LVEF) <35%, under optimal pharmacological treatment. Both ischemic and nonischemic P had comparable clinical and demographic characteristics. Blood samples were collected immediately before and at 2 and 6 months after CRT, in order to evaluate the serum levels of Tumor Necrosis Factor-alpha (TNF-a) and soluble Fas Ligand (sFasL).

Results: There was a statistically significant reduction in TNF-a levels from baseline (4.3±1.3 pg/mL) to 2 months (1.5±1.9 pg/mL) and to 6 months post-CRT (2.4±1.7 pg/mL), with p=0.019 and p=0.001, respectively. There was also a statistically significant variation in sFasL levels from baseline (57.3±25.2 pg/mL) to 2 months (62.6±32.1 pg/mL) and to 6 months post-CRT (60.6±17.3 pg/mL), with p<0.001.

Both groups (ischemic and nonischemic) had similar results.

Conclusions: In this cohort of chronic heart failure patients, there is a significant improvement in inflammatory status and apoptosis after CRT, independently of the ischemic or nonischemic etiology of the cardiomyopathy. Further studies will be needed to correlate these findings with long-term follow-up regarding clinical outcomes.
exercise. The population was divided into two groups according to the degree of functional peak MR: no to mild/moderate MR (no, MR 1+ and MR 2+) vs moderate/severe MR (MR 3+ and MR 4+).

Results: A good correlation (r coefficient 0.49) was found between the degree of dynamic MR and PASP at peak exercise. Despite similar echocardiographic profile at rest patients with significant peak MR (MR 3+) had worse exercise performance (lower peak VO2, O2 pulse and workload) and impaired ventilatory efficiency (higher VE/VCO2 slope).

Methods and results: The hollow cylindrical midventricular segment with fiber angle changing gradually from 60° inside to 60° outside was assumed. Layer-specific FSs at the innermost, mid-, and outermost layer were arbitrarily decided, and measured values of longitudinal strains (LSs) by using STE were entered into the simulated calculation. The required amount of myocardial sheet shear to supply the gap between the leaflet FSs and LS was calculated, and theoretical values of circumferential strains (CSs) and radial strains (RSs) were computed. When entering -22% as FS in 3 myocardial layers, theoretical values of CSs and RSs were consistent with the observed values in 51 normal control subjects. Similarly, FS was estimated to be -22%, -22.5%, and -22% at the inner, mid-, and outer layer, respectively, in 41 hypertensive patients with LV hypertrophy and preserved ejection fraction (HHD). In contrast, in 43 patients with hypertrophic cardiomyopathy (HCM), FS was estimated to be -20%, -20% and -19% at the inner, mid-, and outer layer, respectively.

Conclusion: The results of the present study indicated for the first time that the estimated FS from the wall kinetics measured by STE was preserved normal in HHD but impaired in HCM. This technique might provide unique information regarding active myocardial fiber shortening and give important insight into pathophysiology of myocardial diseases.

P875 BEDSIDE
Prognostic value of global longitudinal systolic strain in patients with anterior myocardial infarction

Introduction: Left ventricular ejection fraction (LVEF) is a potent prognostic parameter in acute myocardial infarction. However, global longitudinal systolic strain (GLS) from 2D speckle-tracking echocardiography is a potent novel method to estimate the left ventricular function. This study was aimed to evaluate the value of GLS as a predictor for 1 year all-cause mortality in patients with anterior myocardial infarction (MI).

Method: Among the 546 first-STEMI patients, who underwent primary percutaneous coronary intervention (PCI), from November 20 to December 2011, 216 patients (mean age 60±12.4, 171 male) with anterior myocardial infarction were enrolled.

Results: Mean LVEF of the patients was 46.1±10.1% and mean GLS was -22.0±3.9%. Receiver operating curve of GLS for 1 year mortality demonstrated that GLS showed excellent prediction for 1 year mortality in anterior MI patients (area under curve [AUC] 0.84, 95% confidence interval [95CI] 0.771 - 0.915). Cutoff value of GLS for mortality prediction was -11.7% (sensitivity 94%, specificity 58%). A Group with high GLS (n=100) showed significantly poor prognosis than low GLS (n=116) group in Kaplan-Meier survival analysis (mortality 16% vs. 9.9%, log rank p<0.001, Fig. 1). Compared with LVEF, GLS showed better prediction for mortality, but not significant (AUC 0.84 vs. 0.79, p=0.31). Univariate analysis showed that age, gender, Killip class, symptom-to-balloon time, systolic blood pressure, estimated GFR, post PCI TIMI flow and GLS were predictors for mortality, but not significant (AUC 0.84 vs. 0.79, p=0.31).

Conclusion: GLS can be a major predictor in patients with anterior myocardial infarction.

P874 | BEDSIDE
Assessing ventricular function
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Background: Left atrial ejection force (LAEJF) reflects LA contractile state, but it is dependent on age. Atrial-ventricular matching that is not influenced by age and has potential for non-invasive clinical use.

Methods: LAEJF was defined as the ratio between LAEJF and the square of annulus area that is little altered by age.

Results: The contraction of left ventricular (LV) myocyte contributes to longitudinal and circumferential myocardial shortening, and radial myocardial thickening by myocardial fiber shortening and by the secondary induction of changes in myocardial fiber and sheet orientation. A simulation study for estimating myocardial fiber strain (FS) using speckle tracking echocardiography (STE) was conducted.

Conclusions: In HF patients the severity of exercise-induced MR is associated with the most unfavorable performance and pulmonary hemodynamic response. A combined approach with CPET and echocardiographic assessment can help to early unmask and target functional MR and its related unfavorable phenotypes.
P877 | BEDSIDE
Short duration of symptoms at presentation is associated with left ventricular recovery in dilated cardiomyopathy: results from a prospective cohort study
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Purpose: Outcome data in dilated cardiomyopathy (DCM) stem from research performed prior to the widespread use of inhibitors of the renin-angiotensin-aldosterone system, beta blockers, cardiac resynchronization therapy (CRT) and left ventricular (LV) assist devices (LVAD). We report prospective outcome data from a cohort of patients with DCM treated according to current guidelines.
Methods: We included 102 patients with idiopathic DCM and LV ejection fraction (LVEF) <40%. Baseline (BL) work-up included echocardiography, measurement of peak oxygen consumption (peak VO2) and right-sided heart catheterisation. Follow-up (FU) was performed after 12 months. Predictors of the absolute change in LVEF (delta EF) were analysed by regression analysis.
Results: At FU, two patients were transplanted and one was on an LVAD. Four patients did not show. In the others, LVEF had increased by 13 % (delta EF) were analysed by regression analysis.
Conclusion: This prospective study confirms that delta EF derived from non-invasive echocardiography is a powerful independent indicator in patients with LV dysfunction. Improving in patients with severely reduced LVEF at BL, delta EF may be a useful adjunct in heart failure diagnosis and management.

P878 | BEDSIDE
Assessment of left ventricular function by strain echocardiography in healthy first degree relatives of non-familial idiopathic dilated cardiomyopathy patients
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Purpose: It has been shown that cardiac deformation parameters detected by strain echocardiography may be impaired in some cardiac diseases although left ventricular ejection fraction (LVEF) and chamber diameters are in normal limits. The aim of this study is to evaluate subclinical myocardial dysfunction with strain imaging in first-degree relatives of patients with non-familial idiopathic dilated cardiomyopathy (IDC).
Methods: Forty-one first-degree relatives of 19 patients with non-familial IDC were recruited in the study. The LV deformation parameters were compared with the age, sex and body surface area healthy control group (n=46) in terms of deformation prospectively.
Results: There were statistically significant reductions in EF (62.3±6.8 vs 65.6±6.3, p<0.002), global longitudinal strain (-17.9±2.32 vs -19.2±2.16, p<0.002), strain rate (0.97±0.14 vs 1.03±0.14, p<0.04), radial strain (3.41±0.8% vs 42.79±11.91%, p<0.001) and circumferential strain (-16.3±3.2% vs 18.29±3.39%, p<0.001) in the study population when compared with the control group.
Conclusion: Left ventricular deformation parameters are impaired in first-degree relatives of patients with IDC. Strain imaging can be used for early detection of subjects who are at risk for development of IDC.

P879 | BENCH
Novel technique to monitor cardiac output by measuring pulmonary electrical impedance, potentially applicable to patients with a cardiac resynchronization/defibrillation device
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Purpose: In heart failure (HF) patients implanted with a cardiac resynchronization/defibrillation device, a device-based algorithm that detects cardiac deterioration may improve the outpatient management of HF. Although several algorithms have been developed to detect pulmonary congestion, there have been no device-based algorithms to detect reduction in cardiac output (CO). We have developed a novel technique to monitor CO, which can be implemented into those devices.
Methods: Our technique estimates CO from pulsatile changes in electrical impedance measured between can electrode (generator) implanted in left thorax subcutaneously and coronary vein electrode (Fig. 1A). The generator and the coronary sinus lead were integrated into an implantable telemetry system for experiments. In canine models of acute HF (n=6) induced by coronary embolization and chronic HF (n=3) induced by rapid right ventricular pacing, we examined whether CO estimated by our technique (COest) reliably tracked CO measured by thermistor pulmonary artery catheter (COref).
Results: In one representative chronic HF dog, COest accurately tracked COref during induction of HF by ventricular pacing and during recovery after pacing was stopped over a long period of time (Fig. 1B). Regression analysis of pooled data (9 dogs) indicated that serial changes in COest and those in COref were significantly correlated with reasonable accuracy (Fig. 1C). Reduction in COest predicted reduction in COref with 86% sensitivity and 100% specificity.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient group (n=41)</th>
<th>Control group (n=86)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37±8.94</td>
<td>34±8.48</td>
<td>0.06</td>
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<tr>
<td>Sex (M/F)</td>
<td>19/22</td>
<td>19/28</td>
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<tr>
<td>BSA (m²)</td>
<td>1.85±0.24</td>
<td>1.81±0.19</td>
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<tr>
<td>LVEDV (cm³)</td>
<td>4.78±0.5</td>
<td>4.60±0.43</td>
<td>0.04</td>
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<td>LVEF (%)</td>
<td>62.3±6.8</td>
<td>65.6±6.3</td>
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<td>E/A</td>
<td>1.2±0.28</td>
<td>1.51±0.51</td>
<td>&lt;0.001</td>
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<tr>
<td>GCS (%)</td>
<td>17.9±3.2</td>
<td>19.21±2.16</td>
<td>0.002</td>
</tr>
<tr>
<td>GLSr (s/l)</td>
<td>0.97±0.14</td>
<td>1.03±0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>GCSr (%)</td>
<td>16±3.2</td>
<td>18.29±3.39</td>
<td>&lt;0.001</td>
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<tr>
<td>GCSr (s/l)</td>
<td>1.3±0.29</td>
<td>1.2±0.25</td>
<td>0.08</td>
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<tr>
<td>GRs (%)</td>
<td>34.9±8.2</td>
<td>42.79±11.91</td>
<td>&lt;0.001</td>
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<tr>
<td>GRSr (s/l)</td>
<td>1.7±0.4</td>
<td>1.75±0.29</td>
<td>0.68</td>
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<td>Torsion</td>
<td>10.6±8.5</td>
<td>12.4±5.78</td>
<td>0.07</td>
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</tbody>
</table>

Conclusion: Highly sensitive and specific detection of CO reduction by our technique may help the outpatient management of HF.
left ventricle non-compaction cardiomyopathy (LVNC). Hypertrophic cardiomyopathy (HCM) shares several morphological features with LVNC. However, prognosis and treatment strategy in LVNC is very different from HCM. We aimed to evaluate if regional LV myocardial function in these diseases may help discrimination between LVNC and HCM.

Methods: We studied 15 patients with LVNC (age 50±15), 25 patients with HCM (age 44±15) and 25 healthy controls (age 40±13), diagnosed according to current guidelines. Global longitudinal strain (GLS) by echocardiography was calculated from a 16 LV segments model with speckle tracking technique. LV basal (6 segments) and apical (4 segments) longitudinal strains were averaged.

Results: Patients with LVNC and HCM had reduced LV function compared to healthy by EF (37±12% vs. 55±5% vs. 61±5%, p<0.001) and by GLS (-11.5±10% vs. -16.3±3.1% vs. -21.2±1.8, p<0.001). LVNC had reduced function compared with HCM (EF: p<0.001 and GLS, p=0.04). LV apical strain was worse in LVNC compared to HCM (-15.3±6.7% vs. -18.9±4.4%, p=0.04), while LV basal strain did not differ (-13.9±5.7% vs. -14.5±3.9%, p=0.69). Function increased from base to apex in HCM (-14.5±3.8 vs. -18.9±4.4%, p<0.001) and in healthy controls (-20.2±1.6% vs. -21.6±2.7%, p=0.008), as opposed to a more homogeneously decreased function in LVNC (-13.9±5.7%, vs. -15.3±6.7%, p=0.34) (Figure).

Conclusion: This study demonstrated a basal to apical gradient with relatively preserved apical function in HCM, while function was homogeneously reduced in LVNC. These characteristics may help to discriminate between these two cardiomyopathies.