TRANSCATHETER AORTIC VALVE IMPLANTATION: WHAT’S NEXT?

4755 | BEDSIDE
Moderate to severe mitral regurgitation in patients undergoing transcatheter aortic valve replacement: a meta-analysis of mortality outcomes and mitral regurgitation evolution in 4,933 patients


Purpose: Transcatheter aortic valve replacement (TAVR) is an effective alternative therapy in selected patients with severe aortic stenosis. We sought to investigate the role of mitral regurgitation (MR) of moderate to severe mitral regurgitation (sMR) in patients undergoing TAVR, which, to date, remain still unclear.

Methods and results: Sixteen studies enrolling 4,933 patients undergoing TAVR, including patients with sMR, were considered in the meta-analysis and analyzed for all-cause-mortality: a further meta-analysis was performed to assess MR evolution post-TAVR. In patients with sMR, all-cause-mortality post-TAVR was significantly increased, at 30-day (ES: -0.18; 95% confidence interval CI: -0.31 to -0.04, I2 = 46.51, p = 0.148) and 2-year follow-up (ES: -0.15; 95% CI: -0.27 to -0.03, I2 = 65.20, p = 0.02), compared to patients with normal or mild MR.

Conclusions: In patients undergoing TAVR, the presence of sMR increases post-procedural mortality. A further meta-analysis of development of devices at higher positions significantly improved MR severity. Whether such recovery in MR severity impacts on mortality after TAVR remains to be defined.

4756 | BEDSIDE
Increased mortality after transcatheter aortic valve implantation (TAVI) in patients with severe aortic stenosis and low ejection fraction: a meta-analysis of 6,898 patients


Purpose: This is conflictive evidence regarding safety and efficacy of transcatheter aortic valve implantation (TAVI) procedures in patients with severe aortic stenosis and low left ventricular ejection fraction (EF). The primary aim of this study was to determine the impact of TAVI on short- and long-term mortality in patients with low EF (EF < 0.50); the secondary aim was to analyze the impact of TAVI procedure on EF recovery in the same setting of patients.

Methods and results: Twenty-six studies enrolling 6,898 patients with severe aortic stenosis undergoing TAVI procedure were included in the meta-analysis and analyzed for all-cause mortality and at 1-month and 1-year EF and at 2-year EF follow-up (overall ES: -0.15, 95% CI: -0.28 to -0.01, I2 = 74.05, p = 0.116), however this improvement reached significance only in patients undergoing TAVI with Edwards SAPIEN valve.

Conclusions: In patients undergoing TAVI, the presence of sMR increases post-procedural mortality. A further meta-analysis of development of devices at higher positions significantly improved MR severity. Whether such recovery in MR severity impacts on mortality after TAVR remains to be defined.

4757 | BEDSIDE
 Coronary artery disease significantly impairs long term outcomes after transcatheter aortic valve implantation

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Background and aims: Coronary artery disease (CAD) is frequent and negatively impacts the prognosis of patients with severe aortic stenosis (AS) who underwent surgical aortic valve replacement (SAVR). However, in patients with severe AS referred for TAVI the impact of CAD on outcomes has not been fully delineated. Furthermore, less is known about the indication and strategy for revascularization in these high risk patients. This study sought to determine in patients with severe AS undergoing transcatheter aortic valve implantation (TAVI) the prevalence and prognostic impact of the presence of CAD as well as to access the safety and feasibility of percutaneous revascularization (PCI) before TAVI.

Methods: Patients who underwent successful TAVI from September 2007 to October 2012 were retrospectively divided into two groups according to the presence of CAD defined as the presence of coronary revascularization or at least one epicardial stenosis ≥50% on coronary angiography. In selected patients, PCI was performed before TAVI either in a planned intervention prior to TAVI (staged PCI) or at the time of TAVI (concomitant). Study outcomes included 30-day, 1-year and 2-year all-cause death plus the safety outcomes, defined according to the Valve Academic Research Consortium (VARC).

Results: Ninety-one patients were included and 46 (51%) had coexisting CAD. Patients with CAD were more frequently men, hypertensive, dyslipidemic, had worse aortic annular filtration ratio (AVR) and more left ventricular dysfunction (LVD) than patients without CAD. EuroScore 2 was significantly higher in CAD group. PCI was performed in 13 patients (28%). There were no more significantly adverse events in patients who underwent PCI before TAVI than in patients who underwent TAVI alone. The 30-day mortality was similar between patients with and without PCI (9% and 5% respectively, p = 0.442), but at long-term the rates of death were significantly higher in CAD group (hazard ratio with CAD of 2.2; 95% CI from 1.2 to 4.6, p = 0.042), at year 2 were 26% in CAD patients and 14% in no-CAD patients, and at 2 years were 50% in CAD patients and 24% in non-CAD patients (Kaplan-Meier analysis).

Conclusions: In severe symptomatic AS who underwent TAVI, CAD is frequent and adversely impacts long term outcomes, but not procedure outcomes. In selected patients, PCI before TAVI appears to be feasible and safe.

4758 | BEDSIDE
Feasibility and outcomes of transcatheter aortic valve implantation in high-risk patients with stenotic bicuspid aortic valves

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Aims: Bicuspid aortic valve (BAV) is the most common congenital heart disease and may lead to aortic valve stenosis. Although Transcatheter Aortic Valve Implantation (TAVI) emerged as an alternative therapy in high-risk patients with tricuspid valve stenosis, presence of a significant stenosis is a contraindication, due to its unique anatomy and increased risk of periprocedural complications. We aimed to assess the feasibility and outcomes of TAVI in high-risk patients with bicuspid aortic valve stenosis.

Methods: The study is a prospective, single-centre registry of patients with BAV stenosis treated with TAVI. Periprocedural safety, hemodynamic and clinical outcome was observed during patient follow-up.

Results: Of 120 high-risk patients with severe aortic stenosis who underwent TAVI from January 2009 to January 2014 in our centre, 1 (0.8%) had documented BAV. Patients were aged 76.1±9 years (range 56-99), with mean EuroScore II of 20±11%, all in New York Heart Association functional class III. The mean aortic valve area was 0.76±0.36 cm², mean gradient was 45.3±15.1 mmHg and mean LVEF was 50.5±12.4%. The procedure was performed using transfemoral access in 13 (87%), transapical in 1 (6.5%) patient. Medtronic CoreValve prosthesis was implanted in 9 (60%) and Edwards Sapien XT in 6 (40%) patients. TAVI procedure was successful in 13 patients (87%). Major adverse events according to the second Valvular Academic Research Consortium definitions were present in 2 patients: in 1 periprocedural death (Edwards Sapien XT 29) and 1 periprocedural stroke (Medtronic CoreValve 26). Importantly, both complications were related to prosisssis dislocation from the bicuspid aortic valve annulus. Postprocedural aortic valve stenosis, presence of a significant stenosis is a contraindication, due to its unique anatomy and increased risk of periprocedural complications. We aimed to assess the feasibility and outcomes of TAVI in high-risk patients with bicuspid aortic valve stenosis.

Conclusions: Our initial experience suggests TAVI using CoreValve and Sapien XT prostheses in high risk patients with stenotic bicuspid aortic valve is feasible, leading to good short term hemodynamic and clinical improvement. However, prosisssis dislocation during implantation carries ominous prognosis warranting further multicentre studies on BAV anatomy and prosisssis matching for this specific group of patients.

4759 | BEDSIDE
Neurological damage after TAVI versus aortic valve replacement in patients with similar EuroScore

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Purpose: There are no studies comparing the incidence of acute silent cerebral ischemic lesions and neurocognitive dysfunction following TAVI vs. conventional aortic valve replacement (AVR) in contemporary patients with comparable surgical risk.

Methods: Fifty consecutive patients (p) undergoing TAVI were compared to 48 contemporary p with log EuroScore (ES) >10% undergoing AVR. Diffuse weighted Magnetic Resonance Imaging (MRI) was performed in 71 p (40 TAVI and 31 AVR) at 30 days, and 41 p (20 TAVI and 21 AVR) at 12 months. Method of Recommendation and Guidelines for neurocognitive assessment in adults undergoing major cardiac surgery.

Conclusions: 21 p (13%) and 20 p (25%) had new acute silent cerebral ischemic lesions at 30 days and 12 months, respectively. There was no significant differences in the frequency of new acute cerebral ischemic lesions between TAVI and AVR at 30 days and 12 months. There were no significant differences in the frequency of new acute cerebral ischemic lesions between TAVI and AVR at 30 days and 12 months. There were no significant differences in the frequency of new acute cerebral ischemic lesions between TAVI and AVR at 30 days and 12 months. There were no significant differences in the frequency of new acute cerebral ischemic lesions between TAVI and AVR at 30 days and 12 months.
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4760 | BEDSIDE
Prevalence of cerebral ischemic lesions and neurocognitive decline after transcatheter aortic valve implantation: insights from the FRANCE 2 registry

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The incidence of silent cerebral ischemic lesions was assessed in the FRANCE 2 registry in patients undergoing transcatheter aortic valve implantation (TAVI) with a CoreValve expandable system versus with or without preparatory balloon aortic valvuloplasty (PBAV).

Methods: A total of 657 patients were included in the analysis, 133 who had undergone TAVI with PBAV and 524 without PBAV. Cerebral imaging was performed using a semi-automated software tool. The incidence of cerebral ischemic lesions was assessed with the Reliable Change Index (RCI).

Results: The prevalence of cerebral ischemic lesions was 13.0% (95% CI: 10.0–16.6) in the patients who underwent TAVI with PBAV and 20.7% (95% CI: 17.8–23.9) in those who did not, with a RCI of 0.124 (95% CI: 0.092-0.156). The prevalence of silent cerebral ischemic lesions in patients who underwent TAVI without PBAV was 29.1% (95% CI: 25.2–33.5) versus 9.1% (95% CI: 5.9–13.2) in those who underwent TAVI with PBAV. The outcome was calculated using the Reliable Change Index (RCI).

Conclusions: The prevalence of silent cerebral ischemic lesions appeared to be lower in patients who underwent TAVI with PBAV. Additional studies are needed to confirm these findings and to determine the clinical relevance of this decrease in cerebral ischemic lesions.

4761 | BEDSIDE
Transcatheter aortic valve implantations after previous coronary artery bypass grafting: insights from the FRANCE 2 registry

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Objectives: The aims of this study were to assess the prevalence of cerebral ischemic lesions and neurocognitive decline after transcatheter aortic valve implantation (TAVI) with and without preparatory balloon aortic valvuloplasty (PBAV) and to determine the clinical relevance of these findings.

Methods: A total of 657 patients who underwent TAVI were included in this analysis. Patients were divided into two groups: those who had undergone TAVI with and without PBAV. Cerebral imaging was performed using a semi-automated software tool. The outcome was calculated using the Reliable Change Index (RCI).

Results: The prevalence of cerebral ischemic lesions was 13.0% (95% CI: 10.0–16.6) in the patients who underwent TAVI with PBAV and 20.7% (95% CI: 17.8–23.9) in those who did not, with a RCI of 0.124 (95% CI: 0.092-0.156). The prevalence of silent cerebral ischemic lesions in patients who underwent TAVI without PBAV was 29.1% (95% CI: 25.2–33.5) versus 9.1% (95% CI: 5.9–13.2) in those who underwent TAVI with PBAV. The outcome was calculated using the Reliable Change Index (RCI).

Conclusions: The prevalence of silent cerebral ischemic lesions appeared to be lower in patients who underwent TAVI with PBAV. Additional studies are needed to confirm these findings and to determine the clinical relevance of this decrease in cerebral ischemic lesions.
Conclusion: Previous bioprosthetic aortic valve does not adversely impact outcomes in patients undergoing TAVI. This result should be taken into account by the heart teams to consider VI as an alternative option for the management of bioprosthetic valve failure in high-risk patients.

4764 | BEDSIDE
Prosthesis choice for transcatheter aortic valve replacement: improved outcomes with the adoption of a patient-specific transcatheter heart valve selection algorithm

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Purpose: Transcatheter aortic valve replacement (TAVR) is routinely performed by using either self-expanding or balloon-expandable prostheses, which are the most widely used TAVR devices. No specific indications for these two valves have been adopted so far. This study prospectively investigated the impact of a patient-specific transcatheter heart valve (THV) selection algorithm on TAVR outcomes.

Methods: Consecutive patients who underwent TAVR using the selection algorithm (Figure 1) since January 2012 (N=184) were compared with earlier consecutive patients in whom the algorithm was not applied (N=193). The primary endpoints were: 1) VARC-defined device success and 2) paravalvular regurgitation (PVR)≥moderate.

Results: Patients in the study group were more likely to have diabetes mellitus (35.3% vs. 24.9%, p=0.027) and renal insufficiency (35.3% vs. 18.5%, p<0.001), whereas COPD was more frequent among the control group (28.4% vs. 39.3%, p=0.027). Device success was obtained in 87.0% of patients included in the study group and in 77.2% of those included in the control group (adjusted OR: 1.85, 95%CI: 1.03-3.31, p=0.039). On echo, PVR≥moderate was present in 5.6% of the study group and in 17.4% of the control group (adjusted OR: 0.35, 95%CI 0.16-0.76, p=0.008).

Figure 1. THV selection algorithm.

Conclusions: The implementation of a patient-specific THV selection algorithm for TAVR, which entails a specific THV implantation (CoreValve or SAPEN XT) for specific aortic root anatomies, may improve clinical outcomes after TAVR by allowing higher device success and reducing the incidence of more than mild PVR.

INNOVATION AND THE HEART 2

4765 | SPOTLIGHT
Association of systolic blood pressure levels with cardiovascular events and all-cause mortality among older adults without antihypertensive medication

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Endpoints were: 1) VARC-defined device success and 2) paravalvular regurgitation (PVR)≥moderate patients in whom the algorithm was not applied (N=193). The primary endpoints were: 1) VARC-defined device success and 2) paravalvular regurgitation since January 2012 (N=184) were compared with earlier consecutive patients in whom the algorithm was not applied (N=193). The primary endpoints were: 1) VARC-defined device success and 2) paravalvular regurgitation (PVR)≥moderate.

Results: Patients in the study group were more likely to have diabetes mellitus (35.3% vs. 24.9%, p=0.027) and renal insufficiency (35.3% vs. 18.5%, p<0.001), whereas COPD was more frequent among the control group (28.4% vs. 39.3%, p=0.027). Device success was obtained in 87.0% of patients included in the study group and in 77.2% of those included in the control group (adjusted OR: 1.85, 95%CI: 1.03-3.31, p=0.039). On echo, PVR≥moderate was present in 5.6% of the study group and in 17.4% of the control group (adjusted OR: 0.35, 95%CI 0.16-0.76, p=0.008).

Figure 1. THV selection algorithm.

Conclusions: The implementation of a patient-specific THV selection algorithm for TAVR, which entails a specific THV implantation (CoreValve or SAPEN XT) for specific aortic root anatomies, may improve clinical outcomes after TAVR by allowing higher device success and reducing the incidence of more than mild PVR.

Conclusion: Previous bioprosthetic aortic valve does not adversely impact outcomes in patients undergoing TAVI. This result should be taken into account by the heart teams to consider VI as an alternative option for the management of bioprosthetic valve failure in high-risk patients.

10,983 participants without hypertension, enrolled in the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort study were categorized into 3 age groups: 55-64, 65-74 and ≥75 years old. All groups were further divided according to baseline SBP levels: <120 (reference group), 120-129, 130-139, 140-149, and ≥150 mmHg. Four main outcomes were analysed in the study: CVD, CHD and stroke incidence, and all-cause mortality rate. Median follow-up was 4.5 years for CVD and CHD, 5.7 years for stroke, and 6.0 years for all-cause mortality.

After multivariable adjustment, there was a linear relation between SBP and the risk of CVD and CHD incidence, and all-cause mortality rate with the highest risk for SBP: ≤140 mmHg among participants aged 55-64 and 65-74 years (HR 3.06, 95%CI: 1.54-6.09; p=0.003 and 1.85, 95%CI: 1.03-3.33; p=0.017 for CVD incidence, 4.10; 95%CI: 1.86-9.06; p=0.003 and 2.37, 95%CI: 1.17-4.80; p=0.014 for CHD incidence, and 2.66, 95%CI: 1.61-4.39, p=0.001 and 1.87, 95%CI: 1.32-2.65; p<0.001 for all-cause mortality, respectively). No relation between SBP and CVD and CHD incidence, and all-cause mortality rate was observed for persons aged ≥75 years. The linear relation between SBP and stroke was observed only for patients ≥75 years, with the highest risk for SBP: ≤140 mmHg (3.52, 95%CI: 1.72-7.22; p=0.001).

The results suggest a hypothesis that for all individuals at age between 55-74 years old the recommended level of SBP should be ≤140 mmHg if tolerated, and due to significant stroke reduction it should be also considered for the oldest patients.

4766 | SPOTLIGHT
Aripazine reverses unfractionated and low molecular weight heparins, fondaparinux and new Xa and Ila oral anticoagulants: report of Phase I/II clinical trial with edoxaban

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Purpose: Aripazine (PER977) is a small molecule designed to bind unfractionated and low molecular weight heparins (UFH, LMWH), fondaparinux, and the new oral anticoagulants (NOACs). Its non-covalent binding to anticoagulants prevents them from binding to their endogenous targets, reversing their anticoagulation. Aripazine is ready for intravenous injection; has no significant toxicity effects in animals at clinical doses; no affects on CYP metabolism; and no drug-drug interaction. Aripazine reverses normal hemostasis in rat tail transection and liver laceration bleeding models. Moreover, aripazine reduced bleeding when given immediately after an induced injury in NOAC anticoagulated rats.

Methods: A first in human, 7 cohort, 2 period, ascending dose (5-300 mg) trial with aripazine alone and after 60 mg edoxaban was completed in volunteers.

Results: Aripazine alone showed no serious adverse events and no procoagulation signal (D-dimer, F1.2, TFP). At 50-300 mg doses, aripazine reversed the anticoagulation of 60 mg edoxaban with no evidence of rebound over 24 hrs (Fig. 1). Aripazine also restored normal clot formation and fibrin integrity within the clot, which had been altered with edoxaban therapy, as shown by scanning electron micrographs.

Figure 1

Conclusions: Aripazine is safe and well tolerated at doses that reverse the an-
Implications of american and european guidelines for cardiovascular disease prevention: the rotterdam study
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Background: Recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines have generated concerns regarding inferences and accuracy of risk models in cardiovascular disease (CVD) prevention. We aimed to determine implications of the ACC/AHA, the Adult Treatment Panel-III (ATP-III) and the European Society of Cardiology (ESC) guidelines in a prospective cohort of individuals ≥55 years.

Methods: The study comprised 4,854 participants (mean age 65.5 years) from the Rotterdam Study. We calculated 10-year risks for hard atherosclerotic CVD including coronary heart disease (CHD) and stroke using the pooled cohort equation (ACC/AHA); hard CVD by the ATP-III estimates; and CVD mortality using the Systematic Coronary Risk Evaluation (SCORE) equation. We computed the proportion of participants recommended for drug treatment based on the 3 guidelines and examined calibration of the 3 risk models underlying the recommendations.

Results: Among the mean age of the participants was 65.5 years. The ACC/AHA guidelines recommended all men and 81% of women as candidates for drug treatment. The inferences were 67% of men, 49% of women for the ATP-III and 97% of men, 90% of women for the ESC guidelines. All 3 algorithms overestimated the risk. The average predicted vs. observed risks were 18.9% vs. 11.4% (men), 10.0% vs. 6.8% (women) using the ACC/AHA; 15.8% vs. 6.8% (men), 5.4% vs. 3.2% (women) for the ATP-III; and 6.8% vs. 3.7% (men), 3.9% vs. 2.1% (women) using the SCORE equation.

Conclusions: All men and more than 80% of women ≥55 years were candidates for drug treatment based on both American and European guidelines. The ACC/AHA algorithm, as well as the ATP-III and SCORE functions, systematically overestimated the risk.

Ideal cardiovascular health is associated with favorable cardiac remodeling and lower incidence of heart failure in the Framingham Offspring Study
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Background: The American Heart Association (AHA) has defined the ideal cardiovascular health (Life’s Simple 7TM) in an effort to promote its AHA2020 Strategic Impact Goal of reducing cardiovascular mortality and increasing cardiovascular health by 20% by the year 2020. Limited data suggest that the AHA Heart Score (AHA score) is inversely related with the incidence of cardiovascular disease (CVD). It is unknown whether an ideal AHA score also lowers the risk of heart failure, and whether cardiac remodeling plays a key mediating role underlining any potential association.

Methods and results: We investigated the relations between the AHA Score and cardiac remodeling cross-sectionally and the incidence of heart failure prospectively in up to 3200 Framingham Offspring Study participants (mean age 59 years, 53% women). We hypothesized that the AHA score is inversely associated with heart failure incidence, mediated in part by the favorable effect of an ideal score on echocardiographic indices of cardiac remodeling, including left ventricular (LV) mass (LVM), left atrial dimensions (LAD), and fractional shortening (FS).

Adjusting for age and sex, an ideal AHA score (non-smoking status, ideal body mass index, regular physical activity, healthy diet, and an optimal profile of total serum cholesterol, blood pressure, and glucose; range of AHA score: 0-7, with 7 representing ideal status) was associated with lower LVM and LAD (beta estimates -0.56 gm and -0.06 cm, respectively; unit-increase in AHA score: p<0.0001) but was not related to FS (p=0.05). In additional analyses, the AHA score was also inversely associated with the two components of LVM, i.e., LV diastolic dimensions (LVDd) and LV wall thickness (beta estimates -0.02 cm and -0.04 mm, respectively, p<0.05). Additionally, the incidence of HF was inversely related to the baseline AHA score in age- and sex-adjusted models (p<0.05) for men and women. The hazard ratio [HR] 0.74 per unit-increase of AHA score, 95% CI 0.66, 0.84, an association that was slightly attenuated upon adjustment for LVM (HR 0.82 per unit-increase of AHA score, 95% CI 0.70, 0.96).

Conclusion: Our findings in a large community-based sample emphasize the impact of an ideal cardiovascular health on cardiac remodeling indices and on heart failure risk, underscoring the public health opportunities to prevent heart failure by promoting a healthier lifestyle.
Interleukin 13 receptor alpha 1 regulates the development of metabolic syndrome and cardiomyopathy in mice

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Aims: Increasing evidence suggests that chronic low-grade inflammation that accumulates in subjects such as those with insulin resistance or type 2 diabetes mellitus, may also be linked to the induction and progression of cardiovascular disease (CVD). Although the role of pro-inflammatory cytokines in CVD has received much attention, the possible role of anti-inflammatory cytokines remains unexplored. Interleukin 13 (IL-13) is a Th-2 mediated anti-inflammatory cytokine that exerts its effects through the interleukin 13 receptor α1 (IL-13Rα1) sub-unit. Thus, we aimed to investigate the potential role of IL-13Rα1 in metabolic syndrome and CVD using a genetically-engineered mouse model.

Methods and results: IL-13Rα1-deficient mice (Il13ra1−/−) developed several metabolic syndrome features: obesity, high fasting glucose, impaired response to glucose tolerance test, and higher total cholesterol levels. Il13ra1−/− mice displayed significantly lower TNF-α and undetectable IL-13 plasma concentrations, ruling out the possibility that the observed phenotype is due to an underlying elevation of pro-inflammatory cytokines. LacZ reporter staining demonstrated that IL-13Rα1 is expressed in the heart. Thus, we assessed the role of IL-13Rα1 in cardiac function and structure using echocardiography. Il13ra1−/− mice developed significant systolic dysfunction, which progressed to LV dilatation and posterior wall thinning at the age of 6 months. Furthermore, Il13ra1−/− mice displayed decreased expression of STAT 3, TGF-β and IGF-1 genes that regulate cardiac growth and extracellular matrix deposition. Strikingly, a high-fat diet improved remodelling and dysfunction in Il13ra1−/− mice, suggesting that the cardiomyopathy was independent of the metabolic syndrome. Next, to evaluate the potential therapeutic target for these serious cardiovascular disorders.

Conclusions: Our findings show, for the first time, that IL-13Ra1 is expressed in heart tissue and regulates the development of metabolic syndrome and dilated cardiomyopathy, the latter being associated with crucial changes in extracellular matrix deposition. Thus, IL-13Ra1 may represent a novel biomarker and therapeutic target for these serious cardiovascular disorders.

Weight change is associated with an increase in mortality risk

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Purpose: Recent findings from clinical cohorts suggest that overweight and obese individuals have a better prognosis than normal weight subjects, a phenomenon called obesity paradox. There is relatively little known about the effects of weight change (gain or loss) in this association. Thus, the purpose of this study was to determine the mortality risk association between weight and body mass index (BMI) changes.

Methods: From 1989 to 2011, we identified 60,972 veterans (54,569 men and 6,402 women; mean age 62±16) with at least two weight assessments at least 6 months apart. Risk factors, medications and mortality status information were extracted from the electronic records. The follow-up period was 9.8±4.5 years (597,078.75 person-years). Initial and final BMI was calculated based on the respective weight (kg) and height (m) of each participant. We formed the following five weight groups based on weight change (initialfinal) per year of follow-up: Weight change ≥±2.5% (Referent); weight increase of 2.6%-5.0%; weight increase of ≥5%; weight decrease of 2.6%-5.0%; and weight decrease of ≥5%. We also formed BMI change groups, based on similar percentages of BMI changes. Cox proportional hazard models were then used to compare risks between the weight and BMI groups using the group with no change as the reference group.

Results: There were a total of 12,771 deaths for an annual mortality rate of 2.2% per year. Risk for mortality proportional hazards models, adjusted on confounders, initial weight assessment, cardiac risk factors, cardiac medica- tions, cancer, kidney failure, and HIV/AIDS revealed that change in weight or BMI were associated with increased risk of mortality for the entire cohort and within the BMI classification groups. The increase in risk was graded and was more pro- nounced (about 2-fold) with weight losses compared to weight gains. Specifically, weight increase of 2.5% to 5% was associated with 40% increase in risk (hazard ratio: 1.40; CI: 1.30-1.52), while the weight for the same magnitude decrease in weight was associated with 51% increase in risk (hazard ratio: 1.50; CI: 1.40-2.30). However, relative to the risk with no change in BMI, the trend in risk was similar when weight changes were examined within the traditional BMI categories.

Conclusions: Weight changes are associated with increased mortality risk. The risk was more pronounced with weight losses than weight gains, for the entire cohort and within the traditional BMI categories.

The clinical utility of the novel endothelium-derived biomarker C-type natriuretic peptide for predicting myocardial infarction in the general community

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Purpose: Identifying subjects at risk for cardiovascular (CV) events in a community-based setting is a high priority and highlights the need to find specific biomarkers for underlying CV disease in such subjects. C-type natriuretic peptide (CNP) is an endothelial cell derived peptide that has been shown to possess vasculo-protective properties. CNP is a coronary vasodilator, is pro-angiogenic secondary to ischemic insult and is activated in the coronary vascular wall in humans with coronary artery disease (CAD). While we and others have reported that CNP circulates, no studies have assessed the prognostic utility of plasma CNP for CV events in the general community. We hypothesized that elevated CNP will have significant and added prognostic value for myocardial infarction (MI) in subjects from the general community.

Methods: Plasma CNP was assessed in 1,841 subjects randomly selected from a general community of our country, MN. Subjects were followed for MI, heart failure (HF), death and cerebrovascular accidents (CVAs) over 12 years. Hazard ratios (HRs) for CNP in the highest quartile (compared to lower three quartiles) were calculated, both unadjusted and with adjustment for standard risk factors (age, sex, BMI, cholesterol, smoking, presence of diabetes, CAD and hypertension). Statistical significance: P<0.05.

Results: Mean age of our cohort was 62±11yrs and 48% were male. Median (Q1,Q3) plasma CNP was 13.2 (10.2, 18.6) pg/ml and the highest quartile of CNP corresponded to values of >16.8 pg/ml. Over the 12 yr follow-up, 189 MI, 232 HF, 328 deaths and 350 CVAs were recorded. Cox modeling demonstrated that CNP in the highest quartile has prognostic significance for MI, HF and death (HRs 1.88, 95% CI 1.40-2.51; 1.76, 95% CI 1.35-2.30 and 1.41, 95% CI 1.12-1.76 respectively). With adjustment for standard RFs, the highest quartile of CNP retained prognostic significance for MI and HF (HRs 1.67, 95% CI 1.24-2.26 and 1.47, 95% CI 1.12-1.94 respectively), but not death. Integrated discrimination analysis suggested that addition of highest CNP to standard RFs significantly improved the prediction of MI and HF, but not death.

Conclusion: We report for the first time that elevated plasma CNP, in subjects from the general community, has prognostic significance and adds value to standard RFs, for MI but not HF, death, or CVA. Our findings advance the clinical value of the endothelium-derived peptide, CNP, as a novel plasma biomarker for the identification of subjects from the general community at risk for MI whom may benefit from preventative MI therapies.

Debate of fast diet preserves glucose tolerance and mitochondrial function

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Background: High fat diet is known to affect glucose handling and mitochondrial function under various conditions. The protein deacetylase SirT1, a known longevity factor, improves insulin sensitivity and affects mitochondrial biogenesis.

Objective: We assessed the influence of high fat diet on glucose handling, cardiac and mitochondrial function in wild type and hemizygote transgenic SirT1 mice.

Methods: Wild type (wt) and hemizygote SirT1 transgenic mice at 8 weeks of age were exposed either to high fat diet (HFD - 60% cal. from fat) or standard chow (SD). After 8 weeks of HFD, cardiac function was assessed by echocardiography and respiratory capacity of isolated mitochondria was measured. Furthermore, glucose tolerance was investigated with a glucose tolerance test (GTT) and insulin sensitivity by oral glucose tolerance test (OGTT). Cytometry of several organs was assessed with Western Blot. SirT1 protein expression was also assessed.

Results: In contrast to wild type mice SirT1 transgenic mice had 2-fold higher SirT1 protein level in heart and skeletal muscle but otherwise displayed normal phenotype. Eight weeks of HFD resulted in increased body mass and epididymal fat weight in both, wild type and SirT1 mice. This weight gain was significantly less pronounced in SirT1 mice. Echocardiography revealed normal cardiac morphology, systolic and diastolic function with HFD. Cardiac mitochondrial function, as assessed by respiratory capacity, oxygen uptake and uncoupling bioenergetics, remained constant. Eight weeks of HFD reduced respiratory capacity in wild type mice by ~30%. In contrast, HFD in SirT1 mice resulted in an increase of respiratory capacity by +41% (glutamate: wt-SD 688±82 vs. wt-HFD 483±116 vs. SirT1-SD 535±85 vs. wt-HFD).
Sirt1-HFD T7±1.90 natomsO/min/mg). HFD led to impaired glucose tolerance in wt and Sirt1 mice. However, Sirt1 mice displayed improved glucose tolerance and lower maximal blood glucose levels during GTT than wt (AUC: 1228±101 vs. 1913±195 vs. 1158±92 vs. 1569±104). Insulin response as assessed by insulin stimulated P-Akt/Akt ratio was decreased in heart and skeletal muscle of wild type mice after HFD. In transgenic Sirt1 mice, this loss of insulin sensitivity was not present.

Conclusion: A moderate overexpression of Sirt1 improves insulin sensitivity and preserves mitochondrial function with short term high fat diet.

4787 | BENCH

Transient hyperglycemia induced persistent cellular senescence in human umbilical vein endothelial cells via Sirt1/p300/p53/p21 pathway

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Transient hyperglycemic exposure has been implicated to induce persistent endothelial dysfunctions, a phenomenon also known as ‘metabolic memory’. Although metabolic memory has been demonstrated to promote microvascular endothelial senescence, whether it enhances macrovascular endothelial senescence remains obscure. Human umbilical vein endothelial cells (HUVECs) were incubated with normal glucose (5 mM) for 6 days, high glucose (30 mM) for 6 days, or high glucose for 1 day followed by normal glucose for 5 days (HN cells). We found that transient exposure to high glucose persistently suppressed SIRT1 expression and its deacetylase activity, while it continuously increased the expression of acetyl-p300 (Lys1499), acetyl-p53 (Lys382), p21/waf1, as well as SA-β-gal positive staining. Treatment of HN cells with resveratrol (a selective SIRT1 activator) significantly upregulated the expression and activity of SIRT1, which subsequently inhibited p53/p21-mediated endothelial senescence through deacetylation of p53 at Lys382, resulting in less SA-β-gal positive staining. Additionally, adding L002 (a selective p300 inhibitor) to HN cells also reduced SA-β-gal positive staining by repressing p300-mediated acetylation of p53 at Lys382. Furthermore, SIRT1 overexpression or activation by resveratrol in HN cells inhibited the acetylation of p300 at Lys1499, which led to suppression on p53/p21-mediated senescence and amelioration of senescent phenotype. Of importance, SIRT1 activation by metformin also suppressed cellular senescence in HN cells.

4788 | BENCH

SIRT1 drives persistent myocardial dysfunction via epigenetic regulation of mitochondrial adaptor p66Shc in the diabetic heart

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Purpose: Recent evidence suggests that diabetic cardiomyopathy phenotype is not only due to direct stress/hypoxia insults. The molecular mechanisms underlying persistent myocardial damage remain to be elucidated. Mitochondrial adaptor p66Shc, critically involved in reactive oxygen species (ROS) production, mediates hyperglycemia-induced cardiomyopathy. The present study investigates the role of p66Shc as determinant of persistent oxidative stress in the diabetic heart after anticipated stressors, such as endotoxemia, and we studied its association with energy homeostasis in the heart.

Methods: Diabetes was induced in wild-type 129sv mice (4-6 months old) by a single i.p. dose of streptozocin. Mice were divided into 5 experimental groups: 1) healthy controls; 2) untreated diabetic; 3) diabetics treated with insulin, 4) diabetics receiving insulin together with p66Shc siRNA or 5) scrambled siRNA (n=6-7/group). Insulin implants were placed subcutaneously 3 weeks after the induction of diabetes for the following 3 weeks. In vivo gene silencing of p66Shc was performed by i.v. administration of p66Shc siRNA. Measurement of superoxide anion (O2-) by ESR spectroscopy and mitochondrial swelling assay were performed in isolated cardiac mitochondria. NF-κB activity was assessed by p66Shc knockdown significantly improved EF and FS in comparison with insulin treatment alone. Persistent p66Shc expression was explained with reduced histone H3 acetylation by SIRT1, leading to chromatin remodelling and decreased gene transcription.

Conclusions: These findings suggest that pharmacological activation of deacetylase Sirt1 may suppress p66Shc overexpression and subsequent NF-κB activation in the setting of diabetes.

4789 | BENCH

Tumor necrosis factor receptor-associated factor (TRAF)-1 regulates monocyte mobilization during diet-induced obesity

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Background: Accumulation of inflammatory leukocytes is a prerequisite of adipose tissue inflammation during the metabolic syndrome. We recently reported that genetic deficiency of Tumor necrosis factor receptor-associated factor (TRAF)-1 attenuates inflammatory cell recruitment in atherosclerosis. Here, we investigated whether genetic deficiency of TRAF-1 modulates diet-induced obesity (DIO) in mice.

Methods and results: To test the association of TRAFs and obesity we screened for expression of different TRAFs in mouse adipose tissue after 20 weeks of feeding with a high fat diet (HFD). HFD induced up-regulation of TRAF-1, -3, -5, -6, and -7 mRNA. Interestingly, the amplitude of gene regulation was highest for TRAF-1 (4.9-fold, p=0.002). To test functional relevance of our findings, WT or TRAF-1−/− mice consumed HFD for 20 weeks (n=10 per group). Interestingly, TRAF-1−/− mice gained less weight during HFD (19.9±7.5% vs. 41.3±7.3% for WT and TRAF-1−/−, respectively). Accordingly, total body weight and weight of fat pads was decreased in TRAF-1−/− mice. Moreover, TRAF-1−/− mice demonstrated lowered glucose levels after intraperitoneal glucose and insulin tolerance tests. Finally, inflammatory cell recruitment was impaired in TRAF-1−/− mice with reduced numbers of adipose tissue macrophages. Functionally, circulating and splenic monocytes were lowered in TRAF-1−/− mice proposing that TRAF-1 modulates monocyte mobilization during inflammation.

Conclusion: We present the novel finding that TRAF-1 is regulated in obese adipose tissue. Genetic deficiency of TRAF-1 attenuates adipose tissue inflammation in mice by limiting monocyte recruitment. These findings identify TRAF-1 as a mediator of cardio-metabolic disease.

4790 | BENCH

A novel role for the stress hormone CRH in myocardial fatty acid metabolism

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Background: Heart depends on energy production. The body responds to stresses in an adaptive systemic response mediated in great part through activation of the hypothalamic-pituitary-adrenal (HPA) axis and the release of glucocorticoid. CRH, the hypothalamic component of the HPA axis, is expressed in several tissues outside the central nervous system, including the heart. We hypothesized that CRH is critical for the basal myocardial function and/or in response to non-anticipated stressors, such as endotoxemia, and we studied its association with energy homeostasis in the heart.

Methods: The stressful inflammatory reaction was induced by LPS administration. Two-D targeted M-mode imaging was obtained from the short axis view at the level of greatest LV dimension. mRNA expression levels were quantified by qPCR. Histological analysis was done by H&E, Masson Trichrome, reticulin and PAS staining, and results were assessed by specifically designed image analysis

Results: Crh−/− mice had significantly compromised cardiac function compared to Crh+/+ (wild-type), as determined by lower FS (%) and EF (%) values. In addition, Crh−/− exhibited altered histological abnormalities, including increased perivascular fibrosis and apoptosis. Expression of genes involved in fatty acid metabolism, including PPARα, PPARγ, AMPKα, ACO and Hadha was significantly reduced in Crh−/− mice. They also had lower levels of CD36, PDK4 and FAS, and of the glycolysis marker Hexokinase II; and they exhibited increased glycogen deposition pattern (90-100% after 16-28h post-LPS), compared to no mortality among Crh+/+. Eighteen hours after LPS administration, Crh−/− had significantly reduced EF (%) and FS (%) values, greater inflammation, monocytes’ infiltration, increased vas-
MicroRNA-33 deficiency leads to high fat diet-induced obesity and insulin resistance in vivo
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Background: MicroRNAs (miRs) are small non-protein-coding RNAs that bind to specific mRNAs and inhibit translation or promote mRNA degradation. Recent reports, including ours, indicated that miR-33 located within the intron of sterol regulatory element binding protein (SREBP)-2 controls cholesterol homeostasis and can be a potential therapeutic target for atherosclerosis. We generated miR-33−/− mice and found that these mice showed significant increase of ABCA1 levels and serum HDL-C and resistance to atherosclerosis. A careful attention for body weight gain and insulin resistance for prevention of obesity under high fat diet (HFD: 45% fat). Computed tomography analysis showed a severe increase in body fat. Adipocyte size of miR-33−/− mice was increased with the accumulation of infiltrated cells in epididymal fat. miR-33−/− mice showed impaired glucose tolerance and insulin tolerance and increased serum insulin and leptin levels, which indicated that miR-33 deficiency showed insulin resistance under HFD. Next, we measured the metabolic rate. Oxygen consumption, activity, body temperature and urinary catecholamine levels did not differ between control and miR-33−/− mice. Food intake was slightly but significantly higher in miR-33−/− mice fed HFD, whereas this difference was not seen when fed normal chow. We searched for potential target genes of miR-33 and found that one of the targets is SREBP-1. We confirmed that miR-33 targeted the 3’UTR of SREBP-1 in vitro and the expression of SREBP-1 was increased in miR-33−/− mice. miR-33−/− mice were crossed with Srebp1+/− mice and fed HFD. The difference in body weight decreased and abnormal glucose tolerance and serum leptin levels were ameliorated in miR-33−/− Srebp1+/− mice compared with miR-33−/− Srebp1+/+ mice.

Conclusions: These results indicated that miR-33 deficiency showed obesity and insulin resistance via up-regulation of SREBP-1 under HFD. miR-33 was also reported to target FGF21, which might work in concert with these unfavorable effects because it promotes the activity of NF-κB and regulates the expression of inflammatory genes. A careful attention for weight gain and insulin resistance formation may be necessary when inhibition of miR-33 is applied to clinical setting.

CONTEMPORARY ISSUES IN ARTERIAL HYPERTENSION

Pulse wave velocity (PWV) represents an established risk factor in cardiovascular risk. We prospectively studied 3243 subjects: a prospective study of 3243 subjects

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Objectives: Pulse wave velocity (PWV) provides an estimated risk factor in hypertensive patients. Increased PWV values are associated with worse outcome and PWV measurement represents a significant marker in order to assess total cardiovascular risk.

Aim and methods: This study has the purpose to assess the biological behavior and characteristics of PWV in hypertensive patients. We prospectively studied 10.103 subjects (3243 controls, 6860 hypertensive patients) from five outpatient hypertensive clinics. In all patients anthropometric characteristics as well as medical history and antihypertensive regimen was recorded. The statistical behavior of PWV was tested with respect to qualitative parameters such as gender and smoking, as well as quantitative variables such us age, BMI, systolic BP, diastolic BP and heart rate. Non parametric-test Kruskal-Wallis was utilized in order to identify the variance of PWV between control and hypertensive patients. Regression analysis was performed for all the previously mentioned parameters. Pearson’s correlation test was used to assess the statistical behavior of PWV compared to the patient’s baseline characteristics.

Results: PWV distribution was weighted by age due to conditionality of variance. Kruskal- Wallis test revealed that PWV has a statistically significant different distribution between controls and hypertensive patients (p < 0.001). The magnitude of PWV increase, was related to BP category classification (from optimal to stage III hypertension) (p < 0.001). Pearson’s correlation revealed a significant association of PWV practically with all major baseline characteristics of hypertensive patients (BMI, Gender, Age, Systolic BP, Diastolic BP, Smoking status and heart rate) (p < 0.001). This association was retained after adjustment of PWV confounders. Multiple regression analysis showed that antihypertensive drug therapy does not affect the statistical significant distribution of PWV in hypertensive patients.

Conclusions: PWV is increased in hypertensive patients, the degree of PWV increase, is associated with baseline blood pressure levels (independently of the antihypertensive drug regimen used as well as anthropometric variables).
Methods: Patients aged 745 years with hypertension were identified from the National Health Insurance Research Database. Medical records of 111,986 patients were reviewed in this study, and 16,402 (14.6%) patients were recognized as having RH. Risk of major adverse cardiac events (MACE) in patients with RH and non-RH was analyzed.

Results: A total of 11,856 patients experienced MACE in the follow-up period. There were more females in the RH group, they were older than the non-RH (63.1 vs. 60.5 years) patients, and had a higher prevalence of cardiovascular co-morbidities. Overall, patients with RH had higher risks of MACE (adjusted HR 1.17; 95%CI 1.09-1.27; p<0.001). Significantly elevated risks of stroke (adjusted HR 1.17; 95%CI 1.08-1.27; p<0.001), especially ischemic stroke (adjusted HR 1.34; 95%CI 1.20-1.48; p<0.001), but not all-cause mortality or acute coronary syndrome were noted in patients with RH compared to those with non-RH. A previous study confirmed this relationship with albuminuria, drug resistance, and renal dysfunction with albuminuria. A sub-analysis showed that RH increased the risks of stroke in female and elderly patients. However, no significant influence was noted in young or male patients.

Conclusions: Patients with RH had higher risks of MACE and stroke, especially ischemic stroke. The risks were greater in female and elderly patients than in male or young patients.

479 | SPOTLIGHT

What is targeted diastolic blood pressure in elderly patients? The results from the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort study

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Objective: To determine the prevalence of masked hypertension (MHT), to assess risk factors intensity, and target organs state in midlife women in screening.

Methods: Participants with hypertension (n=13,948), enrolled in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study group. 1Medical University of Lodz, Dept. of Hypertension, Lodz, Poland; 2School of Public Health, University of Alabama at Birmingham (UAB), Dept. of Epidemiology, Birmingham, United States of America; 3University of Milan, Italy; 4First Second University of Naples, Cardiology, Naples, Italy; 5University of Alabama Birmingham, Birmingham, Alabama, United States of America

There are limited data on the optimal levels of diastolic blood pressure (DBP) in elderly patients with hypertension. The aim of the study was to analyse the association of DBP and cardiovascular outcomes in elderly persons taking anti-hypertensive medication.

Participants with hypertension (n=13,948), enrolled in the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort study were categorized into 3 age groups: 55-64, 65-74 and ≥75 years old. All groups were further divided according to baseline-on-treatment DBP levels: <70, 70-79, 80-89, and ≥90 mmHg. Four main outcomes were analysed in the study: cardiovascular disease (CVD), coronary heart disease (CHD) and stroke incidence, and all-cause mortality rate. Median follow-up was 4.5 years for CVD and CHD, 5.7 years for stroke, and 6.0 years for all-cause mortality.

After multivariable adjustment, DBP ≥70 mmHg was associated with the highest risk of CVD and CHD incidence among participants aged ≥75 years, and DBP ≥90 mmHg with the numerically lowest CVD risk (hazard ratio [HR] 0.38, 95%CI: 0.16-0.91; p-linear=0.013, and 0.22, 95%CI: 0.07-0.69; p=0.002, respectively). No relation between DBP and CVD and CHD incidence was observed for persons aged 55-64 and 65-74 years. There was also no relation between DBP and stroke incidence in individuals aged ≥75 years. For participants aged 55-64 years DBP ≥70 mmHg was associated with the highest risk of all-cause mortality (p-linear=0.009). The J-curve relation was observed in this group, with the increased risk of death also for DBP 90 mmHg (p-quadratic=0.022), however with the highest risk for DBP 90 mmHg (1.54, 95%CI: 1.1-2.13). Among participants aged 65-74 years, there was a linear relation between DBP and all-cause mortality with the highest risk for DBP ≥70 mmHg (p=0.039).

The results suggest a hypothesis that for all individuals ≥55 the recommended level of DBP should be between 70 and 90 mmHg, with the special caution for male or young patients.

4801 | BEDSIDE

Arterial hypertension after successful aortic decoarctation: atenolol vs enalapril

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Background: Late arterial hypertension, a very frequent complication in aortic coarctation (AoC) patients after repair, has been identified as a major predictor for morbidity and mortality in AoC patients. Although the most used in the clinical practice, there is very few data about efficacy and tolerability of ace-inhibitors vs. beta blockers in young AoC patients.

Methods: We evaluated the tolerance and efficacy (24h blood pressure and left ventricular mass [LVM]) of oral administration of atenolol vs enalapril.

Results: We enrolled 51 AoC patients (12.5±1.3 years, BMI: 22.9±4.2kg/m²). Patients were randomly assigned at Atenolol treatment (Group I, n=26) (0.5–2 mg/kg), or Enalapril treatment (Group II, n=25) (0.08–0.6mg/kg). Of them, 42 completed the study, 5 patients had a 6 month follow-up and 4 patients 3 month follow-up.

Efficacy: Both drugs were able to significantly reduce 24-systolic blood pressure [Group I: 132.6±12 vs. 124.1±16mmHg, p=0.02; Group II: 134.6±14 vs. 131.7mmHg, p=0.03], however only enalapril was able to significantly reduce LVM [47.1±12 vs. 39.6±10 g/m², p<0.01]. No changes were induced by the treatment on left ventricular systolic and diastolic function or on ischemic gradient. Also myocardial deformation studied parameters did not change significantly during treatment.

Tolerability: Group I: in two cases (7.7%) drug withdrawal was needed because of side effects. Group II: in no cases drug withdrawal was needed (p=0.49).

Conclusions: Our study demonstrated for the first time in AoC young patients that: 1. Enalapril and Atenolol are similarly effective in reducing 24h systolic blood pressure and determination of independent predictors of RAS.
8420 | BEDSIDE
Periprocedural stroke is not independently affected by the access site during coronary angiography and PCI
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Introduction: All coronary angiography (CA) and percutaneous coronary intervention (PCI) performed in Sweden, including any periprocedural complications, are reported to the Swedish Angiography and Angioplasty Registry (SCAAR). Aim: To see if the incidence of periprocedural stroke during CA and PCI differs between the radial and the femoral access.

Methods: All CA and PCI procedures and all neurological complications registered in SCAAR between 2003 and 2010 were analyzed. Two neurologists evaluated all the periprocedural neurological complications. To identify true periprocedural stroke the SCAAR data was cross-checked with the patients medical records.

Results: A total of 259,045 CA and PCI procedures were compiled, of these 30,804 were excluded due to unknown vascular access site. Of 662 reported neurological complications 12 were unverifiable and thus excluded. Finally 227,304 were included in the present study. Two neurologists evaluated all the periprocedural neurological complications. To identify true periprocedural stroke the SCAAR data was cross-checked with the patients medical records.

Conclusions: In this real-world registry the incidence of CP was quite low. CP occurred more often in patients with complex coronary interventions and was associated with a fourfold increase of hospital mortality.

8422 | BEDSIDE
Comparison of low dose versus standard dose heparin for radial approach in elective coronary angiography
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Objective: The aim of this study is to evaluate the efficacy and safety of two doses of heparin, a low dose (2500 IU) and a standard dose (5000 IU) in patients who underwent trans-radial coronary angiography (TRCAG).

Methods: A total of 458 consecutive patients were included in the present study. 217 in the 2500 -IU heparin group and 242 in the 5000-IU heparin group. Radial artery patency was evaluated one month after the TRCAG with Doppler ultrasound.

Results: The radial artery occlusion (RAO) was observed in 15 (3.3%) patients. The RAO was significantly higher in 2500 IU heparin group than 5000 IU heparin group (5.5% vs 1.2% p<0.010, respectively). Female gender (odds ratio (OR)= 66.135, p=0.002, 95% confidence interval (CI) =4.584-954.131), presence of hypertension (OR= 0.022, p=0.005, 95% CI = 0.002-0.307), sheath removal time (OR= 1.496, p<0.001, 95% CI =1.254-1.794) and administration of 2500 IU heparin (OR= 9.758, p=0.034, 95% CI =1.195-79.695) were the independent predictors of RAO in multivariate regression analysis.

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>2500 IU Heparin (n=217)</th>
<th>5000 IU Heparin (n=242)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n%</td>
<td>166 (76.3%)</td>
<td>182 (75.2%)</td>
<td>0.769</td>
</tr>
<tr>
<td>Age, year</td>
<td>60.75</td>
<td>60.25</td>
<td>0.528</td>
</tr>
<tr>
<td>Body mass index, kg/m2</td>
<td>25.3±4.24</td>
<td>27.65±4.14</td>
<td>0.049</td>
</tr>
<tr>
<td>Hypertension, n%</td>
<td>119 (54.8%)</td>
<td>126 (52.1%)</td>
<td>0.552</td>
</tr>
<tr>
<td>Diabetes Mellitus, n%</td>
<td>121 (55.8%)</td>
<td>158 (65.4%)</td>
<td>0.057</td>
</tr>
<tr>
<td>Glomerular filtration rate, ml/min</td>
<td>90.4 (30.7)</td>
<td>90.3 (34.5)</td>
<td>0.982</td>
</tr>
<tr>
<td>Fluoroscopy time, s</td>
<td>150 (79.5)</td>
<td>142.5 (75.3)</td>
<td>0.065</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>6.5 (2)</td>
<td>6.5 (2)</td>
<td>0.803</td>
</tr>
<tr>
<td>Sheath removal time, min</td>
<td>12 (5)</td>
<td>12 (7)</td>
<td>0.732</td>
</tr>
<tr>
<td>Hematoma, n%</td>
<td>5 (2.1%)</td>
<td>5 (2.1%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Radial artery occlusion, n%</td>
<td>12 (5.5%)</td>
<td>3 (1.2%)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Conclusion: The patients in the standard dose heparin group has lower RAO rates compared to low dose group in this study. This suggests that using the current technique, standard dose of heparin is still required for transradial diagnostic angiography.

8423 | BEDSIDE
Strategies for the prevention of contrast-induced nephropathy: a meta-analysis of randomized controlled trials and observational studies
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Purpose: Studies focusing on statin therapy to prevent contrast-induced...
Conclusion: Our data confirmed that any BAS was associated with lower observed bleeding rates in both sexes undergoing PCI. This lower bleeding risk was associated with lower risk of observed mortality in both men and women. Future prospective studies are needed to evaluate the role of BAS in reducing post-PCI bleeding and mortality.

BIOMARKERS IN HEART FAILURE. NEW INSIGHTS

4824 | BEDSIDE
Association of bleeding avoidance strategies with bleeding and in-hospital mortality in men and women undergoing percutaneous coronary intervention

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Purpose: The use of any of the bleeding avoidance strategies (BAS) (radial access, bivalirudin and/or vascular closure devices) has been shown to be associated with lower bleeding among men and women undergoing percutaneous coronary intervention (PCI). However, the relationship of BAS with sex-related mortality in PCI patients is unknown.

Methods: We examined the relationship of BAS with sex-related bleeding and in-hospital mortality among 96,693 patients undergoing PCI enrolled in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) (2010-2012).

Results: BAS were utilized similarly in men and women undergoing PCI (69.2% vs. 68.9%). For both men and women, in patients where any BAS was utilized the incidence of bleeding events was less than 50% of that observed for patients in whom none of the strategies were employed (Figure). Compared to those without the use of BAS, utilization of this strategy was associated with lower risk of observed mortality in men (0.6 vs. 2.6%, p<0.05) and in women (1.0 vs. 3.7%, p=0.05).

Conclusions: Our data confirmed that any BAS was associated with lower observed bleeding rates in both sexes undergoing PCI. This lower bleeding risk was associated with lower risk of observed mortality in both men and women. Future prospective studies are needed to evaluate the role of BAS in reducing post-PCI bleeding and mortality.

4830 | BEDSIDE
Combined measurements of N-Terminal Pro-Brain Natriuretic Peptide and D-Dimer are useful when predicting in-hospital death in acute heart failure

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Aims: NT-proBNP is an established biomarker for the prediction of in-hospital death in patients with acute heart failure. We therefore hypothesized that a combined approach using both NT-proBNP and D-dimer levels might improve the clinical risk stratification for heart failure.

Methods: In total, 287 patients presented to our emergency room within 24 h of symptom onset were included, and NT-proBNP and D-dimer levels were simultaneously measured. The optimal cut-off level for NT-proBNP and D-dimer to predict in-hospital death was determined by receiver operating characteristics curve anal-
yis. The integrated prognostic impact of NT-proBNP and D-dimer levels above each cut-off value was also examined.

**Results:** In-hospital death occurred with 20 patients (7.0%). The optimal cut-off levels for NT-proBNP and D-dimer were 4900 pg/mL and 4.0 mg/dL, respectively, with corresponding odds ratios (OR) of 5.32 (p=0.001) and 3.54 (p<0.005). Patients with higher cut-off levels of both NT-proBNP and D-dimer exhibited the highest risk for in-hospital death compared with the other patients (24.4% vs. 4.1%; OR = 7.65, p<0.001). Multivariable analysis indicated that the integrated biomarkers remained independent predictors of in-hospital death (OR = 11.20, p=0.002).

**Conclusion:** The combination test with both the NT-proBNP and D-dimer biomarkers was useful for the prediction of death in patients with acute heart failure.

4831 | BEDSIDE
Activation pattern of novel renal biomarkers in acute heart failure: superiority of NGAL
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**Background:** Patients with acutely decompensated heart failure often suffer from deterioration in renal function, also referred to as cardorenal syndrome (CRS). The aim was to assess and compare a set of novel markers of acute kidney injury (AKI) in acute heart failure (AHF).

**Methods:** The new renal biomarkers Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney injury molecule-1 (KIM-1), N-acetylated-D-glucosaminidase (NAG) and Interleukin-18 (IL-18) were assessed from urine samples of 58 patients with AHF and 54 healthy controls.

**Results:** Upon admission, NGAL, KIM-1 and NAG, but not IL-18 (p=n.s.), were significantly higher compared to healthy postpartal women (11%). Patients on diuretics presented with higher cut-off levels of both NT-proBNP and D-dimer and exhibited the highest risk for in-hospital death compared with the other patients (24.4% vs. 4.1%; OR = 7.65, p<0.001). Multivariable analysis indicated that the integrated biomarkers remained independent predictors of in-hospital death (OR = 11.20, p=0.002).

**Conclusion:** The combination test with both the NT-proBNP and D-dimer biomarkers was useful for the prediction of death in patients with acute heart failure.

4833 | BENCH
Correlates and prognostic implications of dipeptidyl peptide IV levels in patients with chronic heart failure
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**Purpose:** Dipeptidyl peptidase IV (DPP-IV) is a serine protease that inactivates various peptide hormones including B-type natriuretic peptide (BNP) and glucagon-like-peptide 1 (GLP-1), an incretin involved in glucose homeostasis. DPP-IV is a target of glucose-lowering drugs glitazins and may be involved in pathophysiology of heart failure (HF). We investigated biochemical correlates of DPP-IV and its impact on HF prognosis.

**Methods:** Patients with advanced HF, referred for pre-transplant evaluation or ICD/CRT implantation, underwent fasting blood sampling, echocardiography and were retrospectively followed for combined endpoint of death, LVAD or heart transplantation. DPP-IV was measured by ELISA (DPP/CD36, R&D, USA), BNP by CMIA (Abbott, USA).

**Results:** 369 subjects (mean age 59±11 years, 84% males, BMI 28±4.7 kg/m², DM in 34%) were included. DPP-IV levels followed normal distribution with mean 351±92 pg/mL. DPP-IV level was unrelated to log BNP (Figure 1A), to severity or etiology of HF (NYHA class, MLHFQ score, p>0.05), to degree of cardiac dysfunction (LV EF, LV diameter, both p>0.05), to BMI, gender or DM. DPP-IV correlated with glucose (r=0.23, p<0.001) and HgbA1C (1B), but not with fasting insulin (r=0.04, p=0.4) or HOMA index of insulin resistance (p>0.05). DPP-IV correlated with ALP (r=0.30, p<0.0001), but not with ALT and AST or IVC diameter. After median follow-up of 536 (IQR318-850) days, 36% subjects experienced adverse event. There was no difference in event-free survival by DPP-IV terciles (1C).

Conclusions: DPP-IV is not related to total BNP, degree of HF or prognosis. Elevated DPP-IV is associated with impaired glucose tolerance in HF, independently of insulin resistance, and may be related to liver steatosis.

4834 | BEDSIDE
Diagnostic and prognostic performance of multiple biomarkers for acute heart failure in older patients presenting to the emergency department
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**Background:** The management of acute heart failure (AHF) in older patients is associated with some diagnostic challenges, which are not adequately considered in current ESC guidelines. An approach to diagnosis and prognosis is to measure pro-BNP (787±1900 pmol/l for natriuretic peptide (BNP)). But the threshold for NT-proBNP increases not only with age often due to an impaired renal function, but also differs for patients presenting with acute onset or worsening of symptoms to an emergency department (ED) and those presenting with a more chronic onset of symptoms. TB485±850 days, 36% subjects experienced adverse event. There was no difference in event-free survival by DPP-IV terciles (1C).
agnostic and prognostic performance of NT-proBNP alone or in combination with other biomarkers for AHF in older patients presenting to the ED.

**Methods:** We consecutively enrolled 302 non-surgical patients ≥70 years present- ing to the ED. In addition to NT-proBNP, mid-regional pro-adrenomedullin (MR-proADM), mid-regional pro-atrial natriuretic peptide (MR-proANP), C-terminal pro-endothelin-1 (CT-proET-1), and ultra-sensitive C-terminal pro-atrial natriuretic peptide (MR-proBNP) were measured at admission. Two cardiologists independently adjudicated the final diagnosis of AHF after reviewing all available baseline data excluding the biomarkers. All patients were followed up for cardiovascular-related death within the following 12 months.

**Results:** AHF was diagnosed in 120 (40%) patients (age 81±6 years). Accuracy to diagnose AHF was significantly higher for MR-proADM and NT-proBNP versus NT-proBNP (area under the receiver operating characteristic curve [AUC] 0.84 versus 0.62; P=0.045) and for CT-proET-1 versus NT-proBNP (AUC 0.86 versus 0.81, P<0.001). No other dual or triple biomarker combination showed higher and significant AUC values than MR-proADM or CT-proET-1 combined with NT-proBNP. When added to NT-proBNP, a continuous net reclassification improvement of 33.3% for MR-proADM and 69.9% for CT-proET-1 could result in significant reclassification of older patients. Cox regression analysis revealed a 1.99-fold risk of death (95% CI 1.61 to 2.45, P<0.001) for an increment of the log-transformed MR-proADM concentration by 1 unit after adjustment for risk factors.

**Conclusions:** In unselected older patients presenting to the ED, CT-proET-1 or MR-proADM and NT-proBNP improve the diagnostic and MR-proADM the prognostic performance in AHF.

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**ORAL ANTICOAGULATION IN PRACTICE**

**4043 | BEDSIDE**

Effect of smoking on comparative efficacy of antithrombotic therapy in patients with atrial fibrillation. A community based cohort study

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Smoking is incorporated in a simple score (SAME-TT2R2) that can predict poor INR control in patients with atrial fibrillation (AF) treated with vitamin K antagonists (VKA). Moreover, the clinical benefit of clopidogrel in reducing myocardial infarction and stroke in randomized clinical trials of antiplatelet drugs (APD) was seen primarily in smokers, with little benefit in nonsmokers. We made the hypothesis that active smoking may differently influence 1) the risk of stroke and 2) the risk of bleeding in AF patients treated with VKA or with APD.

**Methods:** We examined the clinical course of 7,948 consecutive patients with AF and/or atrial flutter seen between 2000-2010. The outcomes in patients with active smoking were compared with those in other patients.

**Results:** Among 7,948 patients with AF (age 71±15 years), 1034 (13%) had active smoking. APD was prescribed on an individual basis for 2761 patients (35%) and VKA for 4534 (57%). During a follow-up of 929±1082 days, 3861 strokes/thromboembolic events, 707 severe bleedings and 248 major BARC bleedings were recorded. Smoking was not independently associated with a higher risk of strokes (OR=1.89, 95% CI 0.75-1.18, P=0.62). By contrast, after adjustment on age, CHADS2 score, HASBLED bleeding risk score, VKA use and APD use, smoking was independently associated with a worse prognosis for the risk of severe bleeding (relative risk=1.23, 95% CI 1.05-1.40, P=0.03). Smoking was associated with a risk of major bleeding in patients treated with VKA (relative risk=1.32, 95% CI 0.97-1.76, P=0.07).

**Conclusions:** In AF, there was a higher risk of bleeding in smokers, mainly in those treated with VKA.

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**4044 | BENCH**

Dabigatran-induced anticoagulant and bleeding effects can be reversed with both prothrombin complex concentrates and a specific antidote (idarucizumab) in a lethal porcine polytrauma model

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**Introduction:** A specific reversal agent in situations of life-threatening bleeding with the direct thrombin inhibitor dabigatran is currently not available and methods used in the clinic to reverse its effects have demonstrated conflicting results. This study assessed the ability of a four-factor prothrombin complex concentrate (PCC) and a specific antidote to dabigatran (idarucizumab) to reverse dabigatran anticoagulation in a porcine polytrauma model.

**Methods:** After ethical approval, the study was performed in 24 anaesthetised male pigs (given orally for 1-3 days 30 mg/kg bid) and, on the 4th day, infused prior to blunt liver injury and bilateral femur fractures. Following hemorrhagic shock, blood loss (BL) was recorded 10 min post-trauma and animals were randomized (n=6/group) to a single injection of PCC (25 and 50 IU/kg), the antidote idarucizumab (60 mg/kg) or vehicle (control). BL and hemodynamic variables were monitored for 300 min or until time of death. Coagulation was assessed by thromboelastometry, coagulation parameters and diluted TT. Data were analysed by ANOVA (± SD).

**Results:** Dabigatran levels were 550±155 ng/mL prior to injury. Except for idaru- cizumab treated animals, plasma levels remained significantly elevated in all ani- mals throughout the observation period. The degree of injury was similar among animals 10 min post injury with comparable BL of 742±13 mL. Anticoagula- tion with dabigatran without intervention resulted in a BL of 3774±628 mL and mean survival within the final 12 min (range: 65-146 min; p<0.05 vs. PCC and idarucizumab treated animals). In contrast, treatment with 50 IU/kg PCC (1767±135 mL) and idarucizumab (1190±167 mL) was associated with a significant reduc- tion in BL (p<0.05 vs. controls) and 100% survival. Although the onset of bleeding appeared delayed, total BL was comparable in PCC 25 and idarucizumab treated animals. Likewise, coagulation parameters improved substantially in PCC 50 IU/kg and idarucizumab treated animals. Due to on going blood loss, coagulopathy in control and PCC 25 animals aggravated over time. Clinically and macroscopically no adverse events were observed with idarucizumab or PCC treated animals.

**Conclusion:** This polytrauma model in pigs shows that therapy with aDabi-Fab is effective and safe to reverse dabigatran anticoagulation under conditions of life- threatening bleeding resulting from severe trauma. However, until idarucizumab becomes available clinically, our data also show that PCCs at sufficiently high dosages may be an alternative to stop trauma- and dabigatran induced bleeding.

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**4045 | BEDSIDE**

Safety of new oral anti-coagulants versus conventional agents with respect to clinically significant bleeding risk: a systematic review and networking meta-analysis of randomized controlled trials

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**Background:** New oral anti-coagulants (NOACs) are well established as conven-iente and safe alternatives to conventional agents (Vitamin K antagonists) across a range of clinical conditions. Bleeding in the absence of a specific antidote is a potential complication associated with NOACs as compared to warfarin. In the absence of head-to-head comparisons of relative safety profiles, the choice of a specific NOAC is challenging. This study seeks to compare bleeding risks among the different NOACs using a networking meta-analysis.

**Methods:** Literature search was conducted using Medline, Embase, Cochrane Central Register of Controlled Clinical Trials and Cochrane Database of Sys- tematic Review (CDSR) from the inception of these databases till the present (August 2013). We included clinical trials reporting the bleeding risk associated with the use of NOACs compared with placebo or conventional agents (low molecular weight heparins, aspirin and warfarin). Networking meta-analyses us- ing meta-regression and rankograms were performed using the R package WINBUGS 1.4. Sub- group analyses were performed for acute coronary syndrome (ACS), atrial fibril- lation (AF), and prevention of venous thromboembolism (VTE) after orthopedic surgery. NOACs were ranked based on their likelihood to cause bleeding using a novel method.

**Results:** A total of 673 titles were retrieved and 42 clinical trials (166,889 patients, 92727 in the NOAC’s group and 74162 in the control group) were included in the final analyses. Results from our networking meta-analysis suggested that over-all, apixaban (OR=0.77, 95% CI=0.69-0.88) and dabigatran (OR=0.87, 95% CI=0.78-0.97) cause significantly less bleeding compared with rivaroxaban which was associated with a significantly increased OR=1.12, 95% CI=1.04-1.20) bleeding risk. In subgroup analyses rankograms showed that apixaban was associated with the least number of bleeding events followed by dabigatran and rivaro- xaban in ACS and AF, whereas rivaroxaban was associated with the least bleeding events followed by apixaban and dabigatran in prevention of VTE.

**Conclusions:** There are clinically important differences in the bleeding risk of NOACs among the commonly prescribed NOACs. In the absence of head to head trials, indirect evidence provides useful information for clinicians to guide the prescription of NOACs for specific clinical conditions. An important limitation of this analysis is that the patient populations studied with the various NOACs differed significantly in their composition.

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**4046 | SPOTLIGHT**

Novel oral anticoagulants in patients with venous thromboembolism and active cancer: 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 this is the case in patients with cancer associated thrombosis remains undefined.
Methods: We performed a meta-analysis of randomized controlled trials with the aim of assessing the efficacy and safety of NOACs in patients with VTE and active cancer. MEDLINE, EMBASE and CENTRAL were searched up to December 2013 with no language restriction. The primary outcome of the analysis was recurrence of VTE. Data on VTE recurrence and major or clinically relevant non-major bleeding (CRB) were collected. Data were pooled and compared by ORs and 95% CIs.

Results: Overall, 10 studies comparing NOACs with conventional anticoagulation for treatment of VTE and reporting on outcomes in patients with active cancer were included in the current review. Five studies were included in the meta-analysis (2 with dabigatran, 2 rivaroxaban and 1 edoxaban), accounting for a total of 859 patients. VTE recurrence occurred in 14 of 455 (3.1%) and in 20 of 404 (4.9%) cancer patients treated with NOACs and conventional anticoagulation, respectively. (OR 0.60, 95% CI 0.30 to 1.21; 1-squared 0%). CRB occurred in 14.9 and 16.6% of patients receiving NOACs and conventional treatment, respectively (OR 0.88, 95% CI 0.57 to 1.35; 1-squared 0%).

Conclusions: NOACs seem as effective and safe as conventional anticoagulant treatment for prevention of VTE in cancer patients. Ad hoc clinical trials should be conducted to confirm these results.

4847 | BEDSIDE Risk of myocardial infarction patients treated with oral anticoagulation, a bayesian network meta-analysis A. Tornyos1, A. Komosci1, A. Voroscucl1, D. Kehl2.1 University of Pécs, Heart Centre, Pécs, Hungary; 2 University of Pécs, Institute of Applied Studies in Business and Economics, Pécs, Hungary

Purpose: The relative safety of oral anticoagulants continues to be debated, and there is a considerable heterogeneity regarding cardiac safety among oral anticoagulants. Differences in risk of myocardial infarction may influence the choice of treatment. Differences in risk of myocardial infarction may in- influence the choice of treatment.

Methods: Randomized controlled trials comparing novel anticoagulants to warfarin were searched using MEDLINE, EMBASE, and Cochrane databases. Inclusion on study design, inclusion and exclusion criteria, sample characteristics, and clinical outcomes was extracted. The primary end-point of the analysis was the occurrence of myocardial infarction (MI). We performed a random-effects model within a Bayesian framework using Markov Chain Monte Carlo simulation to calculate pooled odds ratio (OR) and 95% credibility intervals (CI). We also ranked therapies by their likelihood of leading to the best results for the outcomes.

Results: Twelve trials including 100,524 randomized patients were analyzed. At the longest available follow-up the odds for MI was lower with warfarin when compared against dabigatran and rivaroxaban and higher with apixaban and edoxaban (OR: 0.51 CI: 0.09-1.44, OR: 0.72 CI 0.12-1.98, OR: 0.79 CI 0.12-2.29, OR: 1.17 CI 0.16-4.04, OR: 1.64 CI 0.12-7.16, respectively). In the Bayesian network analysis the posterior probability of being the first best choice of treatment was 33.3% for edoxaban, 26.3% for apixaban, 17.6% for warfarin, 11.7% for rivaroxaban, 7.1% for dabigatran and 8.3% for rivaroxaban. Exclusion of the withdrawn ximelagatran and analysis with the corrected values of MI in the RELY trial did not substantially influ-enced the results.

Conclusion: There is a considerable heterogeneity regarding cardiac safety among oral anticoagulants. Differences in risk of myocardial infarction may influence the choice of treatment.

4848 | BEDSIDE Are the guidelines recommendations followed in the clinical practice in patients with atrial fibrillation undergoing coronary stenting? M. Mutuberrria Urdanzain1, A. Sambola1, B. García Del Blanco1, B. Miranda1, A. Santos1, A. Alonso1, F. Alfonso1, A. Cequier2, J.A. Barrabés1, D. García-Dorado1, H. Hospital Clinic San Carlos, Department of Cardiology, Madrid, Spain; 2Bellvitge University, Hospital, Barcelona, Spain

Background: Patients with atrial fibrillation (AF) submitted to PCI and stenting (PCI-S) have an increased risk of bleeding due to the combination of dual anti-platelet therapy (DAPT; aspirin and clopidogrel) with anticoagulation (TT; triple therapy). The use of TT at 30 to 121 days after PCI-S is a class IIIb recommendation of the ACC/AHA/ESC guidelines. Other recommendations such as the use of drug eluting stent (DES), radial arterial access and closure device in femoral access are preferred. Aim: To assess the adherence to guidelines recommendations.

Methods: A prospective multicenter study was conducted from 2007 to 2011 in- cluding patients with non-valvular AF who underwent PCI-S. Baseline character-istics, CHADS2, CHA2DS2VASc, HAS-BLED scores, PCI details, antithrombotic therapy at discharge and its duration were recorded. Follow-up was 1 year. All bleeding events, thromboembolisms (stroke or systemic embolism), acute myocardial infarction or target revascularization, total deaths, and cardiovascular deaths were analyzed post hoc.

Results: We identified 640 patients with AF and 320 (50%) of them were >75 years (79.8±5.6 years). The 74.2% had HTA, 48.3% were smokers, 37.0% dia-betes mellitus, 55.2% dyslipidemia, 15.9% renal failure, 13.3% peripheral arteri-opathy, and 32.0% previous ischemic heart disease. 419 patients (65.5%) had a CHADS2 score >2. 466 (73%) a CHA2DS2VASc >2 and 164 (25.6%) had a HAS-BLED ≥3. DEs was implanted in 247 (38.6%) patients, in 328 (51.3%) radial access was chosen. In only 61 (9.5%) of patients submitted to femoral access a closure device was used. At discharge, 320 (50.2%) patients submitted TT, 266 (41.8%) DAPT and 50 (7.9%) warfarin plus clopidogrel. Total Bleedings occurred in 116 patients (18.1%), and 37 (5.8%) of them were major bleedings. Bleedings occurred mainly in patients treated with warfarin plus clopidogrel (29.9% TT vs 13.5% DAPT vs 26% warfarin plus clopidogrel, p=0.02). During follow-up, 64 patients (9.9%) died for any cause, and 47 (7.7%) because of a cardiovascular event. A multivariate analysis identified as predictors of cardiovascular mortality the age (OR: 1.05; 95% CI 1.00 to 1.11, p=0.043), renal failure (OR 0.62; 95% CI 0.28 to 1.41), and the use of warfarin plus clopidogrel (OR 4.62; 95% CI 1.68 to 12.7, p=0.03). DEs, the arterial access or the use of closure devices were not predictors.

Conclusions: In patients with AF submitted to PCI-S, guidelines recommenda-tions are not always followed. The use of warfarin plus clopidogrel was associated to mortality while other such recommendations as DES, type of arterial access or closure devices had no effect.
4862 | BEDSIDE

ECG abnormalities in athletes-performance and outcome of athletes with inverted T waves

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Purpose: Evaluate the prevalence of the abnormal ECG findings, according to the Seattle criteria (Sc), detected during the preparticipation screening program in a population of highly-trained athletes and identify those harbouring potential malignant cardiovascular diseases in a retrospective follow-up study.

Methods: We ascertained 682 Caucasian sport athletes (mean age 20.5 ± 4.8 years, 459 males, 223 females). Mean follow-up was 12.3 ± years with a yearly screening program. Abnormal ECGs were identified and the presence of cardiomyopathies or primary electrical diseases was evaluated.

Results: In 20.9% athletes abnormal ECGs appeared. In 640 (93.8%) athletes, ECGs were normal or showed common abnormalities, while 22 (3.2%) athletes presented uncommon ECG abnormalities, not certainly associated with inherited cardiovascular diseases, and thus not included in the Seattle criteria. Abnormal ECGs (Sc) included: negative T-waves in ≥2 adjacent leads in 6 (0.9%), intraventricular conduction delay >140 ms in 21 (1.0%), left QRS axis deviation in 7 (1%), left atrial enlargement in 2 (0.3%), ventricular pre-excitation pattern in 1 (0.1%), long QTc interval in 2 (0.1%), ≥2 premature ventricular contractions in 2 (0.3%). Two athletes (0.3%) with inverted T-waves were diagnosed with ARVC and HCM respectively during follow-up (Picture).

Conclusion: Abnormal ECGs according to the Sc were present in 2.9% of our highly-trained athletes. Follow-up showed that 0.3% of athletes (2/682) presenting pathological inverted T-waves were diagnosed with cardiomyopathy and had affected first-degree relatives that were identified through clinical family screening, while athletes with normal ECG did not present any diagnostic criteria of cardiomyopathy.

4863 | BEDSIDE

High prevalence of malignant early repolarisation patterns in indigenous Australian and Pacific Islander/Maori athletes

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Electrocardiographic early repolarisation pattern (ERP) is a common finding in athletic populations. Certain patterns of ERP, namely inferior ERP with a horizontal ST-segment and/or marked J-wave amplitude have been termed “malignant” given their association with increased risk of sudden cardiac death. ERP is more common in black African than Caucasian (C) individuals. However, there is currently little data on the prevalence of ERP in athletes of other ethnic backgrounds, including Indigenous Australian/Torres Strait Islander and Pacific Islander/Maori (ATSI) individuals. From June 2011 to December 2013, 843 C and 160 ATSI elite male athletes underwent ECG screening. ECGs were analysed for the presence of ERP, defined as J-point elevation of at least 0.1 mV in or more inferior (II, III, aVF) or lateral (I,aVL, V4-V6) leads. J-waves were coded as notched, slurred or discrete. J-wave amplitude was measured and ST-morphology coded as horizontal or ascending. Heart rate, QRS duration and Sokolow-Lyon LVH scores were measured. Demographic differences between ATSI and C are shown in Table 1. ERP was more common in ATSI than C, as was inferior ERP, inferior ERP with a horizontal ST-segment and inferior ERP with a J-wave >2mm amplitude. Lateral ERP occurred with similar prevalence in both groups (Table 1). ERP, including ERP patterns associated with an increased risk of SCD are common in elite athletes, and significantly more prevalent in ATSI than C athletes. The long-term clinical significance of ERP in this population is yet to be determined.

4864 | SPOTLIGHT

Coronary artery disease in asymptomatic male athletes aged 45 years or older with a low ESC SCORE risk: the emerging role of coronary CT angiography


Objective: To assess the feasibility of low-dose 64-slice CTA in asymptomatic male recreational athletes aged ≥45 years who underwent a sports medical evaluation.

Methods: 320 participants underwent prospective ECG-triggered CTA using a 256-slice CT scanner. After exclusion of 44 participants with diabetes, hypertension, or an ESC risk score >4% a group of 276 men with a low SCORE risk (0-4%) remained in whom the presence of CAD was defined as a Coronary Artery Calcium Score (CACS) ≥100 Agatston Units or ≥50% luminal stenosis.

Results: In 41 (15%, 95% CI 10.8 – 19.1) of 276 participants with a low ESC SCORE risk and good exercise tolerance (see table), relevant CAD (CACS ≥100 or luminal stenosis ≥50%) was found. The number needed to screen was 6.7.

Conclusion: Minimally invasive CCTA is feasible and detects relevant coronary artery disease in asymptomatic male athletes aged ≥45 years with a low ESC SCORE risk and normal exercise testing.

4865 | BEDSIDE

Cardiovascular screening in middle-aged individuals engaged in high intensity sport activities: implications, yield and cost-analysis

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Purpose: To assess the implications, yield and costs of this preventive evaluation.

Methods: We observed a prospective observational multicenter study including individuals aged 35 to 65 years engaged in high intensity sport activities and free from cardiac diseases. Athletes were examined following the American Association for Cardiovascular Prevention and Rehabilitation protocol including physical examination, 12-lead resting electrocardiogram (ECG) and risk stratification according to the Systematic Coronary Risk Evaluation (SCORE). Athletes with abnormal findings at screening or at high cardiovascular risk underwent additional examinations. The costs of the overall screening program until diagnosis was calculated according to Swiss medical rates.

Results: From January to December 2013 we enrolled 761 athletes (73% males, 46.8±7.3 years). Running (33%) and cycling (23%) represented the most popular intensity sport activities: implications, yield and cost-analysis
4866 | BEDSIDE
Sudden cardiac death in young athletes - data from the Swiss registry
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Purpose: Sudden cardiac death (SCD) in young athletes is of great public interest. In Switzerland systematic pre-participation screening (PPS) including an ECG exist only for professional athletes in high risk sports like ice hockey or football. The purpose of this study was to analyze the incidence and causes of SCD in this population.

Methods: In a retrospective cohort study we reviewed all forensic reports between 1999 and 2010 of German-speaking parts of Switzerland (with an overall population of 5'617'963) for SCD in young individuals (10-39 years). Data were collected in the Swiss REGistry of Athletic Related Death, swissregard.ch. SCD was divided into the following categories: not-related to sports (NON), during recreational sports (REC), and in competitive sports (COMP). Further subdivision of COMP was made into professional and non-professional athletes. The denominators for the calculation of incidences were derived from the Federal Offices of Statistics and Sports.

Results: In the 11-year period under investigation, a total of 267 (76.5%) males and 82 (23.5%) females succumbed to SCD. Of these, 52 (14.8%) were sports-associated SCDs with male predominance (92.3% male versus 7.7% females), 31 (59.6%) athletes died during REC and 21 (40.4%) during COMP. Of those, 3 (14.3%) were professional athletes. Median age [interquartile range] in NON, REC, and COMP was 32 [10], 32 [15], and 30 [14] respectively. Incidence for NON SCD, REC SCD, and COMP SCD were 1.17/100'000, 0.21/100'000, and 0.57/100'000 respectively. Incidences of NON versus COMP, NON versus REC and REC versus COMP were significantly different (all p < 0.001). SCD in COMP mostly occurred during ball games (55%), in REC mostly during endurance sports (68%). Underlying causes of SCD in COMP were coronary artery disease without acute myocardial infarction in 5 (23.8%) athletes, acute myocardial infarction in 3 (14.3%), dilated cardiomyopathy in 2 (9.5%), aortic valve stenosis in 2 (9.5%), and hypertrophic cardiomyopathy (4.8%) due to hypertrophic cardiomyopathy, arrhythmogenic right-ventricular cardiomyopathy and Wolff –Parkinson-White syndrome. SCD in the 3 professional athletes (aged 26, 28 and 30 years) were all due to acute myocardial infarction.

Conclusion: In this cohort, the incidence of sport-associated SCD was low, especially in professional athletes. Interestingly all SCD in this group were caused by acute myocardial infarction. It appears, that PPS with ECG in professional athletes in high risk sports may prevent SCD caused by inherited diseases, but does not to prevent SCD due to acute myocardial infarction.

ATRIAL FIBRILLATION: HOW TO IMPROVE PROGNOSIS?

4871 | BEDSIDE
Higher risk of death and stroke in patients with persistent versus paroxysmal atrial fibrillation: results from the ROCKET AF trial
B.A. Steinberg1, A.S. Hellkamp1, Y. Lohkrygina1, M.R. Patel1, G. Breithardt2, D.E. Singer2, K.W. Mahaffey3, K.A.A. Fox4, R.M. Califf1, J.P. Piccini1 on behalf of the ROCKET AF Steering Committee and investigators. 1Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 2University of Minnesota, Minneapolis, Minnesota; 3Barnes Hospital, St. Louis, Missouri; 4University of Wisconsin, Madison, Wisconsin

Purpose: The efficacy of apixaban compared to warfarin in patients with atrial fibrillation with high coagulation activity despite anticoagulant treatment

Methods: Patients randomized in the ROCKET AF trial (n=14,264) were grouped by baseline AF category: paroxysmal or persistent. Multivariable adjustment was performed to compare thromboembolic events, bleeding, and death between groups, in high-risk subgroups, and across treatment assignment (rixaroxaban or warfarin).

Results: Of 14,062 patients, 11,548 (82%) had persistent AF at baseline, and 2514 (18%) had paroxysmal AF. Patients with persistent AF were marginally older (73 vs. 72; p=0.03), less likely female (39% vs. 45%; p=0.001), and more likely to have previously used vitamin K antagonists (65% vs. 56%; p=0.001) compared with patients with paroxysmal AF. In patients randomized to warfarin, time in therapeutic range was similar (58% vs. 57%; p=0.94). Patients with persistent AF had higher adjusted rates of stroke or systemic embolism (2.18 vs. 1.73 events/100-pyrs; p=0.048) and all-cause mortality (4.78 vs. 3.52; p=0.006) (Figure). Rates of major bleeding were similar (3.55 vs. 3.31; p=0.77). Rates of stroke or systemic embolism in both AF types did not differ by treatment assignment (rixaroxaban vs. dose-adjusted warfarin; p interaction=0.6).

Conclusions: In patients with AF at moderate to high risk of stroke receiving anticoagulation, those with persistent AF have a higher risk of thromboembolic events and worse survival compared with paroxysmal AF.

Abstract 4872 – Table 1

<table>
<thead>
<tr>
<th>Stroke/SEE (n=96)</th>
<th>Apixaban, %/year Patients</th>
<th>Warfarin, %/year Patients</th>
<th>Apixaban vs Warfarin</th>
<th>HR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1+2 (µmol/L) ≤75</td>
<td>0.62</td>
<td>1.03</td>
<td>0.60</td>
<td>0.8969</td>
<td>-</td>
</tr>
<tr>
<td>&gt;75</td>
<td>76/13</td>
<td>34/1818</td>
<td>(0.27–1.36)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>D-dimer (mg/L) ≤401</td>
<td>0.85</td>
<td>0.93</td>
<td>0.92</td>
<td>0.3652</td>
<td>-</td>
</tr>
<tr>
<td>&gt;401</td>
<td>171/1077</td>
<td>23/1355</td>
<td>(0.49–1.73)</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

*p-value for interaction between treatment and biomarker level.
Methods: In the ARISTOTLE trial 18201 patients with atrial fibrillation (AF) were randomized to apixaban 5 mg twice daily or warfarin. Of these patients 4850 were included in a biomarker study with blood sampling after 2 months of study treatment. Stroke/systemic embolism (SEE) and major/clinical significant (CS) non major bleed were evaluated after 2 months. The median follow-up time was 1.8 years. Cox models including treatment, biomarker level at month 2 and the interaction as covariates were analyzed.

Results: The median prothrombin fragment 1+2 (F1+2) and D-dimer levels at 2 months were 75.9 pmol/L and 401 μg/L, respectively.

Conclusion:High F1+2 and F1+2 levels despite oral anticoagulant treatment identify AF patients at high risk of stroke, and high F1+2 is also associated with risk of bleeding. The beneficial effects of apixaban compared to warfarin were consistent regardless of the coagulation activity evaluated during treatment.

4873 | BEDSIDE
Digoxin use in patients with atrial fibrillation is associated with adverse cardiac outcomes: results from the ROCKET AF trial
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Purpose:Although no large clinical trial has randomly assigned and evaluated digoxin in patients with AF with and without heart failure (HF) in the context of a clinical trial aimed at stroke prevention.

Methods:Patients enrolled in ROCKET AF (rivaroxaban vs. dose-adjusted warfarin for stroke prevention) were included and categorized based on digoxin use at baseline and during the study. Cox proportional hazards regression models adjusted for baseline characteristics and medications were used to test the time-dependent effect of digoxin on all-cause, vascular, and sudden death. Cardiovascular outcomes were adjudicated as part of the trial.

Results:Of randomized patients (n=14,171), baseline digoxin use was reported in 5239 (37.0%). Patients treated with digoxin were more likely to be female (42.4% vs. 37.9%), have a history of HF (73.3% vs. 56.1%), have diabetes (43.0% vs. 38.0%), and have persistent AF (86.0% vs. 77.0%) (p<0.001 for each comparison). Kaplan-Meier curves for all-cause death are shown for patients with and without baseline digoxin. After adjustment, digoxin was associated with increased all-cause (HR 1.22; 95%CI 1.08-1.37), vascular (HR 1.22; 95% CI 1.05-1.42), and sudden death (HR 1.29; 95% CI 1.09-1.51, respectively). The total of fatal bleeding, deaths in which bleeding was a contributing factor, and deaths in patients who had a non-fatal major bleed represented 89% and 86% of the excess in deaths observed in the warfarin arm, as compared to HD and LD edoxaban regimens, respectively.

Conclusions: In ROCKET AF, digoxin therapy was associated with a significant increase in all-cause, vascular, and sudden death in patients with AF. These data do not support the routine use of digoxin in patients with AF with or without HF and suggest the need for re-evaluation of current recommendations.

4874 | BEDSIDE
Reduction in bleeding with edoxaban vs warfarin linked to lower all-cause mortality in 21,105 patients randomized in the ENGAGE AF-TIMI 48 trial
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Background: Edoxaban was associated with significantly less bleeding and lower mortality as compared to warfarin in the ENGAGE AF-TIMI 48 trial of 21,105 patients with atrial fibrillation. The causes of death and relationship between bleeding and death have not been previously described.

Methods: ENGAGE AF-TIMI 48 was a double-blind trial comparing warfarin (TTR 68.4%), with 2 regimens of once-daily edoxaban (high-dose [HD], low-dose [LD]) over a median follow-up of 2.8 years. We analyzed the data on the cause of death and relationship to bleeding as adjudicated by the independent, blinded, clinical endpoint committee (CEC). The CEC determined whether deaths were directly due to a bleed (i.e., fatal bleed), bleeding contributed to death, or death was not directly related to bleeding. Major bleeding was defined per ISTH criteria.

Results: There were 839 deaths (4.35%/yr) in the warfarin arm, compared with 773 deaths (3.99%/yr, p=0.08) with HD edoxaban, and 737 deaths (3.80%/yr, p=0.006) with LD edoxaban. Reductions in fatal bleeding represented 45% and 40% of the excess in deaths with warfarin compared to HD and LD edoxaban, respectively (Table). The total of fatal bleeding, deaths in which bleeding was a contributing factor, and deaths in patients who had a non-fatal major bleed represented 89% and 86% of the excess in deaths observed in the warfarin arm, as compared to HD and LD edoxaban regimens, respectively.

Conclusions: The majority of the reduction in all-cause mortality observed with edoxaban in the ENGAGE AF-TIMI 48 trial was either directly or indirectly associated with lower rates of fatal or non-fatal major bleeding with edoxaban as compared to warfarin.

4875 | BEDSIDE
Time-dependent rate of events after coronary stent implantation in patients with atrial fibrillation
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The optimal regimen of the antithrombotic therapies in patients with atrial fibrillation (AF) who have had a coronary stent is unclear. The incidence of the several cardiovascular events may vary over the first year in these patients, some of whom being greatest in the first months after stent implantation. We tried to evaluate this time dependency and how oral anticoagulation (OAC) may affect the rate of these different events.

Methods: All patients with AF and stent implantation seen between 2000 and 2010 in 3 academic hospitals were identified and followed up for events in each period of 3 months for 12 months.

Results: In 978 AF patients with coronary stent placement (mean age 72, 72% male, CHADS2 score 2.0), OAC was prescribed on an individual basis for 417 patients (43%) and no OAC in the remaining 561 patients (57%). During a 1-year follow-up, whilst death was the predominant event in 1st trimester. Rate of bleeding events was highest in first 3 months after stent implantation. Therapy with OAC was associated with a lower all-cause mortality in the periods 0-3 months
Purpose: The tachycardia screening campaign of atrial fibrillation in general practice: assessment of predictive criteria for atrial fibrillation

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Purpose: Atrial fibrillation (AF) affects nearly 750 000 patients in our country and this number is expected to double by 2050. AF is a severe disease with important consequences in terms of morbidity and mortality but still under-diagnosed. Boehringer ingelheim deployed in 2013 an AF screening campaign (prof FA) among family physicians in 16 national sites with a simple questionnaire based on heartbeat measurement, AF linked symptoms and thromboembolic patient risk.

The main objective of this evaluation was to identify the most predictive factors of the disease to provide a simple tool to improve screening and diagnosis of AF in patients over 65.

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

Results: 4592 patients were screened, 585 were oriented to a cardiology specialist and 129 were diagnosed with AF. The statistical analysis was performed on the sample of oriented patients. The logistic regression model identified 3 predictive factors of AF: irregular heartbeat (OR=12.0, p<0.0001), history of stroke, transient ischemic attack or peripheral embolism (OR=2.0, p=0.07) and presence of at least 2 of the following symptoms: faintness, palpitations, chest pain and shortness of breath (OR=2.3, p=0.0008). An AF prediction based only on irregular heartbeat (1st criteria) showed a sensitivity of 74.2% and a specificity of 81.9%, its positive predictive value was 55.6%. It represents the main predictive criteria of AF.

Improving the tool by adding screening based on the presence of at least two symptoms in patients having a thromboembolic history improves sensitivity (80.0%) while maintaining good specificity (79.4%). Screening campaign showed that applying strictly those latest criteria to patients of the screened cohort could have potentially led to diagnosis of 75 additional AF. However 24 patients (all with regular heartbeats) with FA would have been missed.

Conclusion: The measurement of heartbeat is the main predictive criteria in patients over 65, as pointed in ESC 2012 guidelines, but patients with a regular heartbeat should also be considered. They should systematically be referred to a cardiologist in case of at least two symptoms and a thromboembolic history of unknown origin. The campaign underlined the difficulty to diagnose AF in patients having a regular heartbeat which should encourage systematic heartbeat measurement of AF linked symptoms in patients having a thromboembolic history. The campaign underlined the difficulty to diagnose AF in patients presenting at least two symptoms and a thromboembolism history should also be considered. They should systematically be referred to a cardiologist in case of at least two symptoms and a thromboembolic history of unknown origin. The campaign underlined the difficulty to diagnose AF in patients presenting at least two symptoms and a thromboembolism history of unknown origin. The campaign underlined the difficulty to diagnose AF in patients presenting at least two symptoms and a thromboembolism history of unknown origin. The campaign underlined the difficulty to diagnose AF in patients presenting at least two symptoms and a thromboembolism history of unknown origin. The campaign underlined the difficulty to diagnose AF in patients presenting at least two symptoms and a thromboembolism history of unknown origin.

Results: 100% (8) of the high, 84% (21) of the medium and 10% (13) of the low volume centers answered the survey. Only 44% of the professionals were aware of the recommendations made by the scientific societies, independently of the volume of implants in the center. The total number of ICDs deactivated per center was low (no center deactivated more than 5 devices in 2012). 3 Centers discuss deactivation early (before implant or during clinical visits), 17 in terminally ill patients, 7 in terminally ill with frequent shocks and 16 centers never discuss it. The patients take part in the decision in only 52% of the centers. When asked about the ideal moment to discuss deactivation possibilities 17 centers answered that it should be done early, 13 only in terminal ill patients, 9 in terminally ill patients with frequent shocks and 3 centers answered that deactivation should never be discussed.

Conclusion: Physician attitudes and real life management of terminally ill patients with an ICD differ substantially from the recommendations made by scientific societies. Implanting physicians recognize that deactivation options should be discussed earlier in the clinical history of their patients than it is nowadays done. In only 52% of the cases was the patient part of the discussion and the decision to deactivate.

Management of implantable cardioverter defibrillator on specific populations

P4878 | BEDSIDE

Influence of young age on adverse outcomes of the subcutaneous implantable cardioverter defibrillator

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Purpose: The new subcutaneous implantable cardioverter-defibrillator (S-ICD) eliminates the need for transvenous leads, and therefore has the potential to reduce long-term complications by elongating lead-lifetime, which is particularly important for young ICD patients who are at increased risk of ICD-related complications. It is however unknown whether young S-ICD patients are more at risk for short-term complications.

Methods: From the largest S-ICD implanting center worldwide, we compared ICD harm (i.e. inappropriate shocks and/or complications) in patients aged <50 years (yrs) and >50 years (yrs) in our S-ICD registry, which collects consecutive S-ICD implantation information plus follow-up data.

Results: A total of 82 S-ICD patients were included, of whom 62 were <50 yrs (53% male, age 34±10 yrs) and 20 >50 yrs (50% male, age 58±7 yrs). During a follow-up of 23±14 months 7 (11%) patients <50 yrs and 2 (10%) patients >50 yrs (p=1.00). The composite endpoint of ICD harm occurred in 12 (19%) <50 yrs and 3 (15%) >50 yrs (p=1.00). The probability of S-ICD harm at 2 years was 22% in patients <50 years and 18% in patients >50 years (figure, log-rank p=0.69).

Conclusion: In contrast to transvenous ICDs, there is no difference in the probability of short-term ICD-related harm after 2 years in S-ICD patients <50 yrs vs. >50 yrs. Therefore, the potential benefit of the S-ICD to reduce long-term complications for young patients is not overshadowed by a higher rate of short-term complications.

P4879 | BEDSIDE

Inappropriate shocks are more common in asymptomatic vs symptomatic Brugada syndrome patients implanted a cardioverter-defibrillator

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Background: Brugada syndrome (BrS) is an inherited arrhythmogenic disease characterized by a history of sudden cardiac death (SCD) particularly in young people. Implantable cardioverter-defibrillator (ICD) remains the recommended treatment for secondary prevention. Despite confident data against this approach, some asymptomatic, the so-called "high risk", patients are still being implanted an ICD, regardless of the high rate of device complications. We compared the occurrence of major complications in consecutive BrS patients implanted an ICD.

Method and results: Consecutive Patients implanted an ICD for primary or secondary prevention of BrS were studied. The diagnosis of BrS was based on...
symptoms (syncope or cardiac arrest) in conjunction with the ECG type 1 pattern, either spontaneous or unmasked by drug challenge. Per- and post-implantation complications, and ICD programming controls were recorded. All patients underwent ICD control every 6 months or less depending on device-related event. Patients or relatives were also contacted by telephone to check last news (alive or dead).

We studied 46 patients (mean age of 46.7±10.5 years, 10% of female). Spontaneous type 1 ECG pattern was found in 37 (80.4%) of patients and atrial fibrillation in 5 (10.9%). Prior to ICD implantation, No symptom, Syncope, and aborted cardiac arrest were found in 15 (32.6%), 23 (50%), and 8 (17.4%) patients respectively. During a median follow-up period of 76±41.7 months (at 1 to 192), appropriate ICD shocks occurred in 10 (21.7%) patients of whom 90% had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG, 40% had previous syncope and 60% already had spontaneous coved type ECG.

In accordance with the increasingly broader criteria for device implantation, the number of cardiac devices implanted and its associated complications increased. The risk-benefit of cardioverter-defibrillator and avoid this treatment in asymptomatic patients. Particularly in those with previous cardiac arrest. However, the high rate of device complications, mainly inappropriate therapies recommends to accurately assess the risk-benefit of cardioverter-defibrillator and avoid this treatment in asymptomatic patients.

### P4881 | BEDSIDE

**Complications 1 year after generator only and combined generator and lead replacement operations**

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**Purpose:** CIED implantations continue to rise. With an aging population, at least 1 generator replacement ± lead can be expected during their lifetime. Although considered a greater risk for revision than index implants, evidence is scant. We present complication rates for generator only (Bx) and generator+lead operations (Bx+lead).

**Methods:** Consecutive Bx and Bx+lead operations between April 2008 - March 2011, were followed for complications within 1-year. Complications recorded were: 1) any device-related return to theatre within 1 year, with 2) pneumothorax and 3) pericardial effusion additional for Bx+lead procedures. Deaths within 1 year were recorded.

**Results:** 805 Bx procedures were performed (12 AAI, 156 VVI, 484 DDD, 28 VR, 64 DR, 16 CRTD, 45 CRTD) and 111 Bx+lead (37 Bx+atrial, Bx+A; 34 Bx+ventricular, Bx+V; 5 Bx+A+V; 27 Bx+defibrillator, Bx+ICD; 1 Bx+AV+CICD; 5 Bx+coronary sinus, Bx+CS and 1 Bx+CS+ICD). Male patients constituted 55.3% Bx and 59.5% Bx+lead procedures. Median age was 76 yrs and Bx+lead 69 yrs. 4.2% Bx and 9.9% Bx+lead procedures were performed acutely. Table 1 demonstrates complications according to Bx and Bx+lead.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Bx (n=805)</th>
<th>Bx+lead (n=111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Haematoma surgical evacuation</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Retract</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Lead intervention</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Extraction</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Re-implant</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Upgrade</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>71 (8.8%)</td>
<td>31 (27.9%)</td>
</tr>
</tbody>
</table>

All Bx+lead extractions were for infection, with Bx only extractions for infection (18), a dysfunctional unit (1) and radiotherapy treatment (1). Bx+lead complications by lead intervened upon: Bx+A 48.6% (n=37), Bx+V 26.5% (n=54), Bx+A+V 20.3% (n=22), Bx+ICD 3.7% (n=27), Bx+CS 33.3% (n=36) and 0% Bx+AV+CICD (n=1) and Bx+CS+ICD (n=1).

**Conclusion:** Complication rates for Bx and Bx+lead procedures are 8.8% and 27.9%. Atrial, ventricular or atrial plus ventricular lead procedures should be considered greater risk.
Implantable defibrillator early after primary percutaneous intervention for ST-elevation myocardial infarction: the Defibrillator After Primary Angioplasty (DAPA) trial

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**Purpose:** It is not known which patients after primary Percutaneous Coronary Intervention (PCI) for ST elevation myocardial infarction (STEMI) have survival benefit of prophylactic implantable cardioverter defibrillator (ICD). The aim of the DAPA trial is to evaluate the efficacy and safety of ICD in high risk patients after primary PCI for STEMI.

**Methods:** A prospective randomized, multicenter controlled study to compare ICD plus conventional medical therapy vs. conventional medical therapy alone in patients with primary PCI for STEMI. Inclusion criteria were TIMI flow less than 3 after primary PCI or left ventricular ejection fraction lower than 30%. ICD was implanted between 30 and 60 days after the index STEMI. Primary endpoint was all-cause mortality after at least 3 years follow-up.

**Results:** Among inclusion of 266 patients, enrollment was stopped after advice of the data safety board. Mean age was 60.8 ±11.3 years, 78.2% was male. Baseline characteristics were comparable between the two treatment groups. Cross-over was 15.6% in the non-ICD group and 2.3% in the ICD group. During a median follow-up of 4.6 years (±1.7) AF patients died. ICD was associated with better in-hospital mortality and a higher proportion of all-cause mortality in patients with a high risk of death after primary PCI. ICD lowered-long term mortality. However the results of this trial should be interpreted cautiously, since the study was stopped prematurely.

**Conclusion:** The DAPA trial did not show a survival benefit of ICD in patients after primary PCI for STEMI. However, ICD was associated with better in-hospital mortality.

Clinical implication of the symptom onset in acute heart failure patients: a report from a cardiac care unit network emergency medical service database

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**Background:** Acute heart failure (AHF) is one of the frequently encountered conditions in the emergency department but little information is available in regards to the relationships between its timing, clinical background and outcomes.

**Methods:** A total of 3811 consecutive patients were admitted with AHF between 2009 and 2011 in 67 institutions in a Cardiac Care Unit Network, and registered to the on-going emergency medical service (EMS) registry. The symptom onset time was documented by the EMS team on-site and we divided the patients into two groups according to onset-to-admission (OTA) time. To define early vs. late responders to their AHF symptoms, median OTA time was used for the cutoff value. The primary outcome was all-cause mortality during hospitalization.

**Results:** The average age of registered AHF patients was 76.3 ±12.3 years, predominantly males (54.8%), and the average left ventricular ejection fraction was 43±16%. The median OTA time was two hours; between the early (<2hr) and the late (>2hr) OTA group, the early group was in worse state of respiratory and neurological condition upon presentation, demonstrated by high respiratory rate, low oxygen saturation rate, and low neurological coma scale. Overall, 242 (6.5%) patients died during their hospitalization. Despite their worse clinical profile, shorter OTA time was associated with better in-hospital mortality after adjustment for known prognostic indicators (OR, 0.71; 95% CI, 0.52 to 0.97; P=0.034).

**Conclusion:** Among patients with AHF, shorter OTA time was independently associated with better in-hospital mortality. Identification of the symptom onset may aid in triaging of the patients with AHF.
Conclusions: In NICM patients without CHF history, myocardial fibrosis is a strong and independent predictor of adverse outcome and improves risk stratification beyond clinical data and severity of LV systolic dysfunction.

P4887 | BEDSIDE
Risk factors for periodic breathing in heart failure patients with sleep apnea
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1 University Hospital Regensburg, Internal Medicine II, Regensburg, Germany; 2 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany; 3 ResMed Science Center, Martinsried, Germany; 4 Ruhrlinikum Lung Centre, Essen, Germany; 5 University Medical Center Hamburg-Eppendorf, Hamburg, Germany; 6 University Hospital Cologne, Cologne, Germany

Purpose: The presence of periodic breathing (Cheyne-Stokes respiration, CSR) in patients with congestive heart failure (CHF) is associated with poor prognosis, regardless whether it occurs during day time or at night time during sleep. The aim of the present study was to determine the risk factors for night time CSR in a population of CHF patients with sleep apnea (SA).

Methods: The ongoing multi-center SchlafH-registry included prospectively 8341 CHF patients (New York Heart Association (NYHA) class ≥ II and left-ventricular ejection fraction (LVEF) ≤ 45%) from cardiology practices and departments of hospitals. Patients were studied with a two-channel screening device (nasal airflow, pulse oximetry; ApneaLink, ResMed, Sydney, Australia) that detects CSR based on an algorithm using pattern recognition. Patients with suspected SA received full in-laboratory polysomnography with certified scoring.

Results: Of 1144 CHF patients with sleep apnea (Apnea-Hypopnea Index ≤ 15/hour of sleep) 784 (69%) had CSR. CHF patients with SA and CSR were significantly older (69.1 ± 10 vs 65.1 ± 11), had lower LVEF (33.8 ± 8 vs 36.8%) and arteriocapillary PaCO2 values (37.1 ± 4.5 vs 38.8 ± 1.4 mmHg, p < 0.05 for all comparisons) compared to those without CSR. In a multivariable regression model age (odds ratio, OR [95% confidence interval, CI]: 1.40 [1.22; 1.61] per 10 years) and male gender (OR, [95% CI]: 2.01 [1.37; 2.93], LVEF (OR, [95% CI]: 1.21 [1.11; 1.32] per 5% decrease), atrial fibrillation (OR, [95% CI]: 2.03 [1.47; 2.80]) and PaCO2 (OR, [95% CI]: 0.95 [0.92; 0.98]) were independent risk factors for CSR. Symptoms of CHF such as NYHA class III, nocturnal dyspnea and nocturia as well as body mass index were not significantly associated with CSR.

Conclusion: In contrast to symptoms of CHF, age, male gender, impaired cardiac function, atrial fibrillation and low PaCO2 are independent risk factors for the occurrence of night-time CSR in CHF patients with SA.

Acknowledgement: This study was sponsored by ResMed Germany Inc.

P4888 | BEDSIDE
C-reactive protein and NT-proBNP for predicting mortality in patients with heart failure with preserved ejection fraction
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1Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; 2University Medical Centre of Mannheim, Mannheim, Germany; 3Medical University of Graz, Graz, Austria; 4Bern University Hospital, Bern, Switzerland

Aims: Heart failure (HF) with preserved ejection fraction (HFpEF) has a distinct pathophysiological background but a mortality rate comparable to HF with reduced ejection fraction. Consequently, tailored risk prediction in these separate groups of HF is of major importance. Inflammation may play an important pathogenetic role in HFpEF due to its significant contribution to myocardial fibrosis. We therefore aimed to assess the predictive value of C-reactive protein (CRP) in patients with HFpEF with a particular focus on the prognostic gain in relation to N-terminal pro-B-type natriuretic peptide (NT-proBNP).

Methods: CRP plasma levels were determined in 459 patients (age: 67.9 [60.6 - 73.3] years, 63.4% male) with HFpEF in the Ludwigsrainer and Cardiovascular Health (LURIC) study using a high-sensitivity assay. All patients were in a stable condition and diagnosis of HFpEF was based on current recommendations of the Heart Failure and Echocardiography Associations of the European Society of Cardiology.

Results: During a median follow-up of 9.7 years 40 percent (n=184) of these patients died. The corresponding 5-year mortality rate was 18% (n=82). CRP predicted all-cause mortality with an adjusted hazard ratio (HR) of 1.20 (95% CI: 1.02-1.40, P=0.018) and cardiovascular mortality with an adjusted HR of 1.32 (95% CI: 1.08-1.62, P=0.005) per increase of one standard deviation. Accordingly, stratification into tertiles of CRP showed a significant association with all-cause mortality with an adjusted HR of 1.83 (95% CI: 1.23 - 2.72, P=0.002) for the third tertile compared to the first tertile and with cardiovascular mortality with an adjusted HR of 2.21 (95% CI: 1.33 - 3.66, P=0.002) for the third tertile compared to the first tertile. CRP was a significantly stronger mortality predictor in patients enrolled in a control group of HF patients with reduced ejection fraction (interaction, P=0.015). Furthermore, CRP added prognostic value to NT-proBNP: the lowest 5-year mortality rate of 6.8% was observed for patients in the lowest tertile of NT-proBNP as well as CRP. The mortality risk peaked in the group combining the highest values of NT-proBNP and CRP with a 5-year rate of 36.5%.

Conclusion: CRP turned out to be a strong, specific and independent predictor of mortality in HFpEF, but not in HFpEF, possibly pointing to immunologic processes with adverse impact on the course of HFpEF.

P4889 | BEDSIDE
Abnormal iron status is a key determinant of symptoms and submaximal exercise capacity in chronic heart failure patients
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Purpose: Iron deficiency (ID) is associated with impaired peak VO2 exercise capacity, worse quality of life and poorer outcomes. The influence of impaired iron status on submaximal exercise capacity (SEC) has not been explored in chronic heart failure (CHF). This study was designed to evaluate the effect of ID and anemia on SEC measured with the 6 minute walk test (6MWT) in CHF patients.

Methods: 538 consecutive CHF stable patients with either preserved or reduced LVEF were included. At inclusion, clinical variables were recorded and blood samples were obtained for evaluation of iron status. SEC was evaluated with the 6MWT. Symptoms presented during the test were also recorded. Anemia was defined as haemoglobin <12 g/dL in women and <13 g/dL in men. ID was defined as ferritin <100 ng/mL or % transferrin saturation (TSAT) <20%. As an additional marker of ID, the sTfR (serum soluble transferrin receptor) was evaluated.

Results: Baseline characteristics were: Mean age 71±11 years, 38% were female. 32% were in NYHA class III-IV, nearly half of the patients had preserved LVEF, 61% had ID and 45% had anemia. In univariate unadjusted analysis, patients with ID had a reduced SEC compared to non-ID patients (291±104 meters vs 322±113, respectively; p=0.002). Symptoms during the test were more frequent in ID patients (35% vs 27%; p=0.028) and the most common symptom reported was fatigue. In adjusted multivariable analysis (GAM models, see figure), abnormal iron status but not Hb was significantly associated with impaired SEC.

Conclusion: In CHF ID but not anaemia is associated with impaired submaximal exercise capacity measured with 6MWT.

P4890 | BEDSIDE
Myocardial infarction, stroke or hospitalization for worsening heart failure: which event has the greatest prognostic significance in patients with heart failure?
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Background: The prognostic significance of worsening heart failure hospitalization (WHF) has never been compared to that of myocardial infarction (MI) or stroke in patients with chronic heart failure (HF).

Methods: We studied 4,128 patients with HF and preserved ejection fraction (HF-PEF) in the Irbesartan in Heart Failure with Preserved systolic function trial (I-Preserve; mean age 73 years; 24% women; median follow-up 4.8 years, 24% women; median follow-up 4.8 years). Rates per 100 person-years (py) and hazard ratios (HR) for death were estimated for 0-30 days and ≥30 days after first WHF, MI or stroke hospitalization.

Results: During a median follow-up of 9.7 years 40 percent (n=184) of these patients died. The corresponding 5-year mortality rate was 18% (n=82). CRP predicted all-cause mortality with an adjusted hazard ratio (HR) of 1.20 (95% CI: 1.02-1.40, P=0.018) and cardiovascular mortality with an adjusted HR of 1.32 (95% CI: 1.08-1.62, P=0.005) per increase of one standard deviation. Accordingly, stratification into tertiles of CRP showed a significant association with all-cause mortality with an adjusted HR of 1.83 (95% CI: 1.23 - 2.72, P=0.002) for the third tertile compared to the first tertile and with cardiovascular mortality with an adjusted HR of 2.21 (95% CI: 1.33 - 3.66, P=0.002) for the third tertile compared to the first tertile. CRP was a significantly stronger mortality predictor in patients enrolled in a control group of HF patients with reduced ejection fraction (interaction, P=0.015). Furthermore, CRP added prognostic value to NT-proBNP: the lowest 5-year mortality rate of 6.8% was observed for patients in the lowest tertile of NT-proBNP as well as CRP. The mortality risk peaked in the group combining the highest values of NT-proBNP and CRP with a 5-year rate of 36.5%.

Conclusion: CRP turned out to be a strong, specific and independent predictor of mortality in HFpEF, but not in HFpEF, possibly pointing to immunologic processes with adverse impact on the course of HFpEF.
Mortality after event of worsening heart failure (WHF), myocardial infarction (MI) or stroke, in patients with HF-PEF (I-Preserve) or HF-REF (CORONA)

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Day 0–30</th>
<th>Day 31–</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of deaths per 100 py</td>
<td>HR (95% CI)</td>
<td>No. of deaths per 100 py</td>
</tr>
<tr>
<td>I-Preserve</td>
<td>No. event</td>
<td>3,233</td>
</tr>
<tr>
<td>WHF</td>
<td>632</td>
<td>76</td>
</tr>
<tr>
<td>MI</td>
<td>111</td>
<td>21</td>
</tr>
<tr>
<td>Stroke</td>
<td>147</td>
<td>34</td>
</tr>
<tr>
<td>CORONA</td>
<td>No. event</td>
<td>3,410</td>
</tr>
<tr>
<td>WHF</td>
<td>1,222</td>
<td>111</td>
</tr>
<tr>
<td>MI</td>
<td>216</td>
<td>38</td>
</tr>
<tr>
<td>Stroke</td>
<td>163</td>
<td>43</td>
</tr>
</tbody>
</table>

**Conclusion:** Compared with WHF, MI and stroke are associated with a very high early mortality; thereafter all three events are associated with a similar increase in risk of death.

### THROMBOSIS AND BLEEDING IN VALVE DISEASE

#### P4891 | BEDSIDE

Prosthetic valve thrombosis: about 159 patients


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**Background:** The prosthetic heart valve thrombosis (PVT) is a life threatening complication of mechanical valve prosthesis.

In the aortic and mitral position reported incidence varies from 0.5% to 6% per patient-year, and is highest in the mitral position and up to 20% in tricuspid valve replacement. Medical therapy has emerged as an alternative therapy in high-risk surgical patients, considering that surgical prosthetic valve replacement is related to significant operative morbidity and mortality rates.

**Methods:** From 2000 to 2013, 159 patients were hospitalized in our center for mechanical prosthetic valve thrombosis (PVT). The diagnosis of PVT was mainly assessed by echocardiography and/or fluoroscopy. There were 30 men and 129 women aged 15–75 years. Prosthetic valve location was mitral in 153 patients, tricuspid in 03 and aortic in 3. Predisposing causes of MVT were: poor compliance with warfarin, pregnancy or unknown.

The interval from first operation to PVT was from 1 day to 38 years. Delay from first symptoms to hospitalization ranged from 1 to 4 months.

**Results:** The diagnosis was an incidental finding (echocardiographic: increase in the transvalvular gradient); First clinical symptoms were: systemic embolism, progressive exertional dyspnea (NYHA II to III–IV), muffled opening or closing sounds of the prosthetic valve; left heart failure, stroke, and cardiogenic shock.

**Conclusion:** PVT is a life threatening complication of mechanical heart valve prosthesis with high morbidity and mortality despite aggressive treatment by thrombolysis and/or surgery. Treatment should be the preferred therapeutic modalities for most patients with PVT. Thrombolysis, followed by heparin, warfarin, and aspirin, is advised in high-risk surgical candidates without hemodynamic instability under strict echocardiographic surveillance.

#### P4892 | BEDSIDE

Presentation, management and outcome of heparin induced thrombocytopenia after heart valve surgery - a single center experience


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**Purpose:** Use of unfractionated heparin (UFH) exposes patients to heparin-induced thrombocytopenia (HIT) which is a challenging issue both for diagnosis and treatment of patients after heart surgery. In this study, we seek to describe the clinical and biological presentations, the management and the outcome of a large series of patients with a confirmed diagnosis of HIT in the setting of valvular heart surgery.

**Methods:** All patients who underwent valvular heart surgery at our institution from January 2007 to April 2013 were prospectively identified and included in a single-center registry. Clinical and biological data were screened in order to select patients with a confirmed diagnosis of HIT. Serologestic testing for PF4-heparin antibodies and a platelet aggregation test were performed in all patients. The gold standard test for the diagnosis of HIT was the serotonin release assay. In-hospital and long-term outcomes were assessed.

**Results:** We identified 100 patients during this 76-month period. Mean age was 63±16 years. 48% of female patients. Aortic valve replacement was performed in 72 cases, mitral valve replacement in 31 cases, tricuspid valve replacement in 1 case and mitral valve plasty in 10 cases. The mean time to diagnosis from surgery was 9±3 days. A majority of patients (83) were asymptomatic with only isolated thrombocytopenia at the time of diagnosis. A fall in platelet count >50% was observed in 67 cases. In-hospital diagnosis circumstances or complications were arteriovenous thromboembolic events reported in 10 cases (6 cases of acute ischemic stroke), left atrial thrombus in 7 cases, prosthetic valve thrombosis in 10 patients including 1 case of valve obstruction; dermatologic manifestations in 3 cases. UFH was immediately stopped in all cases followed the introduction of danaparoid sodium (97). Anti-aggregation therapy was associated in 6 cases. No thrombotic therapy, interventional radiology procedure, secondary surgery, intravenous immunoglobulin or plasmapheresis were performed. Mean follow-up time was 38 months during which only 4 patients died (cardiac death=1) including in 30 days. Risk of thromboembolic events were seen in only 5 cases following hospital discharge.

**Conclusions:** To our knowledge this is the largest series of patients with a confirmed diagnosis of HIT occurring in the setting of valvular heart surgery. The incidence of HIT was low as well as the proportion of thromboembolic events. Persistent thrombocytopenia was the most frequent presentation. Early diagnosis and prompt treatment are associated with good in-hospital and long-term outcomes.

**P4893 | SPOTLIGHT**

The role of anti-¨a antibodies in patients with prosthetic heart valve thrombus thrombolysed with recombinant tissue-type plasminogen activator (r-Pa)

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**Purpose:** Thrombolytic therapy (TT) is effective for the treatment of prosthetic heart valve thrombosis (PVT). Due to its high fibrin specificity recombinant tissue-type plasminogen activator (r-Pa) is widely used in the management of PVT. Infusion of r-Pa may induce the production of antibodies. In this study, we aimed to evaluate the relationship between anti-r-Pa antibody (ATA) levels and presence of thrombus (THR), responsiveness to TT with r-Pa and development of rethrombosis in patients with prosthetic heart valves.

**Methods:** The study is designed as double blind fashion in 2 centers (Turkey,Italy). In order to detect ATA, plasma samples were collected from 28 PVT patients at baseline and then 15, 30, 45, 90 and 180 days after TT and from 31 controls at baseline only. ATA levels were assayed in human plasma by an enzyme-linked immunosorbent assay that uses r-Pa for capture and mouse monoclonal anti-human immunoglobulin G (IgG) or M (IgM) followed by peroxidase-conjugated anti-mouse immunoglobulin antibodies for detection.

**Results:** There was a significant difference in median levels of ATA between the PVT patients before TT and controls in terms of IgG and IgM (17.88±24.7 vs 3.33±3.48, p:0.005 for IgG and 30.32±22.97 vs 15.78±14.03, p:0.01 for IgM). IgM levels peaked 15 days and IgG levels peaked one month after r-Pa infusion. TT failed in 6 patients (21%) and rethrombosis occurred in 9 patients (32%). In failed TT group baseline IgM levels were significantly higher compared to successful TT group (50.46±34.58 vs 24.28±14.59, p:0.023). In rethrombosis group baseline IgG levels were significantly higher than the remaining PVT patients (30.20±32.79 vs 8.01±12.01, p:0.019). Baseline IgG level of > 3.7 yielded an area under the curve value of 0.780 (95% confidence interval 0.597 to 0.963), sensitivity 80%, specificity 60%, p:0.02 for rthrombosis and baseline IgM level of > 3.4 yielded an area under the curve value of 0.808 (95% confidence interval 0.643 to 0.974, sensitivity 83%, specificity 75%, p:0.024) for TT. Also there is a moderate positive correlation between the baseline IgM levels and the dose of r-Pa (r=-0.466, p=0.038) in successful TT group.

**Conclusion:** Native ATA may act in vivo as inhibitors of r-Pa function. Patients with abnormally high levels of ATA may have an additional risk for THR formation, responsiveness to TT with r-Pa and development of rethrombosis. Furthermore, the infusion of r-Pa may trigger the production of specific antibodies that bind to r-Pa, thus potentially may reduce its function and may participate in the hypofibrinolytic status.
**P4894 | BEDSIDE**

Impact of pre- and post-procedural anemia on incidence of acute kidney injury and 1-year mortality after transcatheter aortic valve implantation. Insights from the FRANCE 2 Registry

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**Background:** Among patients with cardiovascular disease, anemia and renal insufficiency have been reported to influence each other negatively. However, how anemia affects the renal function and outcomes after TAVI has not been adequately elucidated. Thus, the aim of this study is to evaluate the influence of pre- and post-procedural anemia on the incidence of renal insufficiency, especially AKI, and outcomes in patients undergoing TAVI.

**Methods and results:** Data from the French national TAVI registry were collected for 3,472 patients who underwent TAVI between January 2010 and December 2012. Of 3,472 patients, 2,137 were in the normoanemia group, 748 were in the moderate anemia group, and 587 were in the severe anemia group before TAVI. Increased anemia severity before TAVI was associated with significantly different rates of 1-year mortality (15%, 19% and 24%, p < 0.01). The incidence of AKI was significantly higher in the moderate and severe anemia groups (5%, 8% and 10%, p < 0.01). Furthermore, we divided 3,472 patients into 3 groups according to post-procedural anemia, as measured by a drop in hemoglobin (Hb) levels after a procedure: < -2 g/dl (n=1633, group 1), 2 to < -4 g/dl (n=1548, group 2), and < -4 g/dl (n=381, group 3). Higher rate of Hb drop was associated with significantly different rates of 1-year mortality (16%, 18% and 23%, p < 0.01), with similar differences in the incidence of AKI (6%, 7% and 10%, p < 0.04). After adjustment for significant influential confounders in logistic regression multivariate model, both pre-procedural anemia and post-procedural Hb drop were associated with an increased risk of 1-year mortality (HR 1.38, 95%CI: 1.23-1.56, p < 0.01; HR 1.81, 95%CI: 1.44-2.28, p < 0.01, respectively). After adjustment for significant influential confounders in COX-regression multivariate model, both pre-procedural anemia and post-procedural Hb drop were associated with an increased risk of 1-year mortality (HR 1.38, 95%CI: 1.23-1.56, p < 0.01; HR 1.45, 95%CI: 1.26-1.67, p < 0.01, respectively).

**Conclusions:** Both pre- and post-procedural anemia was significantly associated with the incidence of AKI and 1-year mortality.

**P4895 | BENCH**

In-vitro comparison of danaparoid, unfractionated heparin and enoxaparin in preventing thrombus formation on mechanical heart valves

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¹Martin Luther University of Halle-Wittenberg, Department of Cardiology, Halle, Germany; ²Central hospital of the Federal Armed Forces in Koblenz, Koblenz, Germany; ³St. Marien-Hospital Siegen, Cardiology, Siegen, Germany.

**Purpose:** Periprocedural switching from oral to parenteral anticoagulants in patients after mechanical heart valve replacement is challenging, especially in patients suffering from HIT - is as efficacious as unfractionated heparin and enoxaparin in preventing thrombus formation on mechanical heart valves.

**Methods:** Blood samples (250 ml) from healthy male volunteers were treated with either UFH 0.9 IU/ml, enoxaparin 0.6 IU/ml, or danaparoid 0.8 IU/ml (n=10, each). Bileaflet mechanical heart valves were placed in an in-vitro device (THAII, Thrombotester) allowing exposure to anticoagulated blood samples under pulsatile circulation conditions at 60 beats per minute for a total exposure time of 60 min.

**Results:** Levels of anagtoprotein were proven to be at therapeutic range by measuring activated clotting times (ACT) for UFH, and mean anti-FXa-activities in porcine valve prosthesis (2.1%) 354 ± 253 days postoperatively, whereas none was observed in pericardial valves (p < 0.001). However, recently considerably higher rates have been reported with a frequent necessity of reapreresistors.

**Patients and methods:** All patients who received a single stented bioprosthetic valve in the aortic position at our institution between 2007 and 2012 were included in the analysis. We investigated clinical, procedural, and follow-up data with the aim to identify the incidence, potential risk-factors and clinical course of patients with obstructive valve thrombosis in aortic position.

**Results:** 1751 patients (75±9 years) required a single stented aortic bioprosthetic valve, 29% in combination with bypass surgery. Four types of pericardial prostheses were implanted in 1003 patients and two types of porcine prostheses in 748 patients. Sixteen patients with obstructive thrombosis were identified in porcine valve prosthesis (2.1%) 354 ± 253 days postoperatively, whereas none was observed in pericardial valves (p < 0.001). Two unstable patients (12%) required reoperation; the remaining fourteen could be successfully treated with platelet aggregation inhibitors. Risk for obstructive thrombosis was 4 times higher [95% CI 2.7-7.3] in porcine compared to pericardial prosthesis. The presence of this bioprostheses was identified as a strong and independent predictor of obstructive thrombosis in a multivariate model including clinical, procedural and postoperative echocardiographic parameters.

**Conclusion:** Obstructive thrombosis of stented bioprostheses in the aortic valve position seems to be restricted to porcine valves and occurs in about 2% of the patients with this type of prosthesis.
CHEST PAIN ASSESSMENT IN THE EMERGENCY DEPARTMENT

P4898 | BEDSIDE
Heart rate at admission is a predictor of in-hospital mortality in patients with acute coronary syndromes - results from 58 European hospitals - the EURHOBOP study

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Purpose: Heart rate is a fundamental clinical parameter and may have prognostic importance in the acute setting. Heart rate at admission and in-hospital mortality in patients with acute coronary syndromes (ACS) was investigated.

Methods: Consecutive ACS patients admitted 2008-2010 across 58 hospitals in six participant countries of the EURHOBOP collaboration (Finland, France, Germany, Greece, Portugal and Spain). Associations between heart rate at admission and in-hospital mortality were estimated by logistic regression models adjusting for cardiovascular risk factors, including known heart failure, kidney disease, previous stroke, and ischemic heart disease. Cardiogenic shock patients were excluded.

Results: A total of 10374 patients were included; 6366 with non-ST-elevation ACS (NSTE-ACS) and 3209 with ST-elevation myocardial infarction (STEMI). For both NSTE-ACS and STEMI patients a U-shaped relationship between admission heart rate and mortality was found (Figure). For NSTE-ACS, an admission heart rate of 60-69 was associated with the lowest risk; a heart rate <40 bpm was associated with a 11-fold increased risk and heart rate categories above 80 bpm with a 3.8 to 8.8-fold increased risk of mortality. The relationship persisted in the multivariable models. For STEMI patients, heart rates between 70-79 bpm were associated with the lowest risk, and a heart rate <40 bpm was associated with a 4.3-fold increased risk and above 80 bpm with 2.2 to 5.3-fold increased risk of mortality (Figure). In the adjusted model heart rates above 80 bpm remained associated with increased risk.

Admission heart rate and mortality.

Conclusion: Heart rate at admission is a very powerful predictor of in-hospital mortality in patients with ACS. ACS patients with admission heart rate above 80 bpm or bradycardia should receive particular attention.

P4899 | BENCH
A novel electrocardiographic biomarker for prediction of inhospital mortality in the medical emergency department

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Purpose: Cardiac autonomic function may yield important prognostic information in emergency patients but is currently not used for clinical decision making. Here, we propose a novel electrocardiographic marker for automated short-term assessment of cardiac autonomic function.

Methods: The method was developed in 700 patients admitted to the medical emergency department (ED) of a large university hospital (training sample) and validated in 5,030 patients (validation sample). Cardiac autonomic function was assessed by means of a modified version of deceleration capacity (DC) of heart rate from routine monitors within the first minutes after ED admission. The developed algorithm allows a fully automatic DC assessment without manual intervention. Primary endpoint was inhospital and 10-day mortality. Multivariate analyses revealed that the predictive value of DC was dependent on physiological parameters, the APACHE II score and biochemical markers.

ROC curve (primary EP).

Conclusions: DC is a strong and independent predictor of short-term mortality among unselected patients of a medical ED that rapidly identifies low risk patients.

P4900 | SPOTLIGHT
Efficacy of nurse-led chest pain assessment within the emergency department

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Our heart centre provides 24/7 Acute Coronary Syndrome (ACS) services including Primary Percutaneous Coronary Angioplasty (PPCI) for a population of approximately 850K people. To support our services we have developed a team of nurse practitioners (NPs) who undertake roles that have been historically delivered by medical staffs for example: first contact in the Emergency Department (ED) and chest pain/arrythmia and heart failure clinics. The advantage of NPs is that once trained the department has a cohort of “middle grade” equivalent staff who are able to deliver sustainable robust services with an focus on evidenced based practice and individualised patient care that are less subject to whims of the labour market and training rotations. This paper discusses our experience in developing this service and how our service could be replicated in other institutions. In the past 2 years the NP’s have reviewed n=5,496 “all comers” chest pain patients in the ED. Of this cohort 58% were discharged within the UK target of 4-hours. Of the admitted patients, 58% were diagnosed as having ACS by a consultant cardiologist. We undertook a retrospective randomised audit of the same patient population who had been seen by ED “middle grade” (registrars and associate specialist) doctors for comparison. Data showed the NP’s were less likely to admit (42% vs. 82%) and were more likely to correctly identify ischemic patients (58% vs. 7%) when the differential diagnosis was confirmed by a consultant cardiologist. A concern raised was that the NP’s were “over discharging” inappropriate patients. N=2,673 patients were followed up for 30-days post discharge. Of this cohort there were no unexpected deaths and 0.19% re-attended our ED with a confirmed ACS. This data compares favourably with published trial and registry data. Patient Reported Outcome Measures (PROMS) consistently show high patient satisfaction with the service and the quality of care provided. To conclude, appropriate trained NPs can provide safe, robust and patient centred chest pain services in the ED and offer a practical alternative to locum/ staff grade doctors in service delivery in acute cardiac care.

P4901 | BEDSIDE
Comparison of exercise electrocardiography and exercise echocardiography for the prediction of outcome in patients referred to a chest pain unit


Purpose: To assess the relative value of exercise electrocardiography (ExECG) and exercise echocardiography (ExEcho) for predicting outcome in patients referred to a chest pain unit for acute chest pain, nondiagnostic electrocardiograms (ECGs) and negative troponin levels.

Methods: ExECG and ExEcho were performed in parallel in 1172 patients with non-traumatic acute chest pain suspected of having an ischemic origin, who had nondiagnostic but interpretable baseline ECGs and negative troponin levels. Patients with repolarization abnormalities precluding a proper interpretation of ExECG were not included. A positive ExECG was defined as the development of ST-segment deviation of ≥ 1 mm which was horizontal or sloping away from the isoelectric line 80 ms after the J point. A positive ExEcho was defined as the demonstration of echocardiographic ischemia, i.e., the appearance of new or worsening wall motion abnormalities with exercise. The tests were considered negative in the absence of exercise-induced abnormalities at >85% of maximum age-predicted heart rate. Otherwise, the tests were considered inconclusive. The
primary endpoint was a composite of cardiac death, nonfatal myocardial infarction or coronary revascularization at 6 months.

Results: The primary endpoint occurred in 4/680 patients (0.6%) with both negative ExECG and ExEcho, 4/66 patients (6.1%) with positive ExECG and negative ExEcho, 69/160 patients (43.1%) with negative ExECG and positive ExEcho, 110/167 patients (65.9%) with both positive ExECG and ExEcho, and 9/19 patients (6.7%) with inconclusive results. The C-index for predicting the primary endpoint of a model based on clinical and resting echocardiographic data (sex, age, cardiovascular risk factors, history of myocardial infarction, prior coronary revascularization, typical angina and resting left ventricular ejection fraction) was 0.679. The sequential addition of ExECG data (exercise-induced chest pain, ischemic ECG changes, exercise workload and rate pressure-product) and ExEcho data (echocardiographic ischemia) significantly increased the C-statistic of the model to 0.876 and 0.942, respectively (p = 0.001 for both steps).

Conclusion: ExEcho provides significant incremental prognostic information for the prediction of cardiac events over clinical, resting echocardiographic and ExECG data in patients referred to a chest pain unit for acute chest pain, nondiagnostic ECGs and normal troponin levels.

P4902 | BENCH

Frequency and prognosis of unstable angina pectoris in the era of the universal definition: a clinical cohort study

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Purpose: To assess the frequency and prognosis of pts with unstable angina pectoris (UAP) in the era of the universal definition of myocardial infarction (MI).

Methods: During a one-year period we prospectively studied unselected pts admitted to a university hospital. All pts having troponin I (cTnI) measured because of a suspected acute coronary syndrome were included. cTnI was analyzed on an Architect c16000, and a value >30 ng/l was considered the decision limit for the diagnosis of a myocardial infarction (MI). UAP was defined as unstable chest discomfort (rest, new onset, or worsening of angina) and dynamic ECG changes. In UAP pts cTnI was <30 ng/l. The MI diagnosis was according to the universal definition, and pts were classified as ST-elevation MI (STEMI) or non-ST-elevation MI (NSTEMI). Follow-up was at least one year with all-cause mortality as the clinical end-point.

Results: From January 2010 to January 2011 a total of 3762 pts were considered. 516 pts had acute coronary syndrome. UAP was present in 37 (7%), STEMI in 133 (26%), and NSTEMI in 346 pts (67%). The mean age (±SD) differed significantly between the three subgroups: UAP 66±13, STEMI 68±14 and NSTEMI 72±13 yrs (p<0.0005). During a median follow-up of 2.1 years 153 pts died, and the mortality rates were: UAP 8%, STEMI 20%, and NSTEMI 36% (p<0.0001; figure).

Conclusion: In the second decade of the new millenium UAP is present in less than 10% of pts with acute coronary syndrome. The long-term prognosis in these UAP pts appears to have improved with an annual mortality rate of 4%. The reason for the reduced UAP frequency is most likely multifactorial including the advent of more sensitive troponin assays and the introduction of the universal definition of MI.

P4903 | BEDSIDE

New left bundle branch block and acute myocardial infarction revisited: insights from a multicentre diagnostic study

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Purpose: The recent introduction of more sensitive cardiac troponin assays 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 cardiac troponins (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 Roche high-sensitivity (hs) cTnT assays in 2813 consecutive patients presenting to the emergency department with symptoms suggestive of AMI, of whom 447 (16%) 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 diagnostic accuracy was further compared to a standard cTn assay (Roche Troponin T fourth generation). The final diagnosis was adjudicated by two independent cardiologists based on hs-cTnT using all available data.

Results: AMI was the final diagnosis in 36% (n=160) of all KD-patients as compared to 18% in patients with normal kidney function (p<0.001). Among KD-patients with other diagnoses than AMI, baseline hs-cTnT-Lvls were elevated above the 99thpercentile in 68%. In patients with KD the diagnostic accuracy at presentation, quantified by the area under the receiver-operator-characteristic curve (AUC), was significantly greater for hs-cTnT as compared to the standard assay (AUC for hs-cTnT, 0.87 vs. AUC for the standard assay, 0.82, p=0.001). In patients presenting within three hours after the onset of chest pain, hs-cTnT remained superior compared to the conventional cTnT (AUC 0.82 vs. 0.72, p<0.001). In patients with KD, the optimal hs-cTnT cutoff derived from the hs-cTnT data was 29.5 ng/l compared to 16 ng/l in patients with normal kidney function (official 99th percentile cutoff-value 14 ng/l).

Conclusions: The investigated hs-cTnT assay has a high diagnostic accuracy among KD-patients and is superior to conventional cTn assays. High cTn levels are common in non-KD patients. However, the test-specific optimal cutoff-level in KD-patients seems to be nearly twice as high as the standard 99th percentile level.

ClinicalTrials.gov number, NCT00470587

FRACTIONAL FLOW RESERVE: OBJECTIVE MEASUREMENT

P4904 | BEDSIDE

Optimal cutoff-values of roche high-sensitivity cardiac troponin T in patients with kidney disease for the early diagnosis of acute myocardial infarction

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Purpose: The recent introduction of more sensitive cardiac troponin assays 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 cardiac troponins (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 Roche high-sensitivity (hs) cTnT assays in 2813 consecutive patients presenting to the emergency department with symptoms suggestive of AMI, of whom 447 (16%) 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 diagnostic accuracy was further compared to a standard cTn assay (Roche Troponin T fourth generation). The final diagnosis was adjudicated by two independent cardiologists based on hs-cTnT using all available data.

Results: AMI was the final diagnosis in 36% (n=160) of all KD-patients as compared to 18% in patients with normal kidney function (p<0.001). Among KD-patients with other diagnoses than AMI, baseline hs-cTnT-Lvls were elevated above the 99thpercentile in 68%. In patients with KD the diagnostic accuracy at presentation, quantified by the area under the receiver-operator-characteristic curve (AUC), was significantly greater for hs-cTnT as compared to the standard assay (AUC for hs-cTnT, 0.87 vs. AUC for the standard assay, 0.82, p=0.001). In patients presenting within three hours after the onset of chest pain, hs-cTnT remained superior compared to the conventional cTnT (AUC 0.82 vs. 0.72, p<0.001). In patients with KD, the optimal hs-cTnT cutoff derived from the hs-cTnT data was 29.5 ng/l compared to 16 ng/l in patients with normal kidney function (official 99th percentile cutoff-value 14 ng/l).

Conclusions: The investigated hs-cTnT assay has a high diagnostic accuracy among KD-patients and is superior to conventional cTn assays. High cTn levels are common in non-KD patients. However, the test-specific optimal cutoff-level in KD-patients seems to be nearly twice as high as the standard 99th percentile level.

ClinicalTrials.gov number, NCT00470587
Contribution. In the 255 remaining target vessels, target vessel HMR was stratified in a low, intermediate, and high HMR group according to reference vessel HMR tertiles.

The magnitude of HMR modulated the relationship between FFR and HSR, illustrated by the difference in regression slopes across the HMR groups (−1.99 (95% CI: −2.21 to −1.78), −2.84 (95% CI: −2.97 to −2.71), and −5.39 (95% CI: −6.04 to −4.74) for low, intermediate, and high HMR, respectively; overall p < 0.001). For a given stenosis severity, characterized by a narrow range of HSR, FFR increased with increasing HMR (Fig. 1). The correlation between FFR and HSR (r=0.54, p < 0.001) improved substantially after adjustment for HMR (HMR-adjusted partial correlation r=0.73, p < 0.001).

Conclusions: Identification of epicardial disease severity by FFR is obscured by the magnitude of coronary microvascular resistance. Appropriate interpretation of FFR requires information on microvascular status, which illustrates the necessity of combined pressure and flow measurements in daily practice.

P4907 | BEDSIDE
The ischemia-inducing potential of FFR-positive coronary stenosis of intermediate severity is dictated by the combination of epicardial and microvascular resistance
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Purpose: Fractional flow reserve (FFR) is considered to be a stenosis-specific index. However, microvascular disease contributes to the occurrence of myocardial ischemia, and FFR values may be obscured by such microvascular involvement. We documented the impact of hyperaemic microvascular resistance (HMR) and hyperaemic stenosis resistance (HSR) on the FFR-guided identification of inducible myocardial ischemia.

Methods: We assessed 299 target vessels by means of intracoronary pressure and flow measurements to determine FFR, HSR, and HMR. Myocardial perfusion scintigraphy (MPS) was used to identify inducible myocardial ischemia. In 178 patients, HMR was also measured in a reference coronary artery. A total of 44 vessels with FFR ≥0.6 were excluded because of the potential neglection of collateral flow contribution. In the remaining 255 target vessels, FFR was stratified in a low, intermediate, and high HMR group according to reference vessel HMR tertiles.

Results: Among 111 stenoses with a positive FFR (FFR >0.80), FFR was equivalent across the HMR groups: median FFR was 0.74 (0.69–0.78), 0.74 (0.70–0.77), and 0.73 (0.69–0.78) for low, intermediate, and high HMR, respectively (p=0.94). Despite equivalent FFR across groups, the prevalence of ischemia was significantly higher when HMR was high (Figure 1: p<0.05 for all comparisons), which was paralleled by a concomitant significant increase in HSR: median HSR was 0.44 (0.34–0.61), 0.70 (0.57–0.81), and 1.04 (0.80–1.50) for low, intermediate, and high HMR, respectively (p<0.001).

Conclusion: The ischemia-generating potential of FFR-positive stenoses is dictated by the extent of epicardial and microvascular resistance to coronary blood flow, which may not be adequately reflected in the stenosis significance as assessed by FFR.

P4906 | BEDSIDE
Coronary flow velocity reserve is an independent predictor of 10-year major adverse cardiac events after deferral of revascularization in patients with stable coronary artery disease

Purpose: Coronary flow velocity reserve (CFVR) is a combined marker of epicardial and microvascular disease. As microvascular involvement in ischemic heart disease is increasingly recognized as a contributor to adverse outcome, CFVR may provide additional prognostic information over specific markers of epicardial disease, such as hyperemic stenosis resistance (HSR) or fractional flow reserve (FFR). Therefore, we evaluated the independent prognostic value of CFVR for long-term clinical outcome in patients with stable coronary artery disease.

Methods: Between April 1997 and September 2006, revascularization was deferred in 157 patients with 186 intermediate stenoses studied with intracoronary pressure and flow measurements. CFVR <2.0 was considered abnormal. In the presence of multi-vessel disease, one of the vessels was randomly selected for subsequent analyses. Ten-year major adverse cardiac event rates (MACE) were estimated with the Kaplan Meier method, and compared with the log rank test. The independent prognostic value of CFVR for long-term MACE was assessed by multivariate Cox regression.

Results: Median follow-up was 11.7 years (Q1, Q3: 9.9, 13.3). CFVR <2.0 was associated with significantly higher 10-year MACE (32.9% vs. 63.1%, p<0.001;
Figure). After adjustment for age, aspirin use, ACE-inhibitor use, and HSR, decreasing CFVR was associated with a 1.8-fold increase in MACE hazard per CFVR unit (95% confidence interval: 1.1–2.8, P=0.01). Results were equivalent after adjustment for FFR (Hazard ratio 1.9, 95% CI: 1.2–3.0, P=0.01).

Conclusion: Low CFVR is associated with adverse long-term clinical outcome after deferral of revascularization, independent of epicardial disease severity as assessed by HSR or FFR.

**P4909 | BEDSIDE**

Doppler-derived hyperemic microvascular resistance predicts the occurrence of microvascular injury and microvascular perfusion deficits after successful percutaneous coronary intervention

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**Purpose:** Between 40 and 50% of patients presenting with ST-segment Elevated Myocardial Infarction (STEMI) develop microvascular injury (MVI) despite complete angiographic restoration of epicardial flow. The purpose of this study was to investigate whether hyperemic microvascular resistance (HMR) immediately following angiographically successful percutaneous coronary intervention (PCI) is related to both occurrence of MVI at cardiovascular magnetic resonance (CMR) and reduced myocardial perfusion at positron emission tomography (PET) as measured in the days following myocardial infarction.

**Methods:** 60 STEMI patients were included in this prospective study. Immediately after successful PCI, intracoronary pressure-flow-derived HMR measurements were performed. CMR cine and late gadolinium enhanced (LGE) imaging and 2D15O PET imaging were performed 4-6 days after successful PCI. Using CMR, MVI was defined as a subendocardial recess of myocardium with low signal intensity within a gadolinium-enhanced area. Myocardial perfusion was quantified using 2H15O PET. To define normal values of HMR, 16 patients referred for invasive coronary angiography served as a control group.

**Results:** Complete datasets were available in 48 patients of which 24 developed MVI. HMR in the culprit artery in patients with MVI was significantly higher than that in patients without MVI (CMR: 3.3±1.5 vs. no MVI: 2.4±1.2, P<0.03). Multivariable analysis showed that HMR was predictive for MVI (p=0.04). High HMR was also correlated with decreased myocardial blood flow (MBF) on PET (CFVR: 2.0: 3.26±1.41 vs. CFVR: 2.0: 2.24±1.19; p=0.03).

**Conclusion:** Elevated Doppler-derived channel flow directly following successful PCI correlates with CMR-defined MVI and decreased myocardial blood flow measured by PET at follow-up.

**P4910 | BEDSIDE**

Comparison of conventional and diastolic fractional flow reserve after adenosine and dobutamine infusions for hemodynamic assessment of myocardial bridging


**Introduction:** Myocardial bridging (MB) is characterized by dynamic systolic compression of the intracoronary arterial segment that may impair epicardial diastolic relaxation, as well. It has been suggested that adequate invasive hemodynamic assessment of MB should include inotropic stimulation with dobutamine. Thus, we hypothesized that diastolic fractional flow reserve (FFR) after dobutamine infusion might provide a better insight into the hemodynamic assessment of MB.

**Objectives:** The aim of the study was to compare conventional and diastolic FFR after adenosine and dobutamine infusions in patients with isolated MB.

**Methods:** The study included 34 patients (9 males, mean age 56±9 years) with angiographic evidence of MB of the left anterior descending artery (LAD) and systolic compression≥50% diameter stenosis. Patients were evaluated by SEHO test for detection of myocardial ischemia, and conventional and diastolic FFR in the distal segment of LAD during iv. infusion of adenosine (ADO: 140 μg/kg/min) and iv. infusion of dobutamine (DOB: 40-50 μg/kg/min), separately.

**Results:** Feasibility for determining FFR during ADO was 32/34 (94%) and during DOB 34/34 (100%), respectively. SEHO test was positive in only 5/34 (15%). Conventional FFR during peak DOB reached similar values as during ADO (0.83±0.04 vs. 0.84±0.05, p=0.11) while diastolic FFR during peak DOB was significantly lower than diastolic FFR during ADO (0.78±0.10 vs. 0.81±0.06, p=0.007).

Conventional FFR during ADO and peak DOB was similar between SEHO positive vs. SEHO negative patients (0.83±0.09 vs. 0.84±0.05, p=0.183; 0.80±0.11 vs. 0.84±0.06, p<0.001, respectively). However, diastolic FFR during peak DOB was significantly lower in SEHO positive vs. SEHO negative patients (0.73±0.04 vs. 0.80±0.10, p=0.038), and of borderline significance for ADO (0.78±0.15 vs. 0.82±0.05, p=0.059), respectively. Receiver-operating curve identifies the optimal diastolic FFR DOB cut-off of 0.76 (AUC 0.793, 95% CI: 0.657–0.937, p<0.001) with a sensitivity and specificity of 100% and 72%, respectively.

**Conclusions:** Diastolic, but not conventional FFR measurement during inotropic stimulation, in comparison to vasodilation, provides more reliable functional evaluation of hemodynamic significance of myocardial bridging.
Cardiopulmonary exercise testing in patients after acute coronary syndrome and PTCA

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Cardiopulmonary exercise testing (CPET) has recently been shown to improve both sensitivity (+89%) and specificity (+15%) of traditional ECG stress test through the analysis of VO2 kinetics that reflects stroke volume and cardiac output during exercise. Between 2009 and 2013 we performed 1113 cardiopulmonary exercise tests (CPET) at the Lancisi Heart Institute's CPET core laboratory in patients (83 (10) years old, 101 women) who underwent PTCA/stenting after acute coronary syndrome (ACS). PTCA/stenting was performed in one (87%) or two coronary vessels (13%). Drug-eluting stents were implanted in 90% of patients. Aim of the study was to discriminate between patients with or without inducible ischemia (I-MI) and to assess prognosis. CPETs were calculated on a cycle-ergometer until exhaustion using a ramp protocol. The diagnosis of I-MI by CPET was considered when the following abnormalities were present: 1 mm ST downsloping in two or more adjacent leads; flattening in VO2/DWR slope (double slope sign); downward flattening in O2pulse.

Results: Of 1113 CPETs, 232 (21%) were positive (CPET+) and 881 (79%) were negative (CPET-). Follow up lasted 28 months on average. Of CPET+ patients, 195 repeated PTCA/stenting for restenosis (75%) or limiting coronary stenosis (15%) or ACS (10%) during the follow-up. Of CPET-, only 5 were hospitalized (ACS in 2, unstable angina in 3). Kaplan Meier analysis showed a significant separation of CPET+ vs CPET- (P =<0.01 by log rank).

Conclusions: Cardiopulmonary exercise testing may predict the clinical outcome in patients with ACS after PTCA/stenting.

Physical fitness predicts early but not late myocardial infarction; a 35-year follow-up study of 2,014 healthy middle-aged men

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Background: Physical fitness (PF) has previously been shown to predict cardiovascular (CV) death and disease. In the present study we aimed to investigate how baseline PF influenced risks of myocardial infarction (MI) during the first and last part of a 35-year observation of healthy middle-aged men.

Methods: Age adjusted PF, total work divided by body weight (kJ/kg), was calculated in 2,014 apparently healthy, middle-aged men after a maximal bicycle exercise ECG test in 1972-75. Incident myocardial infarction was registered in a nationwide scrutiny of charts in Norwegian hospitals, and early vs. late event was set before or after median MI-age (66 years). Impact of predictors and relative risks between baseline quartiles of PF were estimated using Cox proportional hazard model. When estimating risks of late MI, men with events before 66 years were excluded.

Results: During follow-up, we found 224 and 225 events of early- respectively late MI. Age adjusted PF at baseline was a significant predictor of early- but not late MI. Family history of CHD, baseline smoking status and cholesterol were significant predictors of early MI, while baseline blood pressure and cholesterol were significant predictors of late MI. Relative risks were associated with significantly increased risks of early MI as the highest PF quartile (Q4) in unadjusted, age adjusted and multivariable analysis. There were no differences in risks of late MI among the PF-quartiles (Table).

Conclusions: PF was independently associated with risk of early- but not late MI. Most classical CV risk factors were strong predictors of both early and late MI. Low PF at middle-age could be interpreted as a warning sign of an early rather than late MI.

Cardiopulmonary exercise testing in patients after acute coronary syndrome and PTCA

P4913 | BEDSIDE

P4914 | BEDSIDE

Increased mortality is related to a low oxygen uptake efficiency slope and inability to reach peak effort in CAD patients

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Background: Peak exercise capacity is a well known independent predictor for mortality in patients with coronary artery disease (CAD). However, often exercise tests are stopped prematurely and therefore submaximal measures like the oxygen uptake efficiency slope (OUES) have been introduced. This study sought to determine the prognostic value of the OUES in patients with CAD.

Methods: Patients with CAD, who underwent cardiopulmonary exercise testing (CPET) between 2000 and 2011 were included. OUES was calculated by robust regression analysis. Follow-up information on mortality was collected. Cox regression analyses were used to assess the prognostic value of the OUES and ROC curves were performed. Patient subgroups were established based on the optimal OUES cut-off value and on the ability to reach a peak effort during graded exercise.

Results: In the 1409 CAD patients (mean age 60.7 ± 9.9 years; 1205 men, 204 women), mean OUES was 153±8.40. A peak effort could not be reached in 111 (11%) patients. During a follow-up of 7.45 ± 3.20 years (range 0.16 to 14) 158 patients died (68 of cardiovascular causes). OUES was significantly related to all cause (hazard ratio: 0.586, p<0.001) and cardiovascular (hazard ratio: 0.461, p<0.001) mortality. Survival curves are shown in the figure. Survival was highest
Comparison of two aerobic training interventions in patients with coronary artery disease: the SAINT-EXCAD study
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Background: Exercise-based cardiac rehabilitation is considered an important treatment and secondary preventive measure, but the importance of training modalities such as aerobic interval training (AIT) and moderate continuous training (MCT) in patients with coronary artery disease (CAD) are yet not fully under-stood.

Aim: To compare, in a multicentre, well powered, randomized study, the effects of AIT and MCT on peak aerobic capacity (peakVO2) and endothelial function (FMD).

Methods: 200 stable CAD patients, with ejection fraction (EF)≥50%, aged 58±9 yrs, 90% male, were randomized to a supervised 12-week cardiac rehabilitation program (CR) of three weekly sessions of either AIT (90% of peak HR) or MCT (75% peak HR). Primary endpoints were data from maximal cardiopulmonary exercise tests (CPET) and FMD before and after CR. Data are presented as means±SD and comparisons were performed by ANOVA and ANCOVA.

Results: Baseline characteristics and data from the baseline CPET were not significantly different between both groups, except for age (56.5±9 for AIT and 59.2±9 for MCT; p=0.02). 14 and 11 patients dropped out from respectively the AIT and MCT groups, none of them because of exercise related adverse events. Peak VO2 (ml/min/kg) after CR was significantly higher in both groups (F(57.2, p<0.001) and overall higher values were observed in the AIT group (F(4.66, p<0.05). However, no significant time*group interaction was observed and the percent increases of 22.4.9 for AIT and 20.3±15.3% for MCT were also not significantly different. Inclusion of age as covariant did not alter the results. Endothelial function, as evaluated by FMD, increased also similarly in both groups not significantly different. Inclusion of age as covariant did not alter the results. En-

Conclusion: The OUES is an independent predictor for all cause and cardiovas-
cular mortality in patients with CAD, along with the inability to reach a peak effort during CPET.

P4918 | BEDSIDE
Quality of life post-ACS is related to physical exercise but not to therapeutic interventions
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Introduction: Data from UPBEAT study showed that randomisation of depressed patients with coronary artery disease to a physical exercise program leads to bene-
efficial effects on mood. We performed a real-world registry study to answer the related question of whether engaging in physical exercise post-ACS is associated with quality of life (QoL). A second, unresolved question is to what extent QoL post-ACS is enhanced by medical and therapeutic interventions. These issues are important as QoL determines patients’ levels of motivation and compliance.

Methods: The local Swedish SEPHIA registry at our centre which holds data for N=1570 post-ACS patients aged <75 ys was interrogated. QoL was recorded post-ACS at 1 and 12 months as a visual analog scale (EQ-5D) rating, ranging from 0 to 100. Exercise was given in hours/week, non-Scandinavian immigrant status was self-described. Determinants of QoL at 12 months were analysed in backward logistic regression with values above vs. below population median as dichotomous dependent variable. Independent variables were ranked based on Wald statistic.

Results: There were n=1144 cases with complete QoL data (60±9 years; 22% females; 29% non-Scandinavian immigrants). While exercise decreased during follow-up (1 month: 4.9±4.1 vs. 12 months: 4.0±3.0 hrs/wk; p<0.001) and smok-
ing increased (14 vs. 18%; p<0.001), QoL did not change (62±21 vs. 70±21; p=NS). The leading independent predictor of high QoL was exercise (OR 1.1 per hr/wk) followed by being working (OR 5.2 vs. being on sick leave), non-smoking (OR 2.3) and being of Scandinavian origin (OR 1.8; p<0.001 for all). Interestingly, while angina (OR 0.52) dyspnoea (OR 0.46) and diabetes (OR 0.52) indepen-
dently predicted poor QoL, so did medical interventions such as oral treatment with diuretics (OR 0.61), long-acting nitrates (OR 0.58) and ARB (OR 0.55), read-
misson (any; OR 0.40; for angina; OR 0.35) and PCI (OR 0.63; p<0.05 for all). In

Conclusion: In post-ACS patients, physical exercise is strongly associated with high QoL. Whether the “feelgood effect” of exercise translates into better patient compliance and clinical benefit remains to be shown. Disappointly, while comorbid patients suffer from poor QoL, the impact of commonly recommended medical interventions appears to be neutral or even detrimental.

PHARMACOTHERAPEUTIC CHALLENGES IN THE REAL WORLD
P4919 | SPOTLIGHT
Evaluation of effectiveness and cost effectiveness of decision support system in managing hypertension in resource constrained primary health care settings: results from a cluster randomised trial
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Background: With increasing adoption of information technology in healthcare domains and a shortage of healthcare workforce conversant with guideline-based clinical management, there is need to assess the utility of a clinical decision support system for providing evidence based healthcare and in reducing patient out-
comes in resource constrained Primary Health Centre (PHC) settings

Interventions: (1) Clinical Decision Support System (DSS) (2) Chart Based Sup-
port (CBS)

Objective: To test the effectiveness and cost effectiveness of a clinical DSS among hypertensive patients in India.

Abstract P4919 – Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>AT pre</th>
<th>MCT Pre</th>
<th>AT post</th>
<th>MCT Post</th>
<th>F Time</th>
<th>F Group</th>
<th>F Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO2 (mll/min/kg)</td>
<td>23.3±5.8</td>
<td>22.2±5.6</td>
<td>26.8±6.7</td>
<td>57.2; p&lt;0.001</td>
<td>4.66; p&lt;0.05</td>
<td>0.16 (NS)</td>
<td></td>
</tr>
<tr>
<td>Peak HR (b/min)</td>
<td>135±21</td>
<td>129±21</td>
<td>138±22</td>
<td>20.9; p&lt;0.001</td>
<td>7.58; p&lt;0.01</td>
<td>0.04 (NS)</td>
<td></td>
</tr>
<tr>
<td>HR rest (b/min)</td>
<td>68±11.7</td>
<td>67±12.3</td>
<td>64±10.4</td>
<td>3.78; p=0.052</td>
<td>1.38 (NS)</td>
<td>0.33 (NS)</td>
<td></td>
</tr>
<tr>
<td>FMD (%)</td>
<td>5.5±3.18</td>
<td>5.7±2.50</td>
<td>6.75±3.06</td>
<td>11.5; p&lt;0.001</td>
<td>0.35 (NS)</td>
<td>0.00 (NS)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The OUES is an independent predictor for all cause and cardiovas-
cular mortality in patients with CAD, along with the inability to reach a peak effort during CPET.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/35/suppl_1/851/541962 by guest on 07 February 2019
Primary outcome: Mean changes in systolic blood pressure (SBP) from baseline to 12 months among hypertensive patients randomized by PHC to receive the DSS or the chart based algorithmic support system.

Randomisation: Computer generated cluster-randomization.

Blinding/masking: Blinded to participants and statistician.

Methods: The 12 months difference between the CBS and DSS groups adjusted for age, gender, height, waist, body mass index, alcohol intake, pickle and papad (salty food) intake, and portions of vegetable/fruit consumed per day, systolic BP was -6.59 mm of Hg (95% CI: -12.18 to -1.42, p=0.021) and for diastolic BP was -2.83 mm of Hg (95% CI: -5.78 to 0.13, p=0.083). The incremental cost effectiveness ratio for DSS compared with CBS was $335.37 per QALY gained (95%CI: $252.34 – $416.27).

Conclusion: Clinical DSS are effective in the management of hypertension and are not effective in primary care settings.

Trial registration: CTRI/2012/03/002476; Clinical Trial Registry of India

P4920 | BEDSIDE Long-term effects of L- and N-type channel blocker on serum uric acid levels and left atrial volume in hypertensive patients

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This study was designed to investigate whether the L- and N-type channel blocker, Cilnidipine, may affect LV diastolic function differently compared with the L-type channel blocker, Amlodipine, in patients with essential hypertension. We studied 49 patients with untreated hypertension, randomly assigned to Cilnidipine (Cl) or Amlodipine (Aml) for 48 weeks. LV diastolic function was assessed with the Left atrial volume index (LAVI), mitral early diastolic (E) wave, tissue Doppler early diastolic velocity (E') and the ratio (E/E'). Plasma aldosterone (PAC) and uric acid were measured as markers of myocardial fibrosis and inflammation before and after treatment.

Results: Systolic and diastolic blood pressures equally dropped in both groups. LAVI and E/E' decreased in the Cl group but not in the Aml group. There was no significant change in heart rate or PAC in both groups. Serum uric acid significantly increased in the Aml group but not in the Cl group. LV, E/E' and serum uric acid levels significantly decreased after 48 weeks of treatment with Cl group but not with Aml group (-9.34 vs. 23.14%, p<0.05, -7.5 vs. 13.6, p<0.05, -2.1 vs. 12.5%, p<0.05) as percentage reduction from the values before treatment. Larger %drop in serum uric acid and E/E' were associated with larger %reduction of LAVI (r=0.56, p<0.01, r=0.40, p<0.01). Multiple regression analysis showed that the changes in the LAVI is related to the changes in the serum uric acid (%-47, p<0.01).

Conclusions: Cilnidipine but not Amlodipine may improve LV diastolic function in hypertensive patients, at least partially through the attenuation of myocardial fibrosis by regulating oxidative stress.

P4921 | BEDSIDE Chronopharmacotherapy of hypertension is crucial in mortality of hypertensive patients with metabolic syndrome

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Arterial stiffness and wave reflection are independent predictors of cardiovascular events. In a randomized, open, parallel group study we compared the effect on arterial stiffness and wave reflection of three antihypertensive drugs, n 174 (29%) 97 (13%) ns

Nitrates, n 174 (29%) 234 (38%) ns

Use of three or more medications, n 138 (23%) 186 (25%) ns

β-blockers, n 18 (3%) 37 (5%) ns

Calcium channel blockers, n 150 (25%) 186 (23%) ns

ACE-I, n 444 (74%) 589 (79%) ns

ACE-I, inhibitors of angiotensin converting enzyme, ARBs-angiotensin receptor blockers.

ACE-I, inhibitors of angiotensin converting enzyme, ARBs-angiotensin receptor blockers.

Primary outcome: Mean changes in systolic blood pressure (SBP) from baseline to 12 months among hypertensive patients randomized by PHC to receive the DSS or the chart based algorithmic support system.

Randomisation: Computer generated cluster-randomization.

Blinding/masking: Blinded to participants and statistician.

Methods: The 12 months difference between the CBS and DSS groups adjusted for age, gender, height, waist, body mass index, alcohol intake, pickle and papad (salty food) intake, and portions of vegetable/fruit consumed per day, systolic BP was -6.59 mm of Hg (95% CI: -12.18 to -1.42, p=0.021) and for diastolic BP was -2.83 mm of Hg (95% CI: -5.78 to 0.13, p=0.083). The incremental cost effectiveness ratio for DSS compared with CBS was $335.37 per QALY gained (95%CI: $252.34 – $416.27).

Conclusion: Clinical DSS are effective in the management of hypertension and are not effective in primary care settings.

Trial registration: CTRI/2012/03/002476; Clinical Trial Registry of India

P4922 | BENCH Biological properties of adrenomedullin conjugated with polyethylene glycol

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Purpose: Adrenomedullin (AM) is a vasodilator peptide having pleiotropic effects including cardiovascular protection and angiogenesis. Because of these beneficial effects, AM appears to be a promising therapeutic tool for human diseases such as myocardial infarction or peripheral artery disease, while intravenous injection of AM stimulates sympathetic nerve activity due to the short-acting potent vasodilation, resulting in increased heart rate and renin secretion. To lessen those acute unfavorable actions, we conjugated the N-terminal of human AM with polyethylene glycol (PEG), and examined biological properties of PEGylated AM in the present study.

Methods: N-terminal of synthesized human AM peptide was conjugated with PEG5000-NHS, and then PEGylated AM was obtained by purification with HPLC. Biological effects in vitro stimulating intracellular cAMP in cultured HEK-293 cells stably expressing a specific AM receptor. Blood pressure-lowering effects in vivo were tested by intravenous injections of PEGylated or native AM peptides into anesthetized rats. Plasma disappearance curves of peptides were evaluated by the two compartment model.

Results: PEGylated AM stimulated intracellular accumulation of cAMP in cultured HEK-293 cells, as did native human AM peptide, in a dose-dependent manner. pEC50 of PEGylated AM was lower than native AM (8.19±0.10 vs. 8.59±0.90, mean ± SEM, P<0.01), but no difference was noted in the maximum response of cAMP (9.4±0.30 vs. 9.3±0.26 nmol/well). When injected intravenously at the dose of 10 nmol/kg, both peptides lowered blood pressure (BP) in anesthetized rats, while the acute reductions in mean BP of PEGylated AM were substantially smaller than those of native AM at 2 min (-11.5±1.5 vs. -23.5±2.9 mmHg, P<0.01) and at 4 min (-9.7±1.5 vs. -20.0±2.9 mmHg, P<0.05) of the injection. The first and second plasma half-lives of PEGylated AM were 4.87±0.68 and 108±12 min, while those of native AM were 62.6±0.02 and 152.2±1.9 min, respectively. Both half-lives of the PEGylated peptide were significantly prolonged, as compared with the native peptide (P<0.05).

Conclusions: N-terminally PEGylated AM stimulated cAMP production in vitro, showing smaller acute hypotensive action and a prolonged plasma half-life in comparison of native AM peptide in vivo. The present results suggest a possibility for PEGylated AM as a therapeutic tool with lesenned unfavorable effect of acute hypotension of native AM.

P4923 | BENCH Combination therapy with lercanidipine and enalapril improves wave reflection in hypertensive patients with metabolic syndrome

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Aortic stiffness and wave reflection are independent predictors of cardiovascular events. In a randomized, open, parallel group study we compared the effect on arterial stiffness and wave reflection of a combination therapy with an ACE-inhibitor plus calcium channel blocker or thiazide diuretic in 76 hypertensive patients with metabolic syndrome uncontrolled by ACE-inhibitor monotherapy.

Aortic stiffness (c + enalapril (ENA, 20 mg), patients were randomized to a combination therapy with lercanidipine (LER, 10-20 mg) or hydrochlorothiazide (HCT, 12.5-25 mg) for 24 weeks. Aortic stiffness (carotid to femoral pulse wave
velocity, PWV), central blood pressure (BP) and wave reflection (augmentation index, AIx) were measured by applanation tonometry. After run-in office BP was similar in the two groups. (ENA/LEAR: 149±9.5/95±12; ENA/HCT 150±7.5/95±9 mmHg). Office (ENA/LEAR 132±10/82±1; ENA/HCT 133±7/83±5 mmHg), 24-hour (ENA/LEAR 123±11/75±7; ENA/HCT 123±12/77±7) and central BP (ENA/LEAR 121±13/90±9; ENA/HCT 122±13/79±9 mmHg) were similarly reduced after 24 weeks. PWV was similar after run-in and equally reduced by the two treatments (ENA/LEAR from 8.6±1.5 to 8.1±1.3 m/s, p<0.05; ENA/HCT from 8.5±1.2 to 8.2±1.0 m/s, p<0.05). Furthermore, LMIs reduced AIx, but its reduction resulted in a significantly greater (p<0.05) in ENA/LEAR (from 26.8±9.10 to 20.6±9.18%) than in HCT arm (from 28.2±9.0 to 24.7±8.7%).

In conclusion, the combination with LER caused a similar PWV reduction as compared to HCT, but a greater reduction in AIx in hypertensive patients with metabolic syndrome not controlled by ENA alone. These results indicate a possible protective role of both ENA and LER for CV risk, implying a complementary pharmacotherapy for metabolic syndrome.

**Conclusion**

The combination with LER caused a similar PWV reduction as compared to HCT, but a greater reduction in AIx in hypertensive patients with metabolic syndrome not controlled by ENA alone. These results indicate a possible protective role of both ENA and LER for CV risk, implying a complementary pharmacotherapy for metabolic syndrome.
The soluble guanylate cyclase activator cinaciguat prevents pressure overload-induced cardiac hypertrophy

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Purpose: Pathological cardiac hypertrophy is observed in pressure overload of the left ventricle. Increased intracellular cGMP-levels have been reported to prevent the development of pathological myocardial hypertrophy. We investigated the effects of chronic activation of the cGMP producing enzyme, soluble guanylate cyclase (sGC) by cinaciguat in a rat model of pressure overload-induced cardiac hypertrophy.

Methods: We performed aortic banding (AB) to evoke pressure overload-induced cardiac hypertrophy in our rats. Sham operated animals served as controls. Experimental groups were treated with 10 mg/kg/day cinaciguat (Cin) or with placebo (Co) p.o., respectively. Development of cardiac hypertrophy was investigated by echocardiography. We performed left ventricular (LV) pressure-volume analysis with a pressure-conductance microcatheter to assess cardiac function. In addition to our functional experiments, histological and molecular biological measurements were carried out.

Results: Our results demonstrate that chronic stimulation of the NO-cGMP its signaling by pharmacologically activating soluble guanylate cyclase might be a novel therapeutic approach in the prevention of pathological myocardial hypertrophy.

Conclusions: Therefore, the aim of our study was to investigate the role of Wnt pathway attenuation of adverse LV remodeling and improves heart function. Thus, the macrophage-derived Wnt family of proteins could be a potential therapeutic target for cardiac repair and regeneration.

P4930 | BENCH
Nuclear calcineurin is a sensor for detecting Ca2+ release from the nuclear envelope via IP3R

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Background: We hypothesize that decoding Ca2+ signals for hypertrophic signaling in continuously beating cells like cardiac myocytes with rapid alterations of cytosolic Ca2+ levels requires intracellular Ca2+ microdomains that are partly independent from cytosolic Ca2+. Further there is a need for a Ca2+ sensor within this microdomain that translates Ca2+ signals into hypertrophic signaling. Recent evidence suggested that the nucleus of cardiac myocytes might be a Ca2+ microdomain and that calcineurin, once translocated into the nucleus could act as a nuclear Ca2+ sensor.

Methods and results: Performing a transgenic mouse model with conditional calpain inhibition we now demonstrate that calpain-truncated calcineurin escaped further degradation by the UPS in the nucleus and could not be relocated to the cytosol. Truncated nuclear calcineurin was able to act as nuclear Ca2+ sensor detecting local Ca2+ release from the nuclear envelope via IP3R. Nuclear calcineurin mutants defective for Ca2+ activation failed to activate NFAT dependent transcription. Under hypertrophic conditions Ca2+ transients in the nuclear microdomain were significantly higher than in the cytosol providing a basis for sustained calcineurin/NFAT mediated signaling uncoupled from cytosolic Ca2+.

Conclusions: This data provide an explanation how Ca2+ and calcineurin might regulate transcription in cardiomyocytes in response to neurohumoral signals independently from their role in cardiac contraction control.

P4931 | BENCH
Toll-like receptor 2 deficiency preserves cardiac diastolic function in pressure overload induced heart failure

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Introduction: Approximately 50% of the heart failure patients have a preserved ejection fraction (HFPEF). While as deadly as heart failure with reduced ejection fraction (HFrEF) the mechanisms underlying HFPEF remain unclear. Toll-like receptor 2 (TLR2) is part of the innate immune system and detects exogenous bacterial ligands but also endogenous ligands. TLR2 may in part be involved in the inflammatory response ischaemia reperfusion injury and HFREF. Although inflammation is also important in HFPEF, a role in TLR2 in HFPEF has not been explored.

Methods: C57BL/6J and TLR2-deficient mice were subjected to transverse aortic constriction (TAC) via intercostal incision. The presence of TAC was confirmed by echocardiography. Cardiac function was analyzed with echocardiography at baseline, 3 weeks and 8 weeks after TAC. Animals with an Ejection Fraction (EF)< 40% at 3 and 8 weeks (25%) were excluded.

Results: Eight weeks after TAC, 7 wild type (WT) and 11 TLR2 deficient (TLR2KO) mice had an EF > 40%. The end systolic (ESV) and diastolic volumes (EDV) of left ventricle (LV) increased in WT mice but not in TLR2KO mice (EDV: 36.05±15.02 μL for WT vs 27.09±2.2 μL for TLR2KO; p<0.018; EDV: 23.9±5.2 μL for WT vs 15.9±2.0 μL for TLR2KO; p<0.001). After TAC, the LV weight determined by echocardiography increased similarly for WT and TLR2KO mice. The mitral inflow E/A ratio as the parameter for ventricular stiffness, however, significantly decreased in WT mice but not in TLR2KO mice re-
P4932 | BEDSIDE
Predictive ability of right ventricular free wall strain in chronic versus acute pressure overload
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Purpose: Acute pulmonary embolism (PE) is an important cause of morbidity and mortality. Efforts to differentiate right ventricular (RV) failure from chronic (eg. pulmonary hypertension [PHT]) vs. acute pressure overload have had limited success. We proposed that assessment of RV deformation using RV free wall strain (RVS) would discriminate acute PE from chronic PHT.

Methods: 45 PE pts (64±15 yrs, 15 men) were matched for age, gender and RV systolic pressure (TR mmHg + Right atrial pressure) with 45 PHT pts. Standard echo measurements were performed following ASE guidelines. RVS was performed using VIVI. Receiver operating characteristic (ROC) curve analyses and incremental multivariate analysis were performed to analyze significant associations of etiology of RV pressure overload. Anticipated associations were placed into the models (age, sex, RV end-diastolic area [EDA] and fractional area change [FAC]).

Results: RVS was similar in PE (48±18 mmHg) and PHT (46±17, p=0.91). PE pts displayed significantly lower FAC (26±12 vs. 38±12%, p<0.001) and RVS (13.6±5.7 vs. 19.6±4.7, p=0.001), but increased RVEDA (25.1±6 vs. 21.7±7 cm2, p=0.007). ROC analyses revealed that RV strain had excellent discriminative power (AUC 0.82). Recognition of PE in pts with RVS -50 mmHg with RVS (AUC 0.85) showed 84% sensitivity and 88% specificity with a cutoff of -17.4%. With RVSVP -50 mmHg, RVS of -16.3% (AUC 0.79) showed 85% sensitivity and 65% specificity (Figure). In a stepwise model, addition of RVS increased the model chi square from 25 to 31 (p=0.003).

Conclusion: At the same level of PA pressure, RVS is sensitive for detecting acute PE. This relationship changes at different pressure loads within the RV. Strain is superior to traditional markers of RV assessment such as RVEDA and FAC.

P4933 | BEDSIDE
Right ventricular systolic function and exercise capacity in chronic systolic heart failure: right ventricular mechanics outperform conventional echocardiographic parameters
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Background: In patients with chronic systolic heart failure (CHF), decreased peak exercise capacity predicts cardiovascular outcomes and determines advanced heart failure therapies consideration. Right ventricular (RV) function has been previously recognized as a major determinant of exercise capacity in CHF patients. RV function assessment by longitudinal peak systolic strain (TAPSE) has proven to have superior correlation with right heart catheterization indexes of RV function than conventional echocardiographic measurements like tricuspid annular plane systolic excursion (TAPSE) and RV myocardial performance index (Tei index).

Methods: Fifty consecutive ambulatory patients with chronic systolic HF (left ventricular ejection fraction [LVEF] ≤45%) underwent symptom-limited cardiopulmonary exercise testing and transthoracic echocardiography including LPPS, TAPSE, tricuspid annular plane systolic velocity (s'), RV fractional area change (FAC), and RV myocardial performance index (Tei index).

Results: In our study cohort (mean age 52±13 years, 78% male and mean LV ejection fraction 30±7%), the mean RV LPPS was -21±3%, RV s’ 10±2 cm/s, RV FAC 0.43±0.1, Tei index 0.6±0.2 and median TAPSE 18 mm (IQR: 16 to 21). Peak oxygen uptake (pVO2) was 18.5±5.7 ml/kg/min, exercise duration 11.0 minutes (IQR: 9.1 to 12.6), and VE/VCO2 33±15.7. In the univariate analysis, RV LPPS (r=0.46, p=0.003) and RV FAC (r=0.34, p=0.02) had a direct correlation with pVO2, while Tei index showed an inverse correlation (r= -0.32, p<0.02). Additionally, RV LPPS was directly correlated with cardiac output (r=0.39, p<0.02) and inversely correlated with RV FAC (r=0.46, p<0.02). In the multivariate analysis, only RV LPPS and FAC were independently associated to pVO2 after adjusting for age, male gender and LV EF.

Conclusion: In stable CHF patients, RV function by LPPS is an independent predictor of decreased pVO2 and has the best correlation with exercise capacity when compared with conventional echocardiographic parameters.

P4934 | BEDSIDE
Two and three-dimensional echocardiographic assessment of right atrial size and function in relation to clinical, hemodynamic characteristics and mortality in patients with pulmonary hypertension
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Right atrial (RA) size and function can be a good predictor of clinical outcome in patients (pts) with pulmonary hypertension (PH). We aimed to assess the RA volumes (V) and functions by two-dimensional and three-dimensional echocardiography (2D, 3DE), and to evaluate the relationship among 2DE and 3DE measures and invasive clinical characteristics (IIC), HRQoL and survival. In pts with PH, fifty one pts with PH (age 43±14 years, F 31,M 20) and 20 healthy age and sex-matched controls were included into the study. Subgroups of PH were as follows: Idiopathic pulmonary hypertension (IPAH), RA remodelling with tricuspid annular plane systolic excursion (TAPSE) and RV fractional area change (= FAC) as potential target for treatment.

Conclusion: RA maximal volumes determined by RT3DE were smaller than CMR measurements (V) and functions by two-dimensional and three-dimensional echocardiography. RA systolic function was assessed by tricuspid annular planary systolic excursion and tissue velocity (TAPSE and St). Maximum, pre-atril contractile force were greater compared with controls (p<0.0001). Psychological PT subgroups compared were comparable in 3DE RA Vmax, Vmin and FAC. ATRV FAC were significantly higher compared to 2DE volumes (p<0.001 and p<0.05) whereas EF % were similar (p=NS). 3DE RA Vmax,Vmin and TOTEF correlated with Uric Acid (UA) (R=0.31, 0.34 and -0.31, p<0.05), TAPSE (R= -0.46, -0.50 and 0.49, p<0.001, <0.001 and <0.001), St (R= -0.41, -0.47 and 0.50, p=0.003, 0.0001 and <0.01) and inferior vena cava diameter (IVcD) (R=0.64,0.64 and -0.42, p<0.001, 0.0001 and <0.001), respectively. Ageing was associated with a decrease in 3DToTEF (-0.372 p<0.007), TAPSE, St and IVcD showed good correlations with 2DRAVmax, Vmin, Vpeak, 2D ToTEF% (r=0.62; 0.50 and 0.58) and Uric acid (r=0.57, 0.65 and -0.41) (all p<0.001). 6MWD correlated with TAPSE and 2D ToTEF% (r=0.35 and 0.32, p<0.05) and BNP correlated with 2D Vmax and Vmin (r=0.33,0.39, p<0.05, respectively) whereas BMWD (r=0.0001), UA (r=0.003,0.004,0.003 and 0.001 and 0.01), 2D RA Vmax,p=0.003 and 0.01 and 0.013) was associated with an increased mortality.

We conclude that 2DE, Doppler and 3DE measures of RV and RA dysfunction are significantly correlated with 6MWD, BMWD, UA and 3D ToTEF% of the PH etiology. Moreover, 6MWD, 3D and 2D RA Vmax and Vmin were significantly associated with PH mortality.

P4935 | BEDSIDE
Measurement of right atrial maximal and minimal volumes: comparison of a semi-automatic algorithm of real-time 3D echocardiography with cardiac magnetic resonance imaging

Introduction: Real-time full-volume 3D echocardiography (RT3DE) allows rapid measurement of atrial volume without making geometric assumptions. This method has recently been validated against cardiac magnetic resonance imaging (CMR) for the left atrium. However for right atrial (RA) volume 3DE has so far been validated against CMR with reconstructed 3DE based on multiple 2DE images.

Method: 20 patients were studied RT3DE and CMR within 24h. RT3DE RA maximal (Vmax) and minimal (Vmin) volumes have been measured with a semiautomatic border detection method. These volumes were compared with RA volume determined by CMR as reference method.

Conclusion: RA maximal and minimal volumes determined by RT3DE were smaller than CMR derived volumes. Linear regression analysis showed a rather good correlation between RA maximal volume determined by RT3DE with CMR derived volume (r=0.65). Correlation was better for RA minimal volume (r=0.85). Bland-Altman

Remodelling and death of cardiac myocytes / Imaging right 883

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Conclusion: This small preliminary study suggests that RA maximal volumes ml for CMRI volume. Limits of agreement and bias were smaller for RA minimal volumes.

30.6% compared to CMR. Correlation and agreement was better for RA minimal volumes with mean volume underestimation of RA maximal volume by RT3DE of 24.7%. 2D correlated well with CMR. However agreement between both methods was rather moderate with mean volume underestimation of RA maximal volume by RT3DE of 30.6% compared to CMR. Correlation and agreement was better for RA minimal volumes.

P4937 | BEDSIDE
Two and three dimensional echocardiographic assessment of respiratory variation on inferior vena cava size: who's the winner?
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Accuracy in inferior vena cava (IVC) measurement has clinical implications in the diagnosis and management of cardiac disorders. Usually measured by transthoracic echocardiography (TTE), the usefulness of three-dimensional echocardiography (3D) has not been demonstrated in the evaluation of the IVC.

The aims of this study is to develop a methodology to explore the IVC by 3D and analyse the variation of IVC with respiratory motion in comparison with 2D.

Twenty five patients underwent detailed transthoracic 2D and 3D assessment of IVC. 2D measure of IVC diameter was performed according to the ASE guidelines. IVC dilatation speed in 3D was measured according to its longitudinal axis from the junction with the RA.

The cross-section of the IVC was positioned immediately after the junction with the hepatic vein. The large and small diameter (D1 and D2) and the surface (S) of the IVC were measured. After deep breathing, re-adjustment of the section of the IVC and same measures were done. The IVC collapsibility index (IVCCI = (IVCmax - IVCmin) / IVCmax) was calculated in 2D and for its 3D parameter.

Results: Mean IVCmax and D2max was respectively 21.5±3.1mm and 11.5±1.7mm (2D IVCCI = 46%). 3D shows that IVC in cross section has an oval geometric shape. D1max and D1min was 27.6±1.9mm and 22.3±1.5mm (D1 IVCCI = 19%). D2max and D2min was 15.6±1.2mm and 11.1±1.1mm (D2 IVCCI = 28%). S max and min was respectively 3.2±0.6cm² and 2.0±0.4cm² (S IVCCI = 37%). 2D is less than D1 (p<0.001).

2D is not able to measure his maximal diameter IVC and to perform the exact IVC following during the respiration. 3D assessment of IVC added more valuable information that may help in its management.

P4937 | SPOTLIGHT
Right atrial volumes with 3D and 2D echocardiography are better than inferior vena cava size for estimation of elevated right atrial pressure in pulmonary hypertension
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Purpose: To determine whether right atrial volumes (RAV) with 3D-echocardiography (3DE) can assess elevated mean right atrial pressure (mRAP) in patients evaluated for pulmonary hypertension (PH).

Background: PH is characterized by elevated pulmonary arterial pressure (PAP). Predictors of poor prognostic outcome are enlargement of the right atrium (RA) and elevated mRAP due to RV failure.

Methods: 52 patients (64±15 years, 54% women) evaluated for PH underwent right heart catheterization within 48 hours from 3DE. 7% were not feasible to visualize with 3DE. Maximum (RAVmax) and minum (RAVmin) volumes were measured with 3DE. mRAP was obtained from catheterization and >8 mmHg was considered elevated. Cine cardiac magnetic resonance (CMR) was used in 26 patients for comparison of 3DE RA measurements. Receiver-operating characteristics curves with area under the curve (AUC) were calculated.

Results: RAVmax and RAVmin correlated with mRAP (r=0.364 and r=0.304, p<0.05), and so did RA maximum volume with 2D-echocardiography (r=0.423, p=0.003). AUC was 0.736 for RAVmax, 0.716 for RAVmin and 0.769 for 2D RA volume to discriminate elevated mRAP (p<0.05 for both), with optimal 'threshold' point calculated to 57ml/m² for RAVmax, 30ml/m² for RAVmin and 36ml/m² for 2D RA volume. AUC was neither significant for inferior vena cava diameter nor collapsibility for predicting mRAP>8mmHg (NS). Interobserver variability for 3DE was low. Intraclass correlation coefficient was 0.923 for RAVmax and 0.918 for RAVmin. Bias between 3DE and the average of 3DE and CMR was -54±30% for RAVmax and -66±34% for RAVmin.
Conclusion: 3D-TEE allowed a good assessment of the TA shape and orientation, which is significantly different among individuals. This method could be interesting to improve assessment of TA dilation before left-heart valve surgery.

**BIOMARKERS AND DIAGNOSIS OF ACUTE CORONARY SYNDROME IN THE EMERGENCY DEPARTMENT**

**4958 | BEDSIDE**

Incremental value of copeptin to high-sensitivity cardiac troponin T alone in the early diagnosis of acute myocardial infarction

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Purpose: Recently, two novel approaches have shown to improve the early diagnosis of acute myocardial infarction (AMI): high-sensitivity cardiac troponin (hs-cTnT) and copeptin, a sensitive marker of endogenous stress. It is unknown, whether the combination of hs-cTnT and copeptin would further increase diagnostic accuracy.

Methods: In a prospective, international multicenter diagnostic study, copeptin and high-sensitivity cardiac troponin T (hs-cTnT) were measured in 1991 patients presenting to the emergency department with acute chest pain. The final diagnosis was centrally adjudicated by two independent cardiologists blinded for the investigations. The AUC for the ROC analysis was compared for hs-cTnT and copeptin (0.93: 95% CI: 0.92-0.94, p = 0.076).

Results: The single use of hs-cTnT below the 99th percentile (14ng/l) resulted in a sensitivity of 90% and a negative predictive value of 97%. Using the dual marker strategy of copeptin resulted in a significant improvement with a sensitivity of 98% and a negative predictive value of 99% for hs-cTnT below the 99th percentile (14ng/l) and copeptin below 9pmol/l (p = 0.001 for both comparisons).

Conclusions: The additional use of copeptin further improves the early rule-out of AMI in patients presenting with acute chest pain to the emergency department as compared to hs-cTnT alone. The additional use for the rule-in of AMI, however, seems limited.

Trial registration: ClinicalTrials.gov number, NCT00470587

**4959 | BEDSIDE**

Utility of absolute and relative kinetic changes of high-sensitivity cardiac troponin T in risk stratification in patients with and without acute coronary syndrome

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Purpose: We sought to evaluate the prognostic impact of absolute and relative kinetic changes of high-sensitivity cardiac troponin T (hs-cTnT) in comparison to baseline hs-cTnT elevations for risk stratification in acute coronary syndrome (ACS) and non-ACS conditions with increased hs-cTnT.

Methods: hs-cTnT was measured serially in patients presenting with acute symptoms to our emergency department. We assessed the prognostic performance for mortality prediction of baseline and serial hs-cTnT concentrations in all consecutive patients with ACS (n = 406) or hs-cTnT increases not due to ACS (n = 442) within 3-6 h after admission.

Results: In ACS patients, receiver operating characteristics (ROC) revealed optimized cut-off values of 12.2 ng/L for absolute ∆-change (AUC = 0.66, p < 0.001), 31.2 ng/L for baseline hs-cTnT (AUC = 0.71, p < 0.001) and 45.2 ng/L for maximum ∆-change (AUC = 0.76, p < 0.001). C-statistics showed superiority of absolute ∆-change (p < 0.0003), baseline hs-cTnT (p = 0.04) and maximal hs-cTnT (p = 0.02) compared to relative ∆-changes. However, the combination of baseline hs-cTnT values with either absolute or relative ∆-changes did not improve risk prediction compared to baseline hs-cTnT alone (p = ns.). Moreover, a significant incremental value of the 99th percentile cut-off for mortality prediction using net reclassification improvement was only observed for the ROC-optimized baseline hs-cTnT and the max. hs-cTnT, but not for hs-cTnT absolute or relative kinetic changes. In non-ACS conditions, the ROC-optimized cut-off value of 46.2 ng/L for baseline hs-cTnT (AUC = 0.68, p < 0.001) was superior to absolute ∆-change (p = 0.007) and relative ∆-changes regarding prognostication (p = 0.045). Similar to the logistic ROC analysis in the ACS cohort, the combination of baseline hs-cTnT values with absolute ∆-changes (AUC = 0.646) or relative ∆-changes (AUC = 0.609) revealed no significant reclassification to baseline hs-cTnT and was superior to absolute ∆-change (p = ns.).

Conclusions: Our data suggest that the magnitude of baseline hs-cTnT, and not acute dynamic changes, convey superior long-term prognostic information in ACS and non-ACS conditions. Moreover, absolute and relative kinetic ∆-changes of hs-cTnT do not add significant incremental value for mortality prediction in both conditions.

**4960 | BEDSIDE**

Diagnostic utility of copeptin in addition to high-sensitivity cardiac troponin for the early diagnosis of non-ST-elevation acute coronary syndromes

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Aims: Rapid and reliable exclusion of NSTEMI during an Emergency Department (ED) triage is a major unmet clinical need. We aimed at verifying the non-inferiority of a single-sampling strategy of high-sensitivity cardiac troponin I (hs-cTnI) and copeptin compared with the dual hs-cTnI sampling for the early diagnosis of NSTEMI versus Non Coronary Chest Pain (NCCP) in a cohort of patients admitted at the ED.

Methods: Copeptin, hs-cTnI, CK-MB and myoglobin levels were measured at presentation in 196 consecutive patients admitted to the ED for non-traumatic chest pain with onset within the previous 6 hours and without ST elevation on a 12-lead ECG. The comparative diagnostic performance for NSTEMI diagnosis of a combination of hs-cTnI and copeptin, hs-cTnI and CK-MB, hs-cTnI and myoglobin on admission; and of the 3 hours hs-cTnI serial sampling was studied with reference to the adjudicated post-discharge diagnosis. The diagnostic accuracy and the predictive value of the various biomarkers combinations were assessed using both ROC curve and Net Reclassification Improvement (NRI) analysis. A margin to define non-inferiority between the areas under the ROC curves (AUC) was set at < 0.05.

Results: Of 629 consecutive patients admitted at the ED during March 2011, the diagnosis of NSTEMI was done in 29 patients (14.8%). At the time of admission first blood sampling analysis, a copeptin level <14 pmol/L in combination with a hs-cTnI <0.045 mg/L safely ruled out NSTEMI with both a sensitivity and a negative predictive value of 100%. The combination of hs-cTnI and copeptin generated an AUC of 0.91 (95% CI: 0.88-0.94), which was non-inferior with respect to the 3-hours interval hs-cTnI serial sampling, with a trend towards improved diagnostic performance when compared with the 0.89 (95% CI: 0.81-0.97) for hs-cTnI alone, 0.86 (95% CI: 0.77-0.92) for hs-cTnI/CK-MB, and 0.83 (95% CI: 0.73-0.90) for hs-cTnI/myoglobin. When compared with hs-cTnI alone, the combination of hs-cTnI and copeptin yielded a significant positive NRI of 0.459 (p = 0.043). Short-term (<3 months) follow-up of patients with normal copeptin and hs-cTnI serum levels on admission was completely event-free (out-of-hospital major adverse cardiovascular event rate 0%).

Conclusions: The combined single-sampling use of copeptin and hs-cTnI is non-inferior to dual hs-cTnI sampling to allow a rapid and reliable ruling-out of NSTEMI in patients within 6 hours from chest pain onset. The diagnostic utility of single-sampling copeptin/his-cTnI may result in a substantial cost-saving benefit compared with dual hs-cTnI sampling by reducing the total treatment cost of chest pain management in the ED.

**4961 | BEDSIDE**

High sensitivity troponin T serial changes as a gatekeeper for hospital admission and resources utilization


Purpose: The use of high sensitivity cardiac Troponin T (hs-cTnT) assay might lead to overdiagnosis and overtreatment of Acute Myocardial Infarction (AMI), if compared with standard cardiac Troponin T (cTnT) test. This study aimed to assess the impact of introducing hs-cTnT serial measurements in the everyday clinical practice of an Emergency Department (ED) at a tertiary care teaching hospital.

Methods: We compared 597 consecutive patients presenting with suspected Acute Coronary Syndrome (ACS) at the ED during March 2010, when standard cTnT assay was used, and 629 consecutive patients admitted during March 2011, when hs-cTnT test was used.

Results: The two study groups did not differ in terms of baseline characteristics. Patients with suspected ACS whose troponin levels were above the 99th percentile significantly increased when using the hs-cTnT assay (17.4% vs. hs-cTnT 38.6%, p < 0.001). Accordingly, also the mean GRACE risk score increased (124 vs. 135; p = 0.03).

Results: The final diagnosis of AMI did not change significantly (8.7% vs. 6.8%; p = 0.26) by using the above-mentioned pattern of hs-cTnT. When looking at hs-cTnT tested patients, if we used the 99th percentile as a cut-off for the diagnosis of AMI, we observed a significant increase in the number of AMI diagnosis (6.8% vs. 9.9%; p = 0.07). In particular, had we used the hs-cTnT cut-off value of 14 ng/L for the diagnosis of AMI (99th percentile), we would have observed a 50% increase of NSTEMI.
Biomarkers and diagnosis of acute coronary syndrome in the emergency department

4962 | BEDSIDE
Comparison of a high sensitive troponin T and a conventional troponin I assay for the early detection of myocardial injury

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Purpose: More sensitive troponin assays have allowed to detect ischemia induced myocardial necrosis within 3h after onset of cardiac ischemia. The value of troponin assays for detecting myocardial injury (MI) in early (<2h) chest pain presenters is still a matter of debate.

Methods: The “early presenter” model was tested in 103 stable patients (76% male, age (median, interquartile range) 70 (63-77) years) in whom a short period of myocardial ischemia was induced during stenting of a significant coronary artery stenosis. Blood samples for high sensitive troponin T (hsTnT) and conventional troponin I (TnI) were taken at the start of the procedure and 90, 180 and 360 minutes after stent implantation. Myocardial injury was defined on the 90 and 180 min sample as an absolute rise of TnI or hsTnT >50% of the upper limit of normal. The final diagnosis of MI was made on the 360 min blood sample as an hsTnT >14 ng/L and a TnI >45 ng/L and an absolute rise of >50% ULN.

Results: The final diagnosis of MI on the 360 min sample was made in 63% of the patients. MI at 90 min was demonstrated in 18,2% of patients with TnI and in 20, 9% for hsTnT. At 180 min MI was demonstrated for 27,3% of patients with TnI and hsTnT sensitivity. The diagnostic value, expressed as the area under the receiver-operating curve from 0.64 to 0.73 (p<0.01), and remained an independent predictor of ischemia in multivariable analysis (p<0.001). Combining clinical judgment prior to exercise testing with us-cTnI levels increased diagnostic accuracy as quantified by the area under the receiver-operating curve from 0.64 to 0.73 (p<0.001), which tended to be superior also to clinical judgment after exercise testing (0.69, p=0.056). A single resting us-cTnI measurement provided similar diagnostic accuracy as integrated clinical judgment after exercise testing including work load, as well as symptoms and ECG changes (0.70 versus 0.69, p=ns).

Conclusion: Us-cTnI measurements seem to complement non-invasive clinical assessment in the patients with suspected CAD.

4965 | BEDSIDE
Ischemia modified albumin is a new biomarker for early detection of myocardial injury in acute coronary syndromes

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Purpose: This study was designed to assess sensitivity & specificity of ischemia modified albumin (IMA) for the early detection of acute coronary syndromes (ACS). As a new marker, IMA has been compared with high sensitive cardiac troponin I (hs-cTnI) for the early detection of myocardial injury (MI) in acute coronary syndromes (ACS).

Methods: We retrospectively reviewed consecutive cardiology admissions who came without an increase in mortality and resources utilization. Patients were grouped as ACS or non-ACS and the utility of the hs-TnT level and IMA value was assessed. IMA was measured by a competitive chemiluminescent immunoassay from 20 min to 12 h after admission. High sensitive cardiac troponin I (hs-TnI) was measured by ADVIA Centaur and the cut-off for MI was 14 ng/L.

Results: There were 233 patients [87±12 years; 153 (66%) male] with ACS diagnosed in 148 (64%). The area under the ROC (fig.1) was higher for hs-TnT levels (0.757) than for percent change (0.703). The 99th percentile cut-off of 14 ng/L was sensitive but not specific, while a higher cut-off of 75 ng/L was more accurate (table 1). Percent change of hs-TnT was not more accurate.

Conclusion: In high-risk inpatients, a higher hs-TnT cut off was more accurate than the 99th percentile, but no value or was able to rule in and rule out ACS. Correlation to clinical judgment is essential.

4966 | BEDSIDE
Incremental value of a single resting ultrasensitive cardiac troponin I measurement to rule-out myocardial ischemia

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Background: The aim of this study was to investigate the value of a novel “ultrasensitive” cardiac troponin I (us-cTnI) measurement to rule-out exercise-induced myocardial ischemia (MIS) in patients without known coronary artery disease (CAD).

Methods: We included 714 patients without previously known CAD referred for rest/stress myocardial perfusion single photon emission tomography (SPECT). All clinical information available to the treating cardiologist was used to quantify the clinical judgment regarding the presence of MIS using a visual analogue scale twice: once prior and once after bicycle exercise stress-testing. Us-cTnI measurements were obtained before stress-testing in a blinded manner. The presence of MIS was adjudicated based on perfusion SPECT combined with coronary angiography findings.

Results: MIS was detected in 167 (23.4%) participants. Us-cTnI levels were significantly higher in patients with MIS (4.0 ng/L [95% CI 2.8-6.6] versus 2.6 ng/L [95% CI 1.8-4.1]), p<0.001 and remained an independent predictor of ischemia in multivariable analysis (p<0.001). Combining clinical judgment prior to exercise testing with us-cTnI levels increased diagnostic accuracy as quantified by the area under the receiver-operating curve from 0.64 to 0.73 (p<0.001), which tended to be superior also to clinical judgment after exercise testing (0.69, p=0.056). A single resting us-cTnI measurement provided similar diagnostic accuracy as integrated clinical judgment after exercise testing including work load, as well as symptoms and ECG changes (0.70 versus 0.69, p=ns).

Conclusion: Us-cTnI measurements seem to complement non-invasive clinical assessment in the patients with suspected CAD.
modified albumin (IMA) as a new biochemical marker of early detection of myocardial injury in acute coronary syndromes. Methods: This study included 76 patients, who presented to the emergency department (ED) with acute chest pain within 3h of pain onset and 10 people (matched for age, gender and risk factors) as a control group. The blood samples were obtained from patients in the ED, and repeated 4-6 hours after admission to the coronary care unit (CCU) for those subsequently diagnosed with ACS by history, clinical examination, electrocardiogram (ECG) and cardiac markers. IMA level was detected by Albumin-Cobalt Binding (ACB) test, and receiver operating characteristic (ROC) curve was performed to detect the cut off value of IMA with best sensitivity and specificity in diagnosis of ACS. Results: There was a higher IMA level in patients with ACS (5.27±4) compared to control group (1.7±0.8, p=0.007). The ROC curve showed that IMA level could be used to detect cases of myocardial injury in ACS at a level of 3.25u/ml, with 89.5% sensitivity and 100% specificity and 82% accuracy. On admission, there was a highly significant difference between IMA and troponin T (Tn t) regarding sensitivity in STEMI (STEMI=88.5% vs 30.7%, p=0.001) and non ST-elevation myocardial infarction (NSTEMI=94.4% vs 16.7%, p=0.001). On the contrary, there was no significant difference between IMA on admission and cTnI at 4-6 hours after admission in STEMI (88.5% vs 100%, p=0.633) and NSTEMI (94.4% vs 100%, p=0.829) patients. Comparing changes in Tn I at 4-6 hours of admission to IMA results on admission revealed a highly significant difference in favour of IMA in detecting myocardial ischemia in patients with unstable angina (UA=87.5% vs. 0%, p<0.001), but both (IMA and Tn I) had 100% specificity. Conclusions: IMA is highly sensitive for the early diagnosis of ACS in patients presenting to ED within 3 hours of pain onset, compared to other cardiac markers as Troponin I. IMA may be a useful biomarker for the identification of UA patients presenting with typical acute chest pain and/or abnormal electrocardiograms with negative Tn I.

4966 | BEDSIDE
Optimal cutoff-value of a prototype high-sensitivity cardiac troponin I assay by Beckman-Coulter 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 as a diagnostic tool for 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 a prototype hs-cTnI assay by Beckman-Coulter in 1155 patients presenting to the emergency department with symptoms suggestive of AMI, of whom 190 (16%) were determined to have KD (MDRD GFR <60ml/min). We derived the optimal cutoff value for the diagnosis of AMI in patients with KD. The final diagnosis was centrally adjudicated by two independent cardiologists based on hs-cTnI.
Results: AMI was the final diagnosis in 33% (n=63) 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 99thcentile in 54%. In patients with KD the diagnostic accuracy at presentation, quantified by the area under the curve (AUC), was 0.89 (95%CI for AUC, 0.84-0.94). In patients presenting within three hours after the onset of chest pain, the AUC was 0.82 (95%CI 0.70-0.93). In KD, the optimal hs-cTnI cutoff derived from the ROC curve was 25.9ng/l compared to 11.9ng/l in patients with normal kidney function (office 99th percentile 9ng/l, provided by the manufacturer).
Conclusions: The investigated prototype hs-cTnI assay has a high diagnostic accuracy also in KD-patients. Mild elevations are common in non-AMI patients. However, the optimal cutoff-level in KD-patients seems to be about three times as high as the officially recommended cutoff. ClinicalTrials.gov number, NCT00470587

4967 | BEDSIDE
Triple biomarker index added to the troponin test improves laboratory diagnosis of acute coronary syndromes
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Background: Laboratory diagnosis of acute coronary syndromes (ACS) still remains a challenge, especially in patients with initially highly sensitive to detect myocardial damage, but fail in ACS patients without myocardial necrosis. As a result of retrospective multimer analysis, we have selected 3 biomarkers to test in a prospective study: Pregnancy Associated Plasma Protein A (PAPP-A), C-reactive protein (CRP) and haptoglobin (HPT), which reflect different pathological aspects of ACS.
Aim: Prospectively evaluate diagnostic utility of the triple biomarker index (MultiHPC) derived from PAPP-A, CRP, and HPT blood concentrations added to the routine troponin I (Tn I) evaluation in patients presented with suspected ACS.
Methods: Blood samples were obtained in 154 patients (mean age 62.7±11.3 y, 89 females) admitted consecutively to the ED department either after prolonged anginal episode or with the newly developed or worsening angina. Initial ACS diagnosis was based on ESC guidelines clinical criteria. Further diagnostic verification (ROC criteria) according to the in-hospital examination and 4 weeks follow-up. Triple biomarker index MultiHPC was derived as a sum of Log12[PAPP-A]+Log4[CRP]+Log14.2 (e powered by [HPT]) with the threshold value >3.
Results: After in-hospital examination and follow-up evaluation, ACS at admission was considered in 59 patients: according to the TnI test, 17 TnI-positive patients were referred as ‘true-positive’, 42 TnI-negative patients were “false-negative”. Other 95 patients had stable coronary artery disease (SCAD) and were TnI-negative (95 “true negative” and zero “false positive”). Thirty-two TnI-negative patients with ACS and 18 patients with SCAD had MultiHPC>3. When the MultiHPC criterion was added to the TnI, the net reclassification improvement (NRI) was 0.353 (p<0.001).
Conclusion: Addition of Triple biomarker index MultiHPC to the routine TnI test improved laboratory diagnosis of ACS significantly for a net of 35 per cent by increase in sensitivity and slight loss of specificity.

PERCUTANEOUS CORONARY INTERVENTION OUTCOMES: THINK LONG-TERM

4973 | BEDSIDE
The mode of dual antiplatelet therapy cessation is directly associated with adverse events even with 2nd generation DES: Insights from the PARIS registry
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Background: The risk of adverse outcome after stopping dual anti-platelet therapy (DAPT) in patients who have undergone percutaneous coronary intervention (PCI) is dependent on the context of treatment cessation. Whether these associations persist among unselected real-world patients after 2nd generation DES implantation remains unknown.
Methods: The PARIS (Patterns of non-adherence to Anti-platelet Regimens In Stented patients) registry was an observational multinational study of 5018 patients undergoing PCI with stenting, of whom 3533 (70.4%) received a 2nd generation DES. Cessation was categorized into physician-recommended discontinuation, brief interruption for surgery or disruption (due to non-compliance or bleeding). Association between DAPT cessation and adverse events among patients who received 2nd generation DES were examined using Cox regression with DAPT cessation modeled as a time-updated covariate.
Results: Over 2 years follow-up, 46% of patients remained on DAPT. Rates of discontinuation, interruption and disruption were 31%, 8% and 13%, respectively. Most MACE events (n=195) occurred while patients were on (n=149, 76.4%) rather than off (n=46, 23.6%) DAPT. Patients who disrupted DAPT were more often female, current smokers and more likely to present with ACS. Compared to those remaining on DAPT, disruption was associated with a 2-fold increased risk for ST while no ST occurred after interruption or discontinuation (Table). Patients who interrupted DAPT (<5 days) for surgery did not have higher rates of thrombotic MACE compared to patients on-DAPT.

Methods:
<table>
<thead>
<tr>
<th>On DAPT</th>
<th>Discontinuation</th>
<th>Interruption</th>
<th>Disruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=1704)</td>
<td>(N=1092)</td>
<td>(N=284)</td>
<td>(N=453)</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>1.0 (ref)</td>
<td>0.52 (2.21–1.29)</td>
<td>0.80 (0.25–2.61)</td>
</tr>
<tr>
<td>Procedural death</td>
<td>1.0 (ref)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>1.0 (ref)</td>
<td>0.73 (0.32–1.68)</td>
<td>1.72 (0.73–4.07)</td>
</tr>
<tr>
<td>MACE</td>
<td>1.0 (ref)</td>
<td>0.60 (0.32–1.13)</td>
<td>1.18 (0.57–2.46)</td>
</tr>
</tbody>
</table>

DAPT: dual antiplatelet therapy, ST: stent thrombosis; MI: myocardial infarction; MACE: cardiac death, ST, or MI.
Conclusion: Among unselected patients receiving 2nd generation DES, the impact of DAPT cessation on cardiac risk varies by mode and is modest overall with most events occurring among those on DAPT. DAPT is continued in almost half of patients, despite the safety seen for physician recommended discontinuation and brief interruption for surgery.
Impact of diabetes on clinical outcomes among women undergoing percutaneous coronary interventions with drug-eluting stents: a patient-level pooled analysis of 26 randomized trials

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Purpose: To evaluate the impact of diabetes mellitus (DM) on clinical outcomes among women with coronary artery disease undergoing percutaneous coronary interventions (PCI) with drug-eluting stents (DES).

Methods: We pooled patient-level data of 10,448 women undergoing PCI with DES from 26 randomized trials. Baseline characteristics and long-term clinical outcomes were stratified according to diabetes status at baseline. Associations between DM and outcomes were examined using Cox regression with trial entered as a random effect. The primary outcome was the composite of all-cause death and myocardial infarction (MI). Secondary outcomes were target-lesion revascularization (TLR), and definite or probable stent thrombosis (ST).

Results: Out of 10,448 women treated with DES, 3,294 (31.5%) had DM at baseline. Mean age was 67.2±10.6 with no differences according to diabetes status. Women with diabetes presented more frequently with stable CAD (60.9% vs. 54.4%, P<0.001) and had more comorbidities compared to non-diabetics. At 3 years follow-up, women with DM had higher risks of death or MI (12.6% vs. 8.7%; adjHR 1.51, 95%CI 1.27-1.80), death (7.9% vs. 4.5%; adjHR 1.86, 95%CI 1.07-1.10), MI (6.3% vs. 4.8%; adjHR 1.41, 95%CI 1.11-1.77), ST (2.5% vs. 1.2%; adjHR 2.19, 95%CI 1.43-3.36), and TLR (9.0% vs. 6.0%; adjHR 1.50, 95%CI 1.21-1.86) compared to women without diabetes (Fig. 1).

Conclusions: Women with diabetes undergoing PCI present more frequently with stable CAD than acute coronary syndromes and have a higher risk profile compared with women without diabetes. DM is associated with an increased risk of mortality and adverse ischemic events in women with coronary artery disease undergoing PCI with DES during long-term follow-up.

Lower 5-year event rates in the endothelial progenitor cell capturing stent compared with a drug eluting stent in de novo high-risk of restenosis coronary artery lesions; a randomized trial

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Aim: To evaluate the first long-term randomized adjudicated data regarding the safety and efficacy of the bio-engineered endothelial progenitor cell capturing stent (ECS) versus a drug eluting stent (DES).

Methods: In this prospective randomized pilot study, patients with de novo coronary artery lesions carrying a high risk of restenosis (chronic total occlusion, lesion length ≥ 23 mm, vessel diameter ≥ 2.8 mm, any lesion in a diabetic patient) were randomized to the ECS versus a DES (paclitaxel). Dual antiplatelet therapy (DAPT) was prescribed for ≥ 1 month in ECS and ≥ 6 months in DES. The primary endpoint is target vessel failure (TVF) at 5 years, a composite of cardiac death, myocardial infarction (MI) and target vessel revascularization, adjudicated by a clinical event committee. Clinical event rates were estimated by Kaplan-Meier method and compared with a log-rank test.

Results: A total of 193 patients were included with complete follow-up in 97% of the subjects. The primary endpoint of TVF was similar at 5 years with 23.8% in ECS vs 29.5% in DES (p=0.55) (fig 1). Between year two and year five the event rate is 4.1% in ECS vs. 17.2% in DES (p<0.01) (fig 2). DAPT cessation before 6 months after PCI was no independent predictor for the primary endpoint. The composite of death and MI was 6.3% in ECS vs 12.0% in DES (p=0.19). Definite stent thrombosis was observed in 4 cases in DES versus none in ECS.

Conclusions: The first randomized and adjudicated long-term results of the ECS versus a DES at 5 years show comparable performance and safety. Between two and five years a significant higher event rate was observed in the DES group compared with the ECS group. Importantly, no definite stent thrombosis was observed in the ECS treated group, compared with four cases in the DES group.

Long-term clinical outcomes after everolimus- and sirolimus-eluting coronary stents implantation: final 3-year follow-up of the reset

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Background: Long-term clinical outcomes of everolimus-eluting stent (EES) compared with sirolimus-eluting stent (SES) have not been fully evaluated yet, especially whether EES implantation could positively affect late adverse events reported after SES implantation occurring beyond 1 year.

Methods and results: In this all-comer prospective multicenter randomized open-label trial, 3196 patients were randomly assigned to implant either EES (N=1596) or SES (N=1600). At 3-year, EES was non-inferior to SES regarding the primary safety endpoint (all-cause death or myocardial infarction [MI]) (10.1% versus 11.5%, P non-inferiority=0.001, P superiority=0.19). Cumulative incidence of definite stent thrombosis (ST) was very low and was not different be-
tween the 2 groups (0.5% versus 0.6%, P=0.81). There was no significant difference in the efficacy endpoint of target-lesion revascularization (TLR) between the EES and SES groups (6.6% versus 7.9%, P=0.16). However, the cumulative incidence of target-lesion failure (TLF: cardiac death/target- vessel MI/ischemia-driven TLR) was significantly lower in the EES group than in the SES group (8.8% versus 11.4%, P=0.01). By a landmark analysis at 1-year, the cumulative incidence of very late ST and late TLR were not different between the 2 groups (0.2% versus 0.2%, P=0.99, and 2.2% versus 2.9%, P=0.21, respectively).

Conclusions: The efficacy and safety outcomes for this trial after EES implantation were comparable to those after SES implantation through 3-year follow-up. However, improvement of clinical outcome after EES implantation compared with SES implantation was suggested by the significantly lower cumulative incidences of TLF, which has been the most widely utilized endpoint in the stent-versus-stent trials.

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Long term follow-up of lesions with fractional flow reserve > 0.80: 10 year follow-up of patients treated with revascularization according to FFR

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Aim: Fractional Flow Reserve (FFR) assessment is recommended to judge the need for revascularization of coronary stenosis when no ischemia had been demonstrated. The aim of this study was to investigate 10 year outcomes of patients with or without revascularization.

Methods: From January 2000 to October 2003, 407 patients (452 coronary stenoses) were routinely submitted to FFR assessment. Based on FFR results, 136 (33%) underwent revascularization and 271 were left under optimal medical treatment alone. Follow-up was performed at 10 years for Major Adverse Cardiovascular Event (MACE), defined as death, acute coronary syndrome or revascularization. Three groups were defined: gr1 with FFR < 0.80 and immediate revascularization, gr2 without revascularization and FFR between 0.80 and 0.90, and gr3 without revascularization and FFR > 0.90. Outcomes were compared across groups with the adjusted Cox model. Analyses were repeated by lesions for acute coronary syndrome and revascularization.

Results: 10 year follow-up was available for 391 patients (96%): 53 (13.6%) patients died, 31 (8%) had an ACS and 136 (35%) had a MACE. By adjusted Cox model, there was no difference in survival, ACS or MACE-free survival across groups (figure). Analyses by lesion showed no impact of lesion severity according to angiography, or according to FFR on long term acute events or revascularization.

Conclusions: Under optimal medical treatment, patients with angiographic stenosis who are not submitted to revascularization for coronary stenosis based on FFR, have no excess of MACE or need for revascularization after 10 years as compared with those treated by revascularization. Neither angiographic percent stenosis nor FFR value were predictors of events.

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Effect of transient vs permanent no-reflow on long term mortality in patients undergoing primary angioplasty


Aim: Development of no-reflow (final TIMI <3 flow) in patients undergoing primary angioplasty for acute coronary syndrome is associated with increased mortality. However, affects of reflow on long-term mortality with intracoronary medication (transient) or affects of persistent no-reflow after intracoronary medication (permanent) on long-term mortality are not clear. In this study we sought to determine the affects of transient (TIMI 3 flow after intracoronary medication) and permanent (TIMI flow <3 despite intracoronary medication) no-reflow on long-term mortality.

Study design: 2993 patients (mean age 58.3, 675 female) undergone primary angioplasty for acute ST elevation myocardial infarction within first 12 minutes of pain without pretreatment with thrombolytics between 2006 January and 2010 February were investigated. 294 patients had post-procedural final TIMI 3 flow despite intracoronary medication (transient) and 2699 patients without no-reflow created control group.

Results: Patients in permanent no-reflow group were older and mostly diabetic. Pain to door time was longer and Killip class at presentation was higher significantly in permanent no-reflow group. Angiographic thrombus burden was higher and, cut-off occlusion pattern and proximal lesions were more common in permanent no-reflow group. Presence of pre-procedural TIMI 2/3 flow was significantly lower in permanent no-reflow group. In-hospital mortality was significantly higher in permanent no-reflow group (13.9% vs 17.1%, P=0.303). The composite of MACE at 12 months was not different in both groups (27.7 vs. 29.2%, P=0.754). Death, MI, or revascularization at 12 months were also not different in both groups. In multivariable analysis, no-reflow was not associated with increased risk of in-hospital mortality and adverse cardiac outcomes at 12 months when compared to control group.

Conclusions: Development of no-reflow in the management of STEMI was closely related to in hospital and long term mortality. Nevertheless, reversal of no-reflow after no-reflow development do not positively affect survival.
the best invasive strategy for this condition. Intravascular ultrasound (IVUS) can guide PCI. We aimed to describe the IVUS findings of ST and to compare the clinical outcomes between patients treated with additional stent implantation vs. balloon angioplasty (POBA).

Methods: Multicenter registry including all consecutive patients with late or very late ST undergoing IVUS-guided PCI in 5 institutions in 2009-13. The operator was left to decide the PCI strategy according to IVUS findings. IVUS were later analysed by 2 analysts, who performed a qualitative analysis of the images at baseline and after intervention. 4 items were recorded: late incomplete stent apposition (LISA), aneurysm, stent underexpansion and excessive neointimal proliferation.

Results: 86 patients included, 35 (40.7%) were diabetic, 49 (57.0%) of the ST were of drug-eluting stents (57.0%). The median (inter-quartile range, IQR) of the time after stent implantation was 3.5 years (1.1-5.7). The clinical presentation of the ST was STEMI in 72 (83.8%), 47 (54.7%) received an additional stent. Prior to intervention, there were no differences in the presence of LISA (74.4% vs. 70.2%, p=0.67), aneurysm (10.3% vs. 12.8%, p=0.72), stent underexpansion (20.5% vs. 14.9%; p=0.49) and excessive neointimal proliferation (5.1% vs. 10.6%, p=0.35) between patients treated with POBA vs additional stent implantation. After PCI, LISA was still observed in 33.3% of patients treated with POBA and 56.1% of patients treated with additional stent (p=0.08). Persistent stent underexpansion was observed in 10.0% and 7.3% of patients (p=0.67), respectively. Clinical follow-up was obtained from 83 patients at a median (IQR) of 2.0 years (1.1-3.3). Cardiac death was observed in 0% vs. 7.3% of patients treated without and with additional stent implantation (p=0.11), respectively. Definite or probable new ST was observed in 0% vs. 7.5% of patients (p=0.10), respectively.

Conclusions: The most frequent IVUS findings in late and very late ST were LISA and stent underexpansion. A simple strategy with POBA seems to improve the correction of LISA with respect to additional stent implantation. Although further investigations are required, additional stent implantation is associated with a trend towards worse outcomes at follow-up.

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Long-term ischemic and bleeding outcomes after primary percutaneous coronary intervention for ST-elevation myocardial infarction in the very elderly (80+ years)

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Purpose: Uncertainty exists about the appropriateness of primary PCI in patients undergoing pharmacologic and invasive therapies that have undergone clinical testing primarily in younger patients. We aimed to investigate long-term ischemic and bleeding outcomes after primary PCI in STEMI elderly patients aged ≥80 years.

Methods: Patients undergoing PCI in a large tertiary referral hospital between 2003 and 2008 were included and subdivided in 3 age groups: <60, 60-79, and ≥80 years. Endpoints at 3-year follow-up included all-cause mortality, MACE (a composite of cardiac mortality, recurrent myocardial infarction, target lesion revascularization), and bleeding (BARC bleeding ≥3). Multivariable Cox Regression models were constructed.

Results: A total of 2002 STEMI patients were included, 885 (44.2%) aged <60, 921 (46.0%) 60-79, and 196 (9.7%) ≥80 years. The median follow-up duration was 4.9 years (IQR 3.4-6.4 years). Co-morbidities such as diabetes mellitus, prior stroke, malignant disease, anemia, and chronic kidney disease were more prevalent in the very elderly. Three-year mortality, MACE and bleeding rates are shown in figure 1. Age ≥80 years was an independent predictor of mortality (HR 3.1, 95% CI 2.1-4.7, p<0.001), and a significant predictor of non-access site bleeding (HR 2.26, 95% CI 1.46-3.51, p<0.001).

Three-year clinical outcomes

<table>
<thead>
<tr>
<th>Patients aged</th>
<th>Patients aged</th>
<th>Patients aged</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60 years</td>
<td>60-79 years</td>
<td>≥80 years</td>
</tr>
<tr>
<td>Major adverse cardiac events</td>
<td>117/885 (20.3%)</td>
<td>301/921 (33.1%)</td>
</tr>
<tr>
<td>Death</td>
<td>59/885 (6.7%)</td>
<td>181/921 (19.7%)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>50/885 (5.7%)</td>
<td>134/921 (14.8%)</td>
</tr>
<tr>
<td>Recurrent myocardial infarction</td>
<td>87/885 (10.4%)</td>
<td>109/921 (13.3%)</td>
</tr>
<tr>
<td>BARC ≥3 bleeding</td>
<td>115/885 (13.1%)</td>
<td>200/921 (22.4%)</td>
</tr>
<tr>
<td>Non-access site related</td>
<td>57/885 (6.6%)</td>
<td>118/921 (13.4%)</td>
</tr>
</tbody>
</table>

Conclusions: Rates of both ischemic and bleeding events increased with age, with very high event rates in the very elderly. Strategies aimed at tailored pharmaco-invasive therapy for the very elderly to reduce bleeding and optimize control of co-morbidities may improve clinical outcomes in the elderly.

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Short and mid term comparative effectiveness of TAVR vs SAVR in a real world setting: results from the Italian OBSERVANT Study

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Purpose: To describe acute clinical outcomes of a large series of propensity-matched patients at low/intermediate risk undergoing transfemoral TAVR and surgical aortic valve replacement (SAVR).

Methods: OBSERVANT is an observational prospective multicenter cohort study, enrolling patients with severe aortic stenosis (AS) undergoing SAVR or TAVR. Propensity score method was applied to select two groups with similar baseline characteristics.

Results: The enrolled population included 5,864 SAVR and 1,935 TAVR patients. Matched population comprised 1,300 patients (650 patients for each group) with a relatively low risk profile (log-EuroSCORE: 10.2±9.2% vs. 9.5±7.1%; SAVR vs. TAVR; p=0.104). A higher incidence of renal failure occurred in the SAVR group (10.9% vs. 6.1%; p=0.04) whereas a higher incidence of residual aortic regurgitation (50.8% vs. 9.5%; p<0.001), major access site complications (7.9% vs. 5.1%; p<0.001) and permanent pacemaker implantation (15.5% vs. 3.6%; p<0.001) occurred in the TAVR group. Thirty-day mortality was 3.8% and 3.2% (SAVR vs. TAVR; p=0.546). Six-months mortality was 10.4% and 8.8% (HR=0.87; p=0.450).

Conclusions: Transfemoral TAVR and SAVR have comparable 30-day and 6-month mortality in low/intermediate risk patients with AS. SAVR was associated with a higher peri-procedural risk of renal failure and TAVR with a higher peri-procedural risk of residual aortic regurgitation, vascular damage, and permanent pacemaker requirement.

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Transcatheter aortic valve implantation in bicuspid aortic valve stenosis

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Purpose: Bicuspid aortic valve (BAV) stenosis is considered to be a relative contraindication to transcatheter aortic valve implantation (TAVI). We evaluated the TAVI outcomes in patients with BAV stenosis in a multinational registry.

Methods: Clinical characteristics, procedural data and outcomes were analysed in all patients with BAV stenosis at 12 international high-volume TAVI centres. Outcomes were assessed according to the Valve Academic Research Consortium criteria.

Results: The TAVI registry includes 141 patients undergoing TAVI for BAV stenosis (64.3%), regurgitation (0.7%), or mixed stenosis/regurgitation (34.3%). The mean age was 77.7±9.1 years, 66% were male, and the mean logistic EuroSCORE and STS mortality risk score were 14.6±10.6% and 4.9±3.6%, respectively. BAVs were classified as Type 0 (24.4%); Type 1 (65.6%); and Type 2 (4.6%). The Edwards SAPIEN (n=51) and Medtronic CoreValve (n=31) were both implanted. The implanted THV diameters were: 23 mm (7.0%), 26 mm (36.4%), 29 mm (42.7%), and 31 mm (14.0%). Major vascular complications were noted in 6.3%, device malposition in 6.3%, and 3.5% required implantation of a second THV during the index procedure. Overall procedural success was determined in 89.5% of patients. The mean post procedural transvalvular gradient was 11.5±9.8 mmHg and aortic regurgitation ≥ grade 2 occurred in 28.3% of cases. At 30-day follow-up, all-cause mortality or stroke occurred in 7.7% and 1.4%, respectively. A VARC device safety endpoint occurred in 22.4% and VARC efficacy was adjudicated in 83.9%.

Conclusions: TAVI for BAV disease is both feasible and safe, though post-implantation aortic regurgitation ≥ grade 2 occurs more frequently than reported in this group.
with tricuspid aortic valve stenosis. Further follow-up is required to determine the clinical efficacy in these patients.

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Incidence and clinical impact of stroke complicating transcatheter aortic valve implantations (TAVI). Results of the German TAVI Registry

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Background: Transcatheter aortic valve implantation (TAVI) has emerged as a safe and effective treatment option for patients with severe, symptomatic aortic valve stenosis at high surgical risk. However TAVI is still an invasive procedure usually performed in a frail population, carrying a substantial risk for vascular complications, like stroke, which is known as a serious complication of transcatheter interventional procedures like PCI. At present only sparse data exist on the incidence and clinical risk factors of stroke complicating TAVI in clinical practice today.

Methods: We analysed data of the prospective, multicenter German TAVI Registry, which operated from January 2009 until June 2010.

Results: 1413 TAVIs were performed between 01/2009 and 06/2010. Stroke occurred in 3.1% of all patients undergoing TAVI. Patients with stroke showed significantly increased mortality rates at hospital discharge and at 30-day follow-up compared to patients without stroke. Multivariate analysis showed prior stroke and renal impairment as the only independent predictors for stroke complicating TAVI.

Table 1 shows patient’s characteristics, procedural details and clinical outcome.

Table 1

<table>
<thead>
<tr>
<th>Stroke</th>
<th>No stroke</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>(90.9±6.5)</td>
<td>(81.8±6.2)</td>
</tr>
<tr>
<td>Euro-Score</td>
<td>22±12</td>
<td>20±13</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>44.4%</td>
<td>30.2%</td>
</tr>
<tr>
<td>Prior stroke (ischemic or bleeding)</td>
<td>20.0%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>77.8%</td>
<td>59.9%</td>
</tr>
<tr>
<td>Core valve prosthesis implanted</td>
<td>82.2%</td>
<td>81.9%</td>
</tr>
<tr>
<td>Edwards Sapien prosthesis implanted</td>
<td>17.8%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Atrial fibrillation at discharge</td>
<td>32.5%</td>
<td>19.9%</td>
</tr>
<tr>
<td>Clinical events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital death</td>
<td>28.9%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Death rate (30-day FU)</td>
<td>35.6%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Discharge to nursing home</td>
<td>8.9%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Conclusions: Stroke complicating TAVI is a rare but serious complication in clinical practice leading to a five-fold increase in 30-day mortality rate, as well as a significant increase in morbidity and disability of patients, who survive this complication.

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Impact of pre-existing atrial fibrillation on prognosis after transcatheter aortic valve implantation

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Objectives: Atrial fibrillation (AF) is highly prevalent in the elderly population around the world and significant predictors of cardiovascular events/death. Although many studies revealed that new-onset AF following TAVI is associated with poor outcomes, the predictive-value of pre-existing AF has not been thoroughly investigated in a large-cohort of TAVI-patients. The aim of our study was to determine the impact of pre-existing AF on clinical outcome after TAVI in a real-world setting.

Methods: Data were analyzed for 3051 patients (mean logistic-EuroSCORE: 21.9±14.3) enrolled French-national-TAVI-registry, FRANCE2.

Findings: Of the 3051 patients (mean age: 82.6±7.1 years) with TAVI, 820 (26.9%) had pre-existing AF. Compared with patients without AF, patients with AF had a significantly higher 30-day mortality and cumulative 1-year mortality rates (8.3% vs. 11.5%, p=0.007, 14.6% vs. 23.3%, p=0.001, respectively). After adjustment for considerable influential confounders in COX-regression multivariable model, AF was still associated with an increased risk of 30-day mortality, but independently associated with 1-year mortality (HR:1.23;95%CI:0.96-1.59; p=0.104, HR:1.50;95%CI:1.25-1.80; p<0.001, respectively), when compared to non-AF.

Conclusion: In this real-world TAVI registry, patients with pre-existing AF had a significantly worse survival outcome compared to patients without pre-existing AF. Pre-existing AF plays a crucial role in the selection process and is one of the major independent predictors of outcome after TAVI.

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Impact of reduced left ventricular ejection fraction on mid-term mortality after transcatheter aortic valve implantation

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Objectives: Whether patients with reduced left ventricular function present worse outcome after transcatheter aortic valve implantation (TAVI) is controversial. The aim of this study was assess the impact of baseline severe impairment of left ventricular function on mid-term mortality after TAVI.

Methods: Six-hundred-forty-nine patients with aortic stenosis underwent TAVI with the CoreValve system (92.8%) or the Edwards SAPIEN valve system (7.2%). Baseline LVEF was measured by the echocardiographic Simpson method. The impact of LVEF<30% on mortality was assessed by Cox regression.

Results: Patients with LVEF<30% (N=63), as compared to those with LVEF>30% (N=586), had a higher prevalence of NYHA class >2 (p<0.001) and presented with a higher Euroscore (p<0.001). Procedural success was similar in both groups (98.4% vs 97.2%, p=1). After a median follow-up of 436 days, all-cause mortality (23.8% vs 23.7%, p=0.87, HR 0.96, 95% CI 0.56-1.63) and cardiac mortality (19.1% vs 17.6%, p=0.89, HR 1.04, 95% CI 0.57-1.90) were similar in patients with LVEF<30% as compared to those with LVEF>30%. Thirty-day all-cause mortality was not significantly different between the two groups (11.1% vs 6.3%, p=0.14, HR 1.81, 95% CI 0.81-4.06). Patients with LVEF<30%, as compared to those with LVEF>30%, had a trend toward higher risk of 30-day cardiac mortality (11.1% vs 5.3%, p=0.06, HR 2.16, 95% CI 0.95-4.90), which disappeared after multivariable adjustment (p=0.22). In a prespecified subgroup analysis, compared to patients with LVEF>30%, patients with LVEF<30% presented with a mean transvalvular gradient at 1 month of -40 mmHg (lower gradient) presented a non-significant higher risk of all-cause death (31.6% vs 12.0%, p=0.14, HR 2.46, 95% CI 0.69-8.74) and of cardiac death (23.7% vs 12.0%, p=0.32, HR 1.90, 95% CI 0.51-7.03) as compared to patients with mean transvalvular gradient >40 mmHg (higher gradient).

Conclusions: In this multicenter registry, baseline severe impairment of LVEF was not a predictor of increased short-term and mid-term mortality after TAVI. Among patients with severe impairment of left ventricular function, those with low transvalvular gradient deserve a careful evaluation. Selected patients with severe impairment of left ventricular function should not be denied TAVI.
**BACKGROUND:** Transcatheter aortic valve implantation (TAVI) was first performed under general anesthesia (GA) but evidence is growing that TAVI can be done using local anesthesia (LA) when using the transfemoral approach. We compared LA-defined outcomes between patients with LA and those with GA for transfemoral TAVI using data from the French national TAVI registry “France 2”.

**Methods:** All consecutive patients underwent transfemoral TAVI between January 2010 and December 2011 in 34 centers were included in the France 2 registry. Outcomes were analyzed by multivariate analysis including all baseline and procedural variables.

**Results:** A total of 2871 consecutive patients were included; 1002 with LA (34.9%), 1896 (65.1%) with GA. Younger age, female sex, lower STS score, and no peripheral artery disease or porcelain aorta were independent predictors of the choice of LA over GA. The rate of LA increased significantly over time (P < 0.001), representing 28% in the 1st registry year vs. 41.7% in the 2nd year. The rate of device success and immediate mortality did not differ significantly between LA and GA groups (97.0 vs. 97.6%, P = 0.12; 3.6% vs. 2.8%, P = 0.30, respectively). Length of intensive care unit and hospital stay was greater in the GA group vs LA (3.94 ± 4.1 days vs. 3.44 ± 3.1 days, P = 0.002; 9.8 ± 8.3 vs. 8.8 ± 7.6 days, P = 0.001, respectively).

**Conclusion:** In this large real-world registry, we observed that transfemoral TAVI performed under LA was as safe and as effective as procedures performed under GA.

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**NEW MOLECULAR PLAYERS IN ATEROSCLEROSIS**

### 4980 | BEDSIDE

**TAVI in patients with low-flow, low-gradient aortic stenosis and preserved or reduced ejection fraction: results of the German Aortic Valve Registry (GARY)**

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**Objective:** Despite severe aortic stenosis (AS; AVA/BSA ≥ 0.6 cm²/m²), patients may present a mean transvalvular aortic gradient (MPG) > 40 mmHg due to LV dysfunction (“low-flow, low-gradient”; LS-AS) or concentric LV remodelling with reduced stroke volume (“paradoxical” low-gradient; PLG-AS). The impact of these findings on outcome after TAVI is undetermined. Herein, we analyzed the outcome of patients undergoing TAVI for LS-AS (MPG > 40 mmHg) due to LV dysfunction (“low-flow, low-gradient”; LG-AS) or concentric LV remodelling with reduced stroke volume (“paradoxical” low-gradient, PLG-AS). The results of these findings on outcome after TAVI is undetermined. Herein, we analyzed the outcome of patients undergoing TAVI for LG-AS (MPG > 40 mmHg).

**Methods and results:** 3908 pt undergoing TAVI were included in this ongoing non-randomized national multicenter registry. LG-AS, PLG-AS and HG-AS were present in n = 359 (9.2%); MPG: 26.5 ± 7.3 mmHg; EF: 30.3 ± 7.3%; n = 640 (16.4%); MPG: 30.7 ± 6.5 mmHg; EF: 60.2 ± 7.8% and n = 1864 (47.7%); MPG: 55.5 ± 13.8 mmHg; EF: 56.3 ± 12.5%; pt., respectively. EuroScore I (36.7 ± 20.9 vs. 22.6 ± 15.7 vs. 24.3 ± 17.4; P = 0.001) and patient age (79.1 ± 6.1 vs. 80.5 ± 5.6 vs. 81.3 ± 5.8; P = 0.001) were significantly different between groups. However, postoperative low cardiac output occurred more frequently in patients with LG-AS (8.7 vs. 4.0 vs. 4.2%; P = 0.05). Further, patients with LG-AS and PLG-AS required a longer duration of mechanical ventilation compared to HG-AS (30.0 ± 8.3 vs. 37.7 ± 125.0 vs. 24.8 ± 54.1 hours; P = 0.015).

**Conclusion:** Severe aortic stenosis with a mean transvalvular gradient > 40 mmHg is a common finding and present in ~25% of patients undergoing TAVI. In patients with low-flow, low-gradient AS in hospital mortality after TAVI is significantly higher, however, not in patients with “paradoxical” low gradient AS.

### 4989 | BENCH

**Is early discharge feasible and safe after transfemoral transcatheter aortic valve implantation?**

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**Background:** Length of stay after transcatheter aortic valve implantation (TAVI), as for many medical conditions, is more a report of historic performance than medical evidence. Shorter hospital stays may be cost-effectiveness and is also a feature of contemporary medical practice, but evidence is growing that TAVI can be done under local anaesthesia without major complications immediately after TAVI.

**Methods:** We studied the change in PCS between baseline and 1-year follow-up (Cohen’s D), and identified variables predictive of this change with multivariable linear regression analysis.

**Results:** In hospital mortality of pt with LG-AS was significantly higher than with HG-AS (7.8 vs. 4.9%, P = 0.001), in contrast, patients with PLG-AS had a comparable in-hospital mortality (P-LGAS 5.3% vs. HGAS 4.9%; P = 0.67). The rate of TAVI-associated complications was without significant differences (new pacemaker: 34.3 vs. LA group 35.5%, p = 0.09). Further, patients with L-GAS and P-LGAS required a longer duration of mechanical ventilation compared to HG-AS (30.0 ± 8.3 vs. 37.7 ± 125.0 vs. 24.8 ± 54.1 hours; P = 0.015).

**Conclusion:** Severe aortic stenosis with a mean transvalvular gradient > 40 mmHg is a common finding and present in ~25% of patients undergoing TAVI. In patients with low-flow, low-gradient AS in hospital mortality after TAVI is significantly higher, however, not in patients with “paradoxical” low gradient AS.
are presented by antigen-presenting cells like dendritic cells (DCs) and lead to the activation of T cells. Recently it has been shown that DCs are able to induce an antigen-specific tolerance in peripheral T cells, which is necessary to suppress the progression of atherosclerosis. In the present study, the cellular composition of atherosclerotic lesions was investigated to analyze the functional role of DCs as activators of pro-inflammatory T cells.

**Material and methods:** Cross-sections of 29 plaque specimens were classified as stable (14) and unstable (15) atherosclerotic lesions according to histological criteria (size of the lipid core, thickness of the fibrous cap, neovascularization). Carotid specimens (n=12) without signs of atherosclerosis from accident victims were used as control vessels. Immunohistochemical staining was performed to detect different types of myeloid DCs (S100, fascin, CD83, CD209) and plasmacytoid DCs (CD304, CD123), pro-inflammatory T cells (CD3, CD4, CD8, CD161), and regulatory T cells (FoxP3). Results: In stable compared to unstable lesions, significantly higher numbers of myeloid DCs (S100: 1.6-fold, p=0.01, fascin: 1.6-fold, p=0.03, CD83: 5.2-fold, p<0.003, CD209: 2.5-fold, p<0.004) and pro-inflammatory T cells like T helper cells (3.3-fold, p<0.008), cytotoxic T cells (3.4-fold, p=0.001), and natural killer cells (1.5-fold, p=0.03) were detected. A significant correlation between myeloid DCs and pro-inflammatory T cells (fascin-CD4: r=0.66, p<0.001, fascin-CD8: r=0.55, p=0.002, fascin-CD161: r=0.61, p<0.001) was visible. For plasmacytoid DCs no correlation was obvious. Also, there was a significantly higher degree of leukocyte infiltration compared to ApoE−/− animals (90402 vs. 28288 vs. 277590 μg/dl p<0.001 respectively). Aortic root analysis after western diet revealed a significantly less in sgk1−/− than in sgk1+/+macrophages and in control plasmid-transfected THP-1 cells with IKK-inhibitor BMS-345541 (145348 ± 3,356 vs 159,4 ± 4,059ng N=4 p=0.001, respectively). Zymographic MMP-9 production and invasion through matrigel in vitro were significantly higher in S422DSGK1-transfected THP-1 cells as compared to control plasmid- or empty vector-transfected THP-1 cells. As determined by Boyden chamber and thiglycollate-induced peritonitis, migration of SGK1-transfected CD11b+Fluc+ cells was significantly diminished in vitro and in vivo. Ymzagom MPP-9 production and invasion through matrigel in vitro were significantly less in sgk1−/− than in sgk1+/+macrophages and in control plasmid- or empty vector-transfected THP-1 cells compared to control plasmid- or K127NSGK1-transfected THP-1 cells. According to immunoblot analysis IKK- and IkB-phosphorylation was significantly lower in sgk1−/− macrophages than in sgk1+/+macrophages and significantly upregulated in sgk1−/−macrophages and significantly higher in S422DSGK1-transfected THP-1 cells as compared to control plasmid- or S422DSGK1-transfected THP-1 cells. Treatment of S422DSGK1-transfected THP-1 cells with IKK-inhibitor BMS-34544 (10μM) abolished S422DSGK1-induced increase of MPP-9 transcription and gelatinase activity. Since MPP-9 release is critical to the arterial remodeling process, these results indicate that SGK1 may play an important role in the regulation of MMP-9 production and invasion through matrigel in vitro and in vivo.

5010 | BENCH

**Dowregulation of ITCH prevents atherosclerosis through immune as well as metabolic effects**

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**Purpose:** To assess the role of ITCH, an E3 Ubiquitin Ligase involved in T-cell activation, in the generation of pro- or anti-inflammatory T cells.

**Methods:** We crossbred ITCH−/− with the hypercholesterolemic mouse model apoe−/−. The results indicate that mice lacking ITCH show reduced weight gain and a tendency to M2 (anti-inflammatory) T-cell differentiation alone we performed Bone Marrow Transplant (BMT) experiments. Cross-sections of 29 plaque specimens were classified as stable (14) and unstable (15) atherosclerotic lesions according to histological criteria (size of the lipid core, thickness of the fibrous cap, neovascularization). Immunohistochemical staining was performed to classify vessels. Immunohistochemical staining was performed to classify vessels.

**Results:** In stable compared to unstable lesions, significantly higher numbers of myeloid DCs and pro-inflammatory T cells like T helper cells and pro-inflammatory T cells like T helper cells (3.3-fold, p<0.008), cytotoxic T cells (3.4-fold, p=0.001), and natural killer cells (1.5-fold, p=0.03) were detected. A significant correlation between myeloid DCs and pro-inflammatory T cells (fascin-CD4: r=0.66, p<0.001, fascin-CD8: r=0.55, p=0.002, fascin-CD161: r=0.61, p<0.001) was visible. For plasmacytoid DCs no correlation was obvious. Also, there was a significantly higher degree of leukocyte infiltration compared to ApoE−/− animals (90402 vs. 28288 vs. 277590 μg/dl p<0.001 respectively). Aortic root analysis after western diet revealed a significantly less in sgk1−/− than in sgk1+/+macrophages and in control plasmid-transfected THP-1 cells with IKK-inhibitor BMS-345541 (145348 ± 3,356 vs 159,4 ± 4,059ng N=4 p=0.001, respectively). Zymographic MMP-9 production and invasion through matrigel in vitro were significantly higher in S422DSGK1-transfected THP-1 cells as compared to control plasmid- or empty vector-transfected THP-1 cells. As determined by Boyden chamber and thiglycollate-induced peritonitis, migration of SGK1-transfected CD11b+Fluc+ cells was significantly diminished in vitro and in vivo. Ymzagom MPP-9 production and invasion through matrigel in vitro were significantly less in sgk1−/− than in sgk1+/+macrophages and in control plasmid- or empty vector-transfected THP-1 cells compared to control plasmid- or K127NSGK1-transfected THP-1 cells. According to immunoblot analysis IKK- and IkB-phosphorylation was significantly lower in sgk1−/− macrophages than in sgk1+/+macrophages and significantly upregulated in sgk1−/−macrophages and significantly higher in S422DSGK1-transfected THP-1 cells as compared to control plasmid- or S422DSGK1-transfected THP-1 cells. Treatment of S422DSGK1-transfected THP-1 cells with IKK-inhibitor BMS-34544 (10μM) abolished S422DSGK1-induced increase of MPP-9 transcription and gelatinase activity. Since MPP-9 release is critical to the arterial remodeling process, these results indicate that SGK1 may play an important role in the regulation of MMP-9 production and invasion through matrigel in vitro and in vivo.
and plaque destabilization we analyzed neointima formation and plaque rupture in apo−/−sgk1−/− mice. As a result, we found significantly reduced incidence of plaque ruptures (buried caps) in apo−/−sgk1−/− mice compared to apo−/−sgk1+/+ mice.

**Conclusions:** SGK1 plays a pivotal role in vascular inflammation during atherosclerosis induced by hypercholesterolemia and balloon injury.

**Methods:** To investigate the effect of PAR2 in atherosclerosis, we generated PAR2−/−Apoe double deficient mice. Beginning at age of 2 months, animals were either fed standard chow or a cholesterol-rich Western diet over 2 or 4 months, respectively, in comparison with Apoe control mice (both C57BL/6 background).

**Results:** PAR2−/−Apoe mice were fed either fed standard chow or a cholesterol-rich Western diet over 2 or 4 months.

**Discussion:** In PAR2−/−Apoe mice, cholesterol feeding induced neointima formation, increased vascular inflammation, and increased vascular remodeling.

**Conclusions:** PAR2−/−Apoe mice showed a significant decrease in SMC content within the lesions whereas apoptosis was markedly increased after 4 months of cholesterol-rich diet in comparison with PAR2−/−Apoe mice. Infiltration of macrophages was significantly higher in Apoe mice and remained elevated at high levels during cholesterol feeding. In comparison, macrophage content in Apoe mice in early lesions, however markedly increased during cholesterol feeding. Interestingly, the rate of apoptosis greatly increased in Apoe mice at 4 months, while it remained low in PAR2−/−Apoe animals. This may suggest a delayed macrophage infiltration and attenuated apoptosis in the PAR2−/−Apoe mice. In SMC isolated from C57BL/6 mice, incubation with FXa caused a time-dependent increase in expression of IL-6 and MCP-1. This was attenuated in SMC from PAR2 mice, suggesting a regulatory role of PAR2.

**Conclusion:** The deficiency of PAR2 attenuated the development of atherosclerotic lesions in Apoe mice. Furthermore, we observed decreased apoptosis and decreased expression of PAR2 in Apoe mice. A PAR2-dependent regulation of pro-inflammatory mediators such as IL-6 and MCP-1 may contribute to this atherogenic effect of PAR2.

**5014 | BENCH**

**Aerolized coronary atherosclerotic model in a novel low density lipoprotein receptor knockout-knock out swine**


**Purpose:** Accelerated coronary atherosclerotic model in novel low density lipoprotein receptor adenovirus vectorization in P AR2/ApoE mice. In SMC isolated from C57BL/6 mice the incubation with FXa increased the activity of caspase-3.

**Results:** In the subchronic model, the expression of SCF, c-kit and other angiogenic factors was up-regulated in Apoe−/−sgk1−/− mice compared to Apoe−/− mice. As a result, we found significantly reduced activity of PAR2 in SMC isolated from C57BL/6 mice.

**Conclusions:** PAR2−/−Apoe mice showed a significant decrease in SMC content within the lesions whereas apoptosis was markedly increased after 4 months of cholesterol-rich diet in comparison with PAR2−/−Apoe mice. Infiltration of macrophages was significantly higher in Apoe mice and remained elevated at high levels during cholesterol feeding. In comparison, macrophage content in Apoe mice in early lesions, however markedly increased during cholesterol feeding. Interestingly, the rate of apoptosis greatly increased in Apoe mice at 4 months, while it remained low in PAR2−/−Apoe animals. This may suggest a delayed macrophage infiltration and attenuated apoptosis in the PAR2−/−Apoe mice. In SMC isolated from C57BL/6 mice, incubation with FXa induced a time-dependent increase in expression of IL-6 and MCP-1. This was attenuated in SMC from PAR2 mice, suggesting a regulatory role of PAR2.

**Conclusion:** The deficiency of PAR2 attenuated the development of atherosclerotic lesions in Apoe mice. Furthermore, we observed decreased apoptosis and decreased expression of PAR2 in Apoe mice. A PAR2-dependent regulation of pro-inflammatory mediators such as IL-6 and MCP-1 may contribute to this atherogenic effect of PAR2.

**5070 | BENCH**

**Right ventricular functions in patients with breast cancer treated with chemotherapy**

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**Objectives:** To assess the effects of chemotherapy on right ventricular (RV) echocardiographic indices

**Methods:** Echocardiograms (n=200) were performed at baseline and after 4 cycles (101±27 days) of chemotherapy (ChemoRx) in 100 female patients (51±10 years) with breast cancer. The mean cumulative dose of doxorubicin was 234 mg/m².

**Results:** Of 100 patients, 21 and 3 patients developed post-ChemoRx RV and LV systolic dysfunction respectively. RV functions were shown in Table 1. Advanced cancer stage (TNM stage ≥3B) increased risk of RV systolic dysfunction post ChemoRx, Odd ratio=4.62 (1.98-17.881, p=0.02).

Table 1

<table>
<thead>
<tr>
<th>Pre-chemotherapy</th>
<th>Post-chemotherapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial blood pressure (mmHg)</td>
<td>92±9</td>
<td>91±9</td>
</tr>
<tr>
<td>RV systolic function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV fractional area change (%)</td>
<td>56±9</td>
<td>50±11</td>
</tr>
<tr>
<td>Tricuspid annular plane excursion (TAPSE) (mm)</td>
<td>22±3</td>
<td>20±3</td>
</tr>
<tr>
<td>Tricuspid peak systolic annulus area (average S') (cm²)</td>
<td>13±2</td>
<td>12±2</td>
</tr>
<tr>
<td>RV diastolic function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid early annular tissue velocity (e') (cm/s)</td>
<td>10.9±2.8</td>
<td>10.0±2.3</td>
</tr>
<tr>
<td>Tricuspid E/A</td>
<td>5.7±1.1</td>
<td>6.0±1.5</td>
</tr>
<tr>
<td>Tricuspid E deceleration time (msec)</td>
<td>252±77</td>
<td>243±72</td>
</tr>
<tr>
<td>Hepatic venous diastolic reverse velocities (cm/s)</td>
<td>27±9</td>
<td>28±8</td>
</tr>
<tr>
<td>Right atrial volume index (m³/m²)</td>
<td>18±5</td>
<td>19±6</td>
</tr>
<tr>
<td>Global RV function – RV Tei index*</td>
<td>0.28±0.18</td>
<td>0.36±0.17</td>
</tr>
<tr>
<td>RV fractional area change (%)</td>
<td>35%</td>
<td>31%</td>
</tr>
<tr>
<td>RV systolic pressure (mmHg)</td>
<td>27±4.7</td>
<td>27±1.4</td>
</tr>
</tbody>
</table>

**Conclusions:** (1) RV systolic, diastolic, and global functions were significantly impaired after ChemoRx. (2) RV systolic dysfunction post ChemoRx was more severe than LV systolic dysfunction. (3) Further studies regarding prognosis of RV dysfunction in these patients are needed.
and markers of endothelial and mesenchymal stem cells were significantly decreased. We observed a decreased expression of VEGF, but no change for HGF and fibronectin. CMR applied a t-test for paired groups, a value of p<0.05 was considered statistically significant.

Results: There is a statistically significant reduction in LVEF after 18 months follow-up when compared with basal measurements (61.5%±8.3% vs 56.6%±8.3%, p<0.03) Two patients developed late-enhancement in septal area. This is the first report of the relationship between nimotuzumab and cardiac function. It is also relevant because we implement a non-traditional method for LVFE screening in oncologic patients.

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5073 | BEDSIDE

Cardiac sympathetic nerve activity of I-123 MIBG imaging is unrelated to left ventricular dysfunction during trastuzumab therapy

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Purpose: Trastuzumab is a humanized monoclonal antibody that binds to the extracellular domain of the human epidermal growth factor receptor 2 (HER2) and inhibits breast cancer proliferation. Cardiotoxicity has been reported to occur with trastuzumab when administered alone and in combination with anthracyclines. Cardiac iodine-123 metaiodobenzylguanidine (I-123 MIBG) imaging is useful to estimate cardiac sympathetic nerve activity. Many studies indicate that assessment of impaired I-123 MIBG uptake would be useful for the evaluation of antihypertensive cytoxicity. However, it remains unclear that the relationship between trastuzumab-induced cardiac dysfunction and cardiac sympathetic nerve damage using I-123 MIBG imaging. The aim of this study was to assess the value of I-123 MIBG scintigraphy in breast cancer patients treated with trastuzumab who showed a decrease in their cardiac function.

Methods: We performed cardiac I-123 MIBG imaging in 19 female breast cancer patients (mean age 52±12 years, range 31-70 years) who demonstrated a significant cardiotoxicity during trastuzumab therapy. Cardiotoxicity was defined as a left ventricular ejection fraction (LVEF) decrease below 60% measured by echocardiography. I-123 MIBG imaging was obtained at the early (15 min after tracer injection) and delayed (4 hr after) phases. The heart to mediastinum ratio (H/M) and the global washout rate (WR) were calculated.

Results: 20% patients (49%) were treated with trastuzumab alone and 17 patients (89%) were used in combination with anthracyclins-based regimens. 11 patients (58%) had radiotherapy, of whom 6 patients on the breast. The mean of delayed H/M ratio was 2.92±0.73 (1.77-4.48) and the mean of WR was 20.6±7.7% (8.2-35.8). I-123 MIBG scintigraphy showed abnormal H/M ratio (< 2.0) in one patient and slightly increased WR (< 30%) in three patients. LVEF was no correlation with the delayed H/M ratio (r=0.20, p=NS) and WR (r=0.12, p=NS), respectively.

Conclusions: These data indicate that trastuzumab-induced LV dysfunction do not reflect cardiac adrenergic neurone abnormalities. The mechanism of trastuzumab-induced cardiotoxicity may differ from anthracycline-induced cardiac neurotoxicity.

NOVEL ANTICOAGULANTS: TRIALS, COST, REAL LIFE USE

5108 | BEDSIDE

Efficacy and safety of apixaban vs edoxaban for stroke prevention in non-valvular atrial fibrillation: an indirect treatment analysis

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Purpose: Vitamin K antagonists (VKA) have been standard of care for the prevention of stroke in patients with non-valvular atrial fibrillation (NVAF). However, the novel oral anticoagulants (NOACs) apixaban, dabigatran and rivaroxaban offer a therapeutic advantage over standard VKA treatment. Results for an additional NOAC, edoxaban have recently been published and the aim of this analysis was to compare the efficacy and safety of apixaban and edoxaban in the management of stroke prevention in NVAF.

Methods: Data from two phase III, double-blind randomised controlled trials included: apixaban [ARISTOTLE, apixaban 5 mg bid (n=9,120) vs warfarin (n=9,081)]; edoxaban [ENGAGE AF-TIMI, 30 mg od (n=7,034) vs 60 mg od (n=7,035)]; warfarin [WARFARIN, 30 mg od (n=7,034) vs 60 mg od (n=7,035)]. An adjusted indirect comparison using Bucher methodology and a network meta-analysis (NMA) were performed, using warfarin as the common comparator.

Conclusions: Apixaban was significantly more efficacious than edoxaban 30 mg for the prevention of both stroke and intracranial haemorrhage. Apixaban had an intermediate safety profile between the two edoxaban doses, with a significantly lower incidence of major or clinically relevant non-major bleeding (CRNM) vs edoxaban 60 mg, compared with a higher incidence vs edoxaban 30 mg.
Table 1. Results of indirect comparison

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axipaban vs edoxaban 30 mg</td>
<td>0.69 (0.55, 0.88)**</td>
</tr>
<tr>
<td>Axipaban vs edoxaban 60 mg</td>
<td>0.67 (0.50, 0.88)**</td>
</tr>
<tr>
<td>Major or CRNM bleeding</td>
<td>1.14 (0.99, 1.30)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.14 (1.21, 1.94)*</td>
</tr>
<tr>
<td>Intracranial haemorrhage</td>
<td>1.37 (0.85, 2.22)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>1.03 (0.88, 1.20)</td>
</tr>
<tr>
<td>Total discontinuations</td>
<td>0.96 (0.87, 1.06)</td>
</tr>
</tbody>
</table>

CI: confidence interval; CRNM, clinically relevant non-major bleeding; SE, systemic embolism.

*p<0.05.

mg. Compared with apixaban, patients treated with edoxaban 60 mg were more likely to discontinue treatment (Table 1).

Conclusions: Based on this indirect comparison analysis, apixaban offered a significant benefit over edoxaban 30 mg for stroke prevention. When compared with edoxaban 60 mg, apixaban was superior for the reduction of major or CRNM bleeding and had lower discontinuations.

5109 | BEDSIDE

Potential impact of apixaban on formulary budget and clinical outcomes in non-valvular atrial fibrillation patients

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Purpose: The goal of this study was to assess impact of apixaban on resource utilization in patients with non-valvular atrial fibrillation (NVAF) to the NHS in the United Kingdom.

Methods: A model was developed to analyze the impact of introducing apixaban in a representative NVAF population on 5-year total healthcare costs. Treatment patterns and market share projections were based on current market research data, with assumptions of projected future market shares. Model assumes that the apixaban market share is drawn equally from dabigatran, rivaroxaban, vitamin K antagonist (VKA) and aspirin. Effect size of apixaban vs VKA and aspirin were derived from randomized controlled trials and against other novel oral anticoagulants from indirect treatment comparisons. Measured in 2012 values, cost inputs were obtained from the published data sources. Annual discounting rate of 3.5% was applied.

Results: Model projected that 384,400 patients (62% of the treatment eligible population) would be treated with anticoagulants over the 5-year study period. Assuming a 10% uptake of apixaban over 5 years, an increase of 1.2% (∼£25.6 million) in the total healthcare budget was estimated including medical cost savings of ∼£111 million. This translated into net increase of £13.33 per treated patient per year from the NHS perspective. More importantly, 322 strokes, 417 major bleeds, 515 CRNM bleeds, 94 myocardial infarctions and 406 CV hospitalisations were avoided during the 5-year study period with the addition of apixaban (Fig. 1).

Conclusions: Addition of apixaban has a minimal increase in the healthcare budget over a 5-year period. This addition provides better outcomes with drug costs offset by medical cost savings elsewhere.

5110 | BEDSIDE

Cost-effectiveness of high-dose edoxaban compared to adjusted-dose warfarin for prevention of stroke and systemic embolism in non-valvular atrial fibrillation

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Purpose: High-dose edoxaban has been shown to be non-inferior to adjusted-dose warfarin for the prevention of stroke or systemic embolism in non-valvular atrial fibrillation (NVAF) patients; while resulting in lower rates of intracranial haemorrhage (ICH) and cardiovascular death. We assessed the cost-effectiveness of high-dose edoxaban compared to adjusted-dose warfarin for the prevention of stroke and systemic embolism in patients with NVAF.

Methods: A Markov model was constructed to compare the cost-effectiveness of high-dose edoxaban (60 mg once daily, 30 mg daily in patients with a creatinine clearance of 30-50 mL/minute, a body weight of <60 kg or the concomitant use of a potent P-glycoprotein inhibitor) and adjusted-dose warfarin (target international normalized ratio (INR) range of 2.0-3.0) from a United States (US) payer/Medicare perspective. The base-case analysis assumed a cohort of 70-year-old patients with NVAF at moderate-to-high risk of ischemic stroke (CHADS2=2), a creatinine clearance >30 mL/minute and no previous contraindications to anticoagulation. Data sources included the Edoxaban versus Warfarin in Patients with Atrial Fibrillation Trial (ENGAGE AF-TIMI 48) and other studies of anticoagulation. Outcome measures included life-time costs in 2013 US dollars, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs).

Results: In the base-case analysis, patients treated with high-dose edoxaban lived an average of 10.32 QALYs at a lifetime treatment cost of $100,223. Those receiving adjusted-dose warfarin lived an average of 10.12 QALYs and incurred costs of $117,719, suggesting high-dose edoxaban to be a dominant economic strategy. These results were most sensitive to changes in associated costs and utility of edoxaban and warfarin (including INR testing, clinic visits and patient time), the monthly cost of treating ICH and the model’s time horizon. Upon Monte Carlo simulation, high-dose edoxaban was found to be cost-effective in 76% of the 10,000 iterations, assuming a willingness-to-pay threshold of $50,000/QALY.

Conclusion: Our Markov model suggests high-dose edoxaban is a cost-effective alternative to adjusted-dose warfarin for the prevention of stroke and systemic embolism in NVAF patients at an increased risk of stroke.

5111 | BEDSIDE

Uptake in new oral anticoagulation agents in anticoagulant naive atrial fibrillation patients: nationwide data 2011-2013

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Purpose: New oral anticoagulation (OAC) agents have been approved for stroke prophylaxis in atrial fibrillation (AF). In “real-world” registries we investigated how these new drugs are being adopted.

Methods: Using a Danish nationwide administrative dataset we identified all OAC-naïve AF patients initiating OAC from August 22nd, 2011 through October 31st, 2013. Baseline characteristics and temporal utilization trends were compared between initiators of warfarin vs. one of the new OACs: dabigatran, rivaroxaban, or apixaban.

Results: We included 18,611 OAC-naïve AF patients; 9902 (53%) initiated warfarin treatment, 7128 (38%) dabigatran, 1303 (7%) rivaroxaban, and 278 (1%) apixaban. Uptake of dabigatran was quick, and 40% of newly initiated patients were started on dabigatran within the first 4 months of when the drug came on market (Figure). By October, 2013 40% were being started on warfarin and dabigatran, respectively, and another 20% were started on either rivaroxaban or apixaban. Rivaroxaban and apixaban users generally had a higher predicted risk of stroke and bleeding, i.e. higher CHADS2-VASc and HAS-BLED scores, compared to warfarin and dabigatran users. Older age, female gender, and a prior stroke were some of the factors associated with new OAC use vs. warfarin, whereas chronic kidney disease, myocardial infarction, and heart failure showed the opposite association.

Conclusions: In a contemporary setting among OAC-naïve patients with AF who are initiated on an OAC, the use of warfarin has declined since the introduction of dabigatran in August 2011. This shift in treatment patterns could result in major winnings for patients with AF. Compared to warfarin, new OACs are more frequently used in older and female patients.
P5112 | BEDSIDE
Real world discontinuation among early users of apixaban, dabigatran, rivaroxaban or warfarin among atrial fibrillation patients newly initiated on anticoagulation therapy: tell of first 200 days

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Purpose: This study evaluated discontinuation of apixaban, dabigatran, and rivaroxaban in the first 200 days after launch in patients with atrial fibrillation (AF) in the US real-world clinical practice setting.

Methods: A retrospective cohort study was conducted using MarketScan® including the EarlyView data. AF Patients - 18 years (ICD-9 code 427.31 or 472.32) with one year of baseline period were included if they were newly prescribed the novel oral anticoagulants (NOACs) during the first 200 days after their availability in the US market, or newly prescribed warfarin after apixaban launch. Discontinuation was defined as lack of subsequent prescription of the index drug within 30 days after the last supply day of the last prescription. Cox proportional hazards model was used to compute hazard ratio (HR) of discontinuation, adjusting for potential confounders and other important patient characteristics.

Results: Among 17,356 eligible patients, 841 (4.85%) were initiated with apixaban, 5,805 (33.45%) with dabigatran, 2,125 (12.24%) with rivaroxaban and 8,585 (49.46%) with warfarin. The mean age of apixaban, dabigatran, rivaroxaban and warfarin patients were 70.3±12.0 years, 69.1±12.4 years, 69.2±12.1 years and 71.9±12.3 respectively. After adjusting baseline patient characteristics, apixaban was significantly less likely to discontinue versus rivaroxaban (HR: 0.60, CI: 0.48, 0.74) and rivaroxaban (HR: 0.52, CI: 0.45 - 0.67) (Figure).

Conclusion: The risk of discontinuation was lower for apixaban versus rivaroxaban or warfarin among newly anticoagulated AF patients. These early findings with relatively short follow-up should be confirmed in future with larger sample size and longer term follow-up.

Poster Session 6
RESPONSES TO EXERCISE TESTING AND TRAINING

P5114 | BEDSIDE
Impact of low versus upper range intensity exercise training on metabolic markers of endothelial function and oxidative stress in patients with coronary artery disease

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Purpose: To evaluate the impact of low versus upper range intensity exercise training on endothelial function, through assessment of circulating blood markers of endothelial function: the stable end product of nitric oxide (NOx), dimethylarginine (ADMA), symmetric dimethylarginine (SDMA), xanthine oxidase (XO), and advanced oxidative protein products (AOPPs). Marker of oxidative stress in patients (pts) with stable coronary artery disease (CAD).

Methods: Fifty one male pts admitted at residential rehabilitation center were studied. Patients were randomized to low intensity exercise (65% of maximal heart rate; LI group, n=26; mean age 56.9±7.8 years) and to upper range intensity exercise (85% maximal heart rate; UI group, n=25; 53.1±8.0 years). Patients exercised twice a day at residential center over a period of 3 weeks. At baseline and 3 weeks later, in all pts values of NOx, ADMA, SDMA, XO and AOPPs were evaluated and exercise test was performed.

Results: After 3 weeks NOx increased significantly in both groups; in LI group from 36.7±10.1 to 42.0±14.2 μmol/L (P<0.021), and in UI group from 33.4±7.3 to 44.6±19.9 μmol/L (P<0.0005). Value of ADMA as well as SDMA decreased significantly in both groups after 3 weeks: in LI (P<0.005 and P<0.004) and in UI group (P<0.005 and P<0.005).

Conclusion: In patients with CP the novel ex-HFQRS-analysis shows a valuable incremental diagnostic value over the ex-ECG with ST-segment-analysis. In patients with IHD-pos the most significant difference with IHD-neg was in DVO2/DWR slope (7.8 (1.5) vs 8.9 (1.8), P<0.001), and O2pulse at peak exercise (9.2 (2.6) vs 12.4 (2.3) μl/min, P<0.001). Follow up lasted 36 (11) months. Patients with IHD-neg had 12 cardiovascular events (CABG in 6, PCI in 4, ACS in 2), while IHD-neg had only 2 events (PCI in 2; P<0.001). In conclusion, NET – a inexpensive, non-operator dependent, safe and noninvasive test- may be used in patients with LLBB to detect/exclude myocardial ischemia on the basis of VO2kinetics and O2pulse.

P5116 | BEDSIDE
Cardiopulmonary exercise testing in patients with left bundle branch block: A new method to detect or exclude ischemic heart disease

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Between 2007 and 2012 we performed 5,781 cardiopulmonary exercise stress tests (CPET) at our Institute’s CPET core laboratory. Aim of the study was to determine the outcome of patients with left bundle branch block (LLBBB) with diagnosis of ischemic heart disease (IHD). Ischemic heart disease was present in 59% of patients, chronic heart failure (CHF) in 22%, valvular heart disease (VHD) in 13% and hypertension in 6%. Myocardial ischemia (MI) was detected in 21 patients with IHD (pos), and excluded in 338 (neg) on the basis of previously-described criteria. Briefly, MI was considered when double slope sign in DVO2/DWR slope combined with a negative downward flattening in O2pulse are both evident (AUC 0.84), while MI was excluded when the above abnormalities were not present. All CPET studies were stopped for exhaustion (92%) or dyspnea (8%) at a RER>1.05. In 21 IHD-pos the most significant difference with IHD-neg was in DVO2/DWR slope (7.8 (1.5) vs 8.9 (1.8), P<0.001), and O2pulse at peak exercise (9.2 (2.6) vs 12.4 (2.3) μl/min, P<0.001). Follow up lasted 36 (11) months. Patients with IHD-neg had 12 cardiovascular events (CABG in 6, PCI in 4, ACS in 2), while IHD-neg had only 2 events (PCI in 2; P<0.001). In conclusion, CPET – a inexpensive, non-operator dependent, safe and noninvasive test- may be used in patients with LLBBB to detect/exclude myocardial ischemia on the basis of VO2kinetics and O2pulse.

Poster Session 6 / Responses to exercise testing and training
P5117 | BEDSIDE
Patients with primary microvascular angina present functional capacity impairment comparable to systolic heart failure patients
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**Purpose:** The primary microvascular angina (PMA) is a chronic condition associated with impaired myocardial perfusion and an increased risk of cardiovascular events. Despite this evidence, there is scarce information about the functional capacity and chronotropic response in patients with PMA. We aimed at assessing the functional capacity and cardiopulmonary test variables obtained in patients with PMA, patients with systolic heart failure (HF) and healthy controls.

**Methods:** We studied 15 patients with PMA, defined as presence of typical angina associated with reversible perfusion defects in myocardial perfusion scintigraphy and no obstructive epicardial coronary lesions on coronary angiography (6 men, 54.4±8.9 years and BMI = 31.1±5.5 kg/m²); 14 HF patients (10 men, 55.8±13.2 years, NYHA class II – III and BMI = 29.7±4.5 kg/m²) and 15 healthy controls (8 men, 48.6±11.6 years and BMI = 28.1±5.3 kg/m²). The 3 groups underwent maximal cardiopulmonary exercise testing (RER >1.1) using a treadmill protocol.

**Results:** No significant difference was found between groups regarding age and BMI (p=0.05). PMA patients presented higher values for left ventricular ejection fraction (65.8±11.7%) when compared to HF patients (33.4±17.6%), p<0.0001. PMA and HF groups showed similar peak VO2 (19.7±5.4 and 17.6±3.2 ml/kg/min, p=0.05), but both values were reduced as compared dysvascular control group (27±5.6 ml/kg/min, p<0.0001). VO2 at anaerobic threshold also presented comparable values between PMA (11.8±2.6 ml/kg/min) and HF patients (11.4±2.1 ml/kg/min), p=0.05, being both values reduced as compared to controls (15.7±2.2 ml/kg/min), p<0.0001. The chronotropic reserve in PMA (60.2±20.1 bpm) and HF patients (49.4±23.9 bpm) were also similar (p=0.05), but reduced as compared to control group (87.3±15.1 bpm), p<0.0001.

**Conclusion:** Our results indicate that patients with PMA present a significant reduction in functional impairment. This is similar to that exhibited by patients with systolic HF. The mechanisms responsible for these changes demand further investigation.

P5118 | BEDSIDE
Impact of cardiovascular risk factors and pre-test symptoms on relationship between age and peak heart rate during treadmill testing in women
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**Background:** We sought to determine the effects of cardiovascular risk factors (CVRFs) and pre-test symptoms on the intercept and slope of the linear relationship between peak heart rate (pHR) and age during exercise treadmill testing (ETT).

**Methods:** Consecutive women who underwent symptom-limited Bruce protocol ETT at Mayo Clinic from 1994 - 2010 were included. Women with cardiovascular disease or on beta blockers were excluded. The relationship of pHR to age, pre-test symptoms, current smoking, diabetes, obesity, hypertension, and hyperlipidemia added to the model. P<0.01 was considered significant.

**Results:** 11,029 women (90% Caucasian, age 52±12 years, Duke Treadmill Score 4.9±4) were included. Baseline pre-test symptoms were reported in 3632 women (32.9%). CVRFs included: smoking 8.4%, diabetes 3.5%, obesity 26.4%, hypertension 15.8%, hyperlipidemia 16.9%. Peak HR was predicted as 201 - 0.67 age only included; second, age, pre-test symptoms, current smoking, diabetes, obesity, hypertensive medications and BMI (p<0.0001). T able shows the effect of CVRFs on pHR. Smoking was a weak negative predictor of late mortality (likely a consequence of associated hypertension). Male gender and smoking were associated with increased peak VO2, peak METs and HRR. Hypertension and hyperlipidemia were associated with reduced peak VO2 and peak METs, but increased HRR.

**Conclusion:** The associations between arterial stiffness and slow HRR/reduced EC in apparently healthy individuals could be partially explained by impaired baroreflex sensitivity and endothelial dysfunction. Further experimental research is required to illuminate the underlying mechanisms.

P5120 | BEDSIDE
Chronotropic incompetence detected on screening exercise treadmill testing: a strong predictor of long-term mortality when present in individuals on a beta blocker or calcium channel antagonist
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**Purpose:** To test the hypothesis that chronotropic incompetence (CI) is predictive of mortality in individuals screened for cardiovascular disease.

**Methods:** 34,551 consecutive exercise treadmill tests (TMET) in individuals without previously documented heart disease, but including treated hypertensives were analyzed using impaired heart rate reserve as a marker for CI.

**Results:** 5327 (15.4%) had CI - 67.9% were male. There were 1275 deaths over a median follow-up of 12.4 years. The mortality in individuals with CI was over twice that for non CI patients - 6.89% versus 3.11% (P<0.0001). Multivariate analysis demonstrated that chronotropic incompetence was a strong predictor of long-term mortality in this large cohort of individuals undergoing screening TMET, with a hazard ratio of 1.99 [95% confidence interval 1.76 to 2.25, P<0.0001]. CI retained its predictive power for long-term mortality both in the presence and absence of heart rate modifying medications. CI was a more powerful predictor of late mortality than a positive exercise ECG response, which had a hazard ratio of 1.31 [1.10 to 1.57, P<0.0027].

**Female sex was protective for better late survival, with a hazard ratio of 0.64 [0.56 to 0.73, P<0.001], while treatment with a negatively chronotropic drug was a weak negative predictor of late mortality (likely a consequence of associated hypertension) with a hazard ratio of 1.22 [1.06 to 1.40, P<0.005].

**Conclusions:** Chronotropic incompetence during TMET is a strong predictor of long-term mortality, even in the presence of heart rate modifying drugs. Chronotropic incompetence overall had a stronger predictive power for long-term mortality than a positive exercise ECG response in this study.

P5119 | BEDSIDE
Associations of exercise capacity and heart rate recovery with carotid-femoral pulse wave velocity
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**Purpose:** Arterial stiffness and exercise variables such as exercise capacity (EC) and heart rate recovery (HRR) are known cardiovascular risk predictors. The purpose of this study is to investigate the associations between treadmill test variables and arterial stiffness.

**Methods:** Study population consisted of 139 subjects, 81 men and 58 women, age 40-65 years old, free of cardiovascular disease history that underwent treadmill test which showed no evidence of ischemia. EC was assessed through peak metabolic equivalents (METs) and HRR was measured at 2 min post exercise. Arterial stiffness was evaluated through carotid-femoral pulse wave velocity (CF-PWV).

**Results:** Pearson’s correlation revealed that CF-PWV is associated with HRR (r=−0.262, p=0.000) and Spearman’s correlation with EC (rso=−0.183, p=0.036). Linear regression analysis revealed that both HRR and peak METs are predictors of arterial stiffness (table).

**Conclusion:** The associations of HRR and EC with CF-PWV after adjusting for common confounders

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<tr>
<th>r2</th>
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<tr>
<td>Model HRR:</td>
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<tr>
<td>Model EC:</td>
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<tr>
<td>Peak METs, Gender, Age, Smoking, b-blockers, Hypertension</td>
<td>0.236</td>
<td>0.0238</td>
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<td>Hypertension</td>
<td>0.232</td>
<td>0.0212</td>
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CF-PWV was also associated with age, male gender and smoking.

**Conclusion:** The associations between arterial stiffness and slow HRR/reduced EC in apparently healthy individuals could be partially explained by impaired baroreflex sensitivity and endothelial dysfunction. Further experimental research is required to illuminate the underlying mechanisms.

Conclusions: Chronotropic incompetence during TMET is a strong predictor of long-term mortality, even in the presence of heart rate modifying drugs. Chronotropic incompetence overall had a stronger predictive power for long-term mortality than a positive exercise ECG response in this study.

**Downloads from:** https://academic.oup.com/eurheartj/article-abstract/35/suppl_1/851/541962/541962?guest=1&ppid=PD/2019
**P5121 | BEDSIDE**

**Effect of bosentan on cardiopulmonary exercise testing in patients with pulmonary arterial hypertension or inoperable chronic thromboembolic pulmonary hypertension**

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**Purpose:** Cardiopulmonary exercise testing (CPX) was reported to be useful for patients with pulmonary arterial hypertension (PAH). However, few reports exist in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH). We investigated whether an oral endothelin receptor antagonist (ERA), bosentan, affected parameters of CPX in CTEPH similar to those in PAH.

**Methods:** We examined PAH and CTEPH patients who visited our hospital from September 2009 to June 2013. Patients who had a clinical diagnosis of PAH or inoperable CTEPH base on the Dana Point criteria and whose World Health Organization functional class (WHO-FC) were from II to IV were included. Bosentan was administered to 17 PAH and 12 CTEPH. Bosentan was given at a dose of 62.5 mg twice daily for 4 weeks, followed by 125 mg twice daily, thereafter. All patients underwent CPX, which was performed before bosentan therapy and at 3 to 6 months of the treatment.

**Results:** The mean age of the patients was 47 ± 17 (16-80) years old. There were 8 (28%) men and the mean disease duration was 1.7 years. Bosentan was well tolerated by all patients, and there was no evidence of drug-related liver dysfunction. No accidents were reported during CPX in either of the groups. In PAH patients, peak VO2 significantly increased after bosentan treatment (p < 0.009). On the other hand, in CTEPH patients, there were no significant differences in the peak VO2. However, the peak PETCO2 was significantly increased from 23.9 ± 5.2 to 29.3 ± 2.6, during the baseline to 30.7 ± 0.7 mosl after the bosentan treatment (p < 0.040). Peak heart rate during exercise and plasma BNP levels tended to decrease after the bosentan therapy in both PAH and CTEPH (p = 0.089 and p = 0.067, respectively). Interestingly, the change from baseline in peak VO2 was correlated with pulmonary vascular resistance in PAH (r = -0.489, p = 0.048). However, in CTEPH, they were not correlated (r = 0.060, p = 0.85).

**Conclusions:** Bosentan therapy partially improved the exercise capacity in patients with inoperable CTEPH demonstrated by an improvement of the peak PAH, indicating that inoperable CTEPH improved the exercise capacity, indicated by the peak VO2 and VE/VO2 slope in patients with PAH. CPX is quite helpful for assessing exercise capacity of patients with inoperable CTEPH as well as PAH under the treatment with an ERA.

**Parameter of training volume increase**

**Conclusion:** Patients were trained with high intensity and most of them reached a considerable increase of their TV. Because fitness at the end of CR was influenced by age, exercise capacity at admission and increase of TV during CR, especially patients from the age of 50 could continue in training after care programs to preserve work ability.

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**P5124 | BEDSIDE**

**Effect of 3 weeks of aerobic exercise training on neuropsychological status of patients undergoing coronary artery bypass grafting**

O. Trubnikova, Y. Argunova, A. Mamontova, O. Barbarash.


**Purpose:** To evaluate the effect of the three weeks of aerobic exercise training on neuropsychological status in patients with coronary artery disease (CAD) after on-pump coronary artery bypass grafting (CABG).

**Methods:** 92 male patients with CAD, who have undergone on-pump CABG, were examined and assigned into 2 groups: group 1 with cycling training program (n=39, the mean age - 55.1±5.3 years) and group 2 without cycling training program (n=53, the mean age 57.2±6.21 years). Cycling training began on post-operative day 14 and continued for 3 weeks. The patients in both groups were comparable by clinical and demographic data as well as by neuropsychological and intraoperative parameters. Neuropsychological status was assessed using the automated software complex “Status PP” on days 5-7 before CABG and 1 month after it. The following parameters were assessed: complex visual-motor reaction time, functional mobility of nervous processes and brain performance (reaction time and missed target signals) attention (Burdon’s attention test), memory (10 numbers memorizing test). The statistical analysis was conducted using Statistics 6.0.

**Results:** No focal neurological symptoms were seen 1 month after CABG in both groups. Faster complex visual-motor reaction time was observed in patients with cycling training (500.7±55.1 ms vs. 535.1±64.1 ms, p = 0.03) as well as lower rate of missed target signals during the functional mobility of nervous processes test (10.1±1.2 vs. 14.0±1.3, p = 0.04), a great number of processed signs on minute 1 (102.1±27.7 vs. 77.7±33.5, p = 0.01) and minute 3 (118.1±28.4 vs. 101.2±25.5, p = 0.03) and attention coefficient (60.9±20.9 vs. 48.4±19.9, p = 0.03) while com-
pleting the Burden's attention test compared to the patients without cycling train-
ing. No significant differences in memory performance were seen in both groups.

Conclusions: Three weeks of aerobic exercise training improves neuropsycholog-
ical status in patients undergoing CABG.

P5125 | BEDSIDE
Necessary dosage adjustments in post myocardial infarction pharmacotherapy to optimize exercise performance during cardiac rehablitation programs
Regional University Hospital Carlos Haya, Malaga, Spain

Purpose: Classical post myocardial infarction pharmacotherapy may need dosage adjustments when serious modifications in health habits are taken, as it happens in participants in cardiac rehabilitation programs (CRP), who generally improve quickly their blood pressure, lipid and glycaemic profiles, leading to reductions in doses of ACEIs/ARAII, statins, and anti-diabetics respectively.

Methods: We analysed our data from the cardiac rehabilitation unit, including 108 patients who completed the program in 2013. We assessed all modifications in drug doses necessary to optimize the pharmacotherapy to fit best progressive improvements in pressure, lipid and glycaemic parameters during the three-month CRP.

Results: Mean systolic and diastolic blood pressure decreased 26.02 mmHg and 12.4 mmHg respectively from the beginning to the end of the program, (systolic 95% CI 19.32 mmHg; p<0.01 and diastolic 95% CI 7.15 mmHg; p<0.05), which supposed that 78 participants (72.2%) needed readjustments to half doses of ACEIs in the final weeks of the CRP, remaining normotensive and with better tolerance to exercise after dose readjustment. Furthermore, lipid profile in the last blood test, that is to say 12 week after the beginning of the CRP, revealed that 64 patients (58.25%) had less than 50 mg/dl of LDL cholesterol, and therefore, reduction to half doses of statins was also applicable to them. 7 participants who were taking Ezetimibe and 12 with Fenofibrate were prescribed to stop these treat-

Conclusions: Cardiac rehabilitation modifies intensively health habits, involving mainly improvement in lipid, blood pressure and glycaemic profiles. Therefore, treatment adjustments during the program become necessary to optimize their physical performance, without forgetting the remarkable pharmacological savings and the better quality of life that treatment reductions suppose.

CARDIOVASCULAR HEALTH UP IN SMOKE

P5127 | BEDSIDE
Fifteen year follow-up of patients with premature (<36 years) myocardial infarction: the impact of smoking status on recurrent coronary events
Attikon University Hospital, Athens, Greece

Purpose: There are few data regarding the long-term prognosis in very young survivors of myocardial infarction (MI). The present study sought to explore the long-term outcome in individuals who had sustained a MI at the age of <35 years.

Methods: We recruited 261 consecutive patients who had survived their first MI <35 years of age. Patients were followed-up for up to 15 years. Clinical end points were: readmission for acute coronary syndrome, cardiac death or coronary revas-
cularization due to clinical deterioration.

Results: The most prevalent risk factor at presentation was smoking (93.6%). Follow-up data were obtained from 236 patients (32±4.3 years old, 203 men). The median period of follow-up was 8.8 years (interquartile range: 5-13 years). During follow-up 138 (58.5%) patients reported continuation of smoking. Eighty-nine (37.7%) patients presented cardiac events (12 deaths, 58 acute coronary syndromes, 19 revascularizations). Multivariable Cox regression analysis showed that persistence of smoking was an independent predictor of cardiac events after adjustment for conventional risk factors (sex, age, diabetes mellitus, hypertension, hypercholesterolemia, family history of coronary artery disease) [hazard ra-
ting (HR): 2.43; 95% confidence interval (CI): 1.49 to 4.02; p<0.001]. Continuation of smoking remained an independent predictor for recurrence of cardiac events when additional adjustment for ejection fraction at presentation was performed (HR: 2.24; CI: 1.34 to 3.75; p<0.002). The figure shows the unadjusted Kaplan-

Conclusions: Persistence of smoking is a predictor of poor long-term prognosis in patients with premature MI.

P5128 | SPOTLIGHT
Time-dependent relation between smoking cessation and improved exercise tolerance in apparently healthy middle-age men and women
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Background: Smoking is an independent cardiovascular risk factor and corre-
lates with reduced exercise tolerance. Data on the time dependent effect of smok-
ing cessation on exercise tolerance are limited.

Methods: We investigated 17,115 men and women who were annually screened at the Institute for Medical Screening of the Chaim Sheba Medical Center. All subjects had their smoking status documented and performed an exercise stress testing (EST) according to Bruce protocol at each visit. Subjects were divided at baseline into four groups: active smokers (N=2,858), recent quitters (smok-
ing cessation <2 years before baseline EST; N=861), remote quitters (smok-
ing cessation >2 years before baseline EST; N=3,856) and never smokers (N=9,810). Baseline and follow up EST duration were compared among the four groups.

Results: Recent quitters demonstrated a 2.4-fold improvement in their EST dura-
tion compared to active smokers (improvement of 24±157 vs. 10±157 seconds, respectively; p<0.02; figure). Multivariate logistic regression showed that recent quitters were 26% more likely to improve their exercise tolerance compared with active smokers (95% CI [1.08-1.47], p=0.003). Assessing smoking status as a time-dependent covariate during 4 consecutive visits demonstrated that recent quitters were 17% more likely to improve their exercise tolerance compared to active smokers (CI 1.02-1.34, p=0.02), with a less pronounced benefit among remote quitters (HR=1.11, CI 1.02-1.21, p=0.01).

Conclusions: Smoking cessation is independently associated with improved ex-
ercise tolerance. The benefits of smoking cessation are evident within the first 2 years of abstinence.

P5129 | BEDSIDE
Characteristics of persistent smokers and quitters after an acute coronary syndrome
M. Snaterse-Zuidam, M. Minneboe, H.T. Jorstad, W.J.M. Scholte Op Reimer, R.J.G. Peters on behalf of RESPONSE. Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands

Purpose: To identify the characteristics of persistent smokers after ACS, com-
pared to patients who quit smoking.

Methods: We analysed data from RESPONSE, a multicenter RCT. Patients (18-
80 years) were included within 8 weeks after an acute coronary syndrome (ACS). As part of the main study patients were randomised to a nurse-coordinated pre-
vention program in addition to usual care (intervention) or usual care alone. For this analysis, we omitted the group assignment. Quitters are defined as smoker at 2 years before the baseline EST; N=3,856), remote quitters (smok-
ing cessation >2 years before baseline EST; N=3,856) and never smokers (N=9,810). Baseline and follow up EST duration were compared among the four groups.

Results: Recent quitters demonstrated a 2.4-fold improvement in their EST dura-
tion compared to active smokers (improvement of 24±157 vs. 10±157 seconds, respectively; p<0.02; figure). Multivariate logistic regression showed that recent quitters were 26% more likely to improve their exercise tolerance compared with active smokers (95% CI [1.08-1.47], p=0.003). Assessing smoking status as a time-dependent covariate during 4 consecutive visits demonstrated that recent quitters were 17% more likely to improve their exercise tolerance compared to active smokers (CI 1.02-1.34, p=0.02), with a less pronounced benefit among remote quitters (HR=1.11, CI 1.02-1.21, p=0.01).

Conclusions: Smoking cessation is independently associated with improved ex-
ercise tolerance. The benefits of smoking cessation are evident within the first 2 years of abstinence.
ers more often had a positive history in CVD compared to quitters (26% vs. 13%), more often a BMI ≥ 25 (32% vs. 24%) and less often a higher education profile (15% vs. 33%).

Characteristics of quitters vs. smokers

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Quitters (n=156)</th>
<th>Smokers (n=168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive history of CVD, n (%)</td>
<td>19 (13%)</td>
<td>44 (26%)</td>
</tr>
<tr>
<td>Risk profile at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (≥ 140 mmHg syst)</td>
<td>36 (24%)</td>
<td>33 (20%)</td>
</tr>
<tr>
<td>LDL ≥ 2.5 mmol/L</td>
<td>46 (31%)</td>
<td>66 (39%)</td>
</tr>
<tr>
<td>Overweight (BMI ≥ 25)</td>
<td>35 (24%)</td>
<td>53 (32%)</td>
</tr>
<tr>
<td>Education rates, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fewer than 8 years</td>
<td>41 (28%)</td>
<td>63 (38%)</td>
</tr>
<tr>
<td>College or university</td>
<td>49 (33%)</td>
<td>25 (15%)</td>
</tr>
<tr>
<td>Risk profile at 12 months follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (≥ 140 mmHg syst)</td>
<td>41 (28%)</td>
<td>43 (26%)</td>
</tr>
<tr>
<td>LDL ≥ 2.5 mmol/L</td>
<td>32 (22%)</td>
<td>62 (37%)</td>
</tr>
<tr>
<td>Overweight (BMI ≥ 25)</td>
<td>127 (81%)</td>
<td>112 (67%)</td>
</tr>
</tbody>
</table>

Conclusion: The majority of quitters stopped immediately after their ACS event and were more successful than subsequent quitters. To improve strategies for smoking cessation we should focus on relapse prevention for these late stoppers.

P5130 | BEDSIDE

Risk factor profile of patients with myocardial infarction: smoking in younger patients

H.P. Theres1, B. Maier2, S. Behrens3, R. Schoeller4, H. Schuehle2 on behalf of SMIR.

Background: The Berlin Myocardial Infarction Registry collects data on hospital treatment of MI patients prospectively since 1999. Part of data collection is asking patients anamnestically for their risk factors. We examined 5 age groups with ≥ 55 years, n=6009 with 55-64 yrs., n=8214 with 65-74 yrs., n=6174 with 75-84 yrs. and n=2523 with ≥ 55 years.

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Results: The risk factor profile differed across ages, 76% of those with 75-84 yrs. and n=2523 with ≥ 55 years.

Conclusion: The risk factor profile profile at baseline and at 12 months follow-up differed across ages, 76% of those with 75-84 yrs. and n=2523 with ≥ 55 years.

P5131 | BEDSIDE

Tobacco smoke exposure is associated with alterations of cardiac geometry and function in children

K. Harada, Y. Harada. Harada Kid’s Clinic, Akita, Japan

Background: Passive smoking (PS) is associated with increased risk for cardiovascular events, however, there has been little information on cardiac function in children with PS. The purpose of this study is to assess left ventricular (LV) function in PS children.

Methods: Echocardiography with tissue Doppler imaging was performed in 93 children (age:10±3 years) who have been exposed to tobacco smoking since intrauterine life and 124 age-matched children without PS. Left atrial anteroposterior diameter, LV end-diastolic volume, ejection fraction, LV mass, and mass-to-volume ratio were measured. Transmural peak flow velocities during early (E) and late diastole (A) and mitral annular myocardial velocities during early (Em) and late diastole (Am) were measured. Left atrial systolic force was calculated. Isovolumic relaxation time and tissue Doppler-derived myocardial performance index were assessed. Effective arterial elastance was estimated by end-systolic pressure-volume ratio.

Results: Body mass index and heart rate were similar between the 2 groups (p>0.05). Systolic and diastolic blood pressures were significantly higher in PS children than in controls (112±10 vs. 109±9 and 83±8 vs 80±8 mmHg, p<0.05, respectively). Compared with controls, left atrial size, LV mass, mass-to-volume ratio, and left atrial systolic force were significantly higher (2.6±0.40 vs. 2.4±0.31 cm, 90v s60 46 vs. 79±31, 1 g, 1.07±0.22 vs. 1.01±0.22, and 3.86±2.05 vs. 3.24±1.69 kdyne, p<0.05, respectively) and Em/Am ratio was significantly lower (2.97±0.67 vs. 3.16±0.77, p<0.05) in PS children. Ejection fraction,isolovolumic relaxation time, myocardial performance index, effective arterial elastance,end-systolic elastance, and intima-media thickness did not differ between the 2 groups.

Conclusions: The present study indicates that tobacco smoke exposure can adversely affect LV geometry and function in childhood. Passive smoking may contribute to the increased prevalence of later cardiovascular diseases.

P5132 | BEDSIDE

Adolescent smoking and vascular function in the SAPALDIA youth study

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Background: In 1991, 2880 adolescents from Switzerland were included in the Swiss Study on Air Pollution and Lung and Heart Disease in Adults (SAPALDIA) cohort, investigating the association between active smoking and functional vascular properties. Fewer than 8 years 41 (28%) 63 (38%)

Conclusion: Early exposure to tobacco smoke is associated with various adverse health outcomes in children and adolescents. However, little is known on the impact of active smoking on cardiovascular health (CVH) in adolescence. The SAPALDIA Youth Study, a nested study in the Swiss Study on Air Pollution and Lung and Heart Disease In Adults (SAPALDIA) cohort, investigated the association between active smoking and functional vascular properties.

Methods: In 288 SAPALDIA offspring underwent a clinical examination following a standardized protocol: blood pressure (BP), ultrasound assessment of the CCA, anthropometry, blood draw for cardiovascular biomarkers and serum cotinine. Smoking and parental habits gave information on early life, health and lifestyle of the child, including smoking status. We conducted multivariable regression analyses to further distill the effect of smoking status on cardiopulmonary function. Smoking and parental habits gave information on early life, health and lifestyle of the child, including smoking status. We conducted multivariable regression analyses to further distill the effect of smoking status on cardiopulmonary function.

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Conclusions: The analyses yield evidence of an early adverse impact of active tobacco exposure on vasculature in adolescence, independent of parental smoking. This short-term impact is suggestive of potential long-term cardiovascular health consequences of early smoking and underlines the need for early prevention of uptake of cigarette smoking in youth.

P5133 | BEDSIDE

Impact of smoking habit on coronary plaque vulnerability as assessed by integrated backscatter intravascular ultrasound

A. Iwata, Y. Uehara, S. Miura, K. Saku. Harada Kid’s Clinic, Akita, Japan

Background: Smoking is well-established risk factor for coronary artery disease (CAD). Little is known about the relationship between smoking habit and coronary plaque vulnerability.

Objectives: We assessed the association between smoking habit and the coronary plaque vulnerability of nonculprit lesions as assessed by integrated backscatter intravascular ultrasound (IB-IVUS).

Methods: Eighty-four consecutive patients with stable CAD who received statin treatment and underwent percutaneous coronary intervention were enrolled. Non-culprit coronary lesions with mild to moderate stenosis were measured by IB-245 mmHg (8.5) and of PP 49mmHg (10.6) Regression analyses yielded significant effect estimates for weekly smoking (compliance -0.076; 0.005; PP: 0.18 mmHg, 95%CI 0.02;0.3). Results remained consistent after adjusting for parental smoking.

Conclusion: The analyses yield evidence of an early adverse impact of active tobacco exposure on vasculature in adolescence, independent of parental smoking. This short-term impact is suggestive of potential long-term cardiovascular health consequences of early smoking and underlines the need for early prevention of uptake of cigarette smoking in youth.

P5134 | BEDSIDE

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were significantly higher than those in the non-smoking group (27.7±14.9mm³ vs. 21.1±9.9mm³; \( P = 0.023 \) and 42.7±12.8% vs. 36.2±11.6%, \( P = 0.019 \), respectively). Furthermore, multiple regression analysis with other metabolic variables revealed that smoking habit was independently associated with %LV (\( P = 0.036 \)) among IVUS parameters.

**Conclusions:** Noncrupt coronary lesions in patients with smoking habit were associated with more lipid-rich plaque content, indicated that the patients with smoking habit may increase vulnerable plaque and the risk of CAD events.

**P5134 | BEDSIDE**

*Relation of airflow limitation and smoking status to carotid atherosclerosis in patients with coronary artery disease*

S. Suzuki, H. Ishii, Y. Shibata, Y. Tatami, N. Noguchi, T. Ota, Y. Kawamura, A. Tanaka, T. Murohara. Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

**Purpose:** Chronic obstructive pulmonary disease (COPD) is associated with an increased risk of morbidity and mortality from cardiovascular disease. However, the effects of smoking seem to be insufficient to explain all of cardiovascular risk in COPD. The aim of this study was to evaluate the combined effects of smoking and airflow limitation (AF) on severity of carotid atherosclerosis among patients with coronary artery disease (CAD).

**Methods:** A total of 223 patients with stable CAD were classified into the smokers with AF group (56), the smokers without AF group (56), and the never smokers group (n=82). All subjects underwent spirometry and carotid ultrasonography. Current or past smokers were classified as smokers. AF was defined as ratio of forced expiratory volume in one second to forced vital capacity. Carotid plaque score (PS) was calculated by summing all plaque thicknesses in both of the carotid systems. Severe carotid atherosclerosis was defined as the carotid PS > 10.

**Results:** The prevalence of severe carotid atherosclerosis was significantly higher in the smokers with AF group (53.6%) than in the smokers without AF group (35.3%) (\( P = 0.038 \)) and the never smokers group (25.6%) (\( P = 0.001 \)). On multivariate logistic regression analysis, the smokers with AF group was an independent predictor of severe carotid atherosclerosis (odds ratio, 3.16; 95% confidence interval, 1.25-7.38; \( P = 0.008 \)). Associations were consistent in subgroups, including smoking status, the duration of smoking, and the amount of cigarettes smoked per day.

**Conclusions:** In patients with CAD, the smokers with AF were more likely to have carotid atherosclerosis than in those without. Our findings might explain the increased risk of future cardiovascular events in such patients.

**P5135 | BEDSIDE**

*Effect of smoking cessation on HDL function*

E. Kawachi, S. Imaiizumi, K. Takata, S. Abe, Y. Yahihiro, Y. Uehara, B. Zhang, S. Miura, K. Saku. Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

**Background:** Smoking cessation reduces cardiovascular disease (CVD) and improves health outcomes. Although the oxidative modification of HDL by smoking could reduce the functionality of HDL, the impact of smoking cessation on HDL function has not been studied.

**Purpose:** We studied the effect of smoking cessation on HDL function.

**Methods:** Thirty-two smokers were randomly treated with varenicline or nicotine patches. Plasma nicotine profile, malondialdehyde level, and the cholesterol efflux capacity and anti-oxidative capacity of HDL were measured before and after treatment.

**Results:** The rate of smoking cessation was 78.6%. There was a significant correlation between efflux capacity and body mass index (BMI) (\( r = 0.44, p = 0.01 \)). After the study period, BMI and plasma uric acid were significantly increased (\( p < 0.001, p < 0.05 \), respectively) and plasma malondialdehyde, pulse rate, hemoglobin, systolic blood pressure and the carbon monoxide (CO) level were significantly decreased in the successful smoking cessation group (\( p = 0.05, p = 0.05, p < 0.001, p < 0.05, p < 0.001 \), respectively). The change in the cholesterol efflux capacity was inversely associated with the reduction of CO (\( r = -0.45, p = 0.02 \)). Although there was no difference in HDL fractions as analyzed by capillary isocaphoresis between the successful and unsuccessful smoking cessation groups, there were significant differences in the anti-oxidative and cholesterol efflux capacity of HDL between the groups.

**Conclusion:** These results indicate that cigarette smoking reduces HDL function and smoking cessation leads to the improvement of HDL functionality, which may involve the mechanism by which smoking cessation has beneficial effects against CVD.

**P5136 | BEDSIDE**

*Twelve weeks of successful smoking cessation therapy with varenicline increases serum apolipoprotein A-1 and high-density lipoprotein cholesterol levels*

M. Iwaoka. Tokyo-Kita Social Insurance Hospital, Cardiology, Tokyo, Japan

**Purpose:** Cigarette smoking adversely affects lipid profiles, and smoking cessation should improve lipid profiles in the long term. However, it remains unclear whether intensive, medication-based smoking cessation therapy can affect lipid profiles in the short term. Thus, we evaluated the short-term effects of smoking cessation therapy with varenicline on lipid profiles.

**Methods:** Participants included 90 consecutive subjects who received 12 weeks of smoking cessation therapy. All subjects were treated with varenicline, and no concomitant medication was made to their current lipidotropic and anti-diabetic medications during treatment. At first and last visits, lipid profiles and fasting blood glucose and hemoglobin A1c levels were evaluated and physical examination was performed. The success group, comprising subjects who attained exhaled carbon monoxide confirmed 4-week continuous abstinence, included 73 subjects, whereas the failure group, comprising those who did not achieve complete smoking cessation, included 17 subjects. The number of cigarettes consumed per day was reduced in all subjects in the failure group.

**Results:** Serum apolipoprotein A-1 (apoA-I) and high-density lipoprotein cholesterol (HDL-C) levels significantly increased from baseline to 12 weeks in the success group (apoA-I: 150.1±28.3 vs. 157.6±27.5 mg/dL, respectively, \( p < 0.01 \); HDL-C: 53.9±15.7 vs. 57.1±14.4 mg/dL, respectively, \( p < 0.01 \)). There were no statistically significant differences observed in the failure group (apoA-I, 145.9±33.4 vs. 146.8±34.2 mg/dL, respectively, \( p = 0.87 \); HDL-C, 52.6±15.7 vs. 53.3±16.3 mg/dL, respectively, \( p = 0.80 \)). The effect sizes (Cohen's d) of apoA-I and HDL-C in the success group were 0.56 and 0.47, respectively. The post-hoc statistical power of apoA-I and HDL-C in the success group were 0.97 and 0.98, respectively.

**Conclusion:** These findings suggest that successful smoking cessation therapy with varenicline improves serum apoA-I and HDL-C levels in the short term.
Conclusion: Smoking cessation with varenicline therapy significantly increased FMD without significant changes of nitroglycerin-induced vasodilatation and baIMT from before to 20 weeks. It appears to improve vascular function which depends on endothelial function, not on vascular smooth muscle function or changes in vascular structure in smokers.

P5141 | BEDSIDE
Major adverse cardiac events (MACE) and all-cause mortality in levothyroxine substituted individuals with subclinical hypothyroidism: a large cohort study
M. Nygaard Andersen1, A.M. Schjerning-Olsen1, J. Clausager Madsen2, J. Faber3, C. Torp-Pedersen4, G.H. Gislason3, C. Selmer1,2, Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Gentofte Hospital, Gentofte, Denmark;2-Copenhagen General Practitioners’ Laboratory (KPLL), Copenhagen, Denmark;3-Herlev Hospital - Copenhagen University Hospital, Department of Endocrinology, Copenhagen, Denmark; 4-Aalborg University, Department of Health Science and Technology, Aalborg, Denmark
Purpose: Subclinical hypothyroidism is associated with a number of cardiovascular risk factors such as hypertension, hypercholesterolemia and diastolic dysfunction, but only limited data exist on long-term outcome of levothyroxine substitution therapy. Therefore we examined effects of levothyroxine substitution treatment on all-cause mortality and major adverse cardiac events (MACE) in patients with subclinical hypothyroidism.
Methods: Patients > 18 years consulting their general practitioner from 2000–2009 in Copenhagen, Denmark, who underwent thyroid blood tests, were identified by individual-level linkage of nationwide registries. Only patients with subclinical hypothyroidism (elevated TSH (Thyroid-Stimulating Hormone) with normal FT4 (Free Thyroxine)) at baseline were included. History of thyroid disease, related medication or treatment with lithium, amiodarone and glucocorticoids were excluded. Levthyroxine treatment was only considered if initiated within 6 months from baseline. Incidence Rate Ratios (IRR) of MACE (combined endpoint of non-fatal myocardial infarction, stroke, or cardiovascular death) and all-cause mortality were analyzed using Poisson regression models.
Results: The total cohort comprised 12,212 patients who had subclinical hypothyroidism (mean age 55.2 (SD ± 18.8) years; 79.5% female). Within the first 6 months, 2,452 patients (20.1%) claimed prescription of levthyroxine. The remaining 9,760 patients (79.9%) either initiated levothyroxine therapy later than 6 months after their initial blood test, or did not receive any substitution treatment. During a mean follow-up of 5.0 (SD ± 2.6) years, 1,165 MACE events were observed and 1,566 patients died. MACE rate was 20/1000 person-years (py) among untreated and 17/1000 (py) among levthyroxine treated. Overall mortality rate was 26/1000 person-years (py) and 21/1000 (py) among untreated and levthyroxine treated, respectively. No influence on MACE. (IRR 1.02 [95% CI: 0.88–1.17]) was found in patients substituted with levthyroxine.
Conclusions: In patients with subclinical hypothyroidism substitution with levthyroxine does not affect the risk of MACE and all-cause mortality.

P5142 | BEDSIDE
Angiotensin receptor blockers reduce the incidence of malignant tumors in hypertensive patients at high risk of cancer
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Purpose: Whether new onset cancer is reduced by angiotensin II type 1 receptor blocker (ARB) therapy is controversial. The aim of this study was to examine this issue in hypertensive patients.
Methods: Patients treated for hypertension for ≥1 year with no previous history of cancer were enrolled into the study from January 2003 to December 2008 and divided into 2 groups (with and without ARBs). Kaplan-Meier time-event curves were used to predict time to onset, and the log-rank test was performed. Incidence rates were calculated using the Cox proportional hazards model with a 95% confidence interval (CI). Sub-group analyses of age, sex, and smoking status were also performed.
Results: Among the 2,313 patients in the ARB group and the 1,375 patients in the non-ARB group, 58 patients in the ARB group (2.51%) and 52 patients in the non-ARB group (3.78%) developed malignant tumors (log-rank test p = 0.014). The Cox proportional hazards model revealed a significant decrease in the incidence of malignant tumors in the ARB group (incidence ratio: 0.82, 95% CI 0.43-0.91). In all sub-groups with cancer at baseline, Kaplan-Meier analyses showed that new-onset cancer development was significantly lower in the ARB group in the non-ARB group (over 60 years p = 0.025; male p = 0.022; current smoker p = 0.003, log-rank test).
Conclusions: The effect of ARB on cancer incidence

P5138 | BEDSIDE
Comparison of two strategies for smoking cessation in hospitalized patients
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Background: Hospitalization is considered a window of opportunity for smoking cessation. There is little data in the literature about smoking treatment for hospitalized patients. Smoking is a major risk factor for cardiovascular global risk.
Objectives: To compare the effectiveness of two smoking cessation strategies based on cognitive behavioural therapy initiated in hospitalized patients and to evaluate the factors related to relapse.
Methods: A prospective randomized study with 90 smokers hospitalized in the University Hospital Antonio Pedro (HUAP), Niteroi, Brazil, from January to December 2012 was carried out. The degree of nicotine dependence was assessed by the Fagerstrom test and the degree of craving by the Questionnaire of Smoking Urges-Brief (QSU-B).
Results: Patients were divided into 2 treatment groups: Bi ( Brief Intervention, n=45) and I ( Intensive Intervention with the presentation of an educational video produced by the authors, n=45). All patients were assessed by telephone at the third, fifth and sixth month. Hospitalized patients relapsed. Abstinence was confirmed by carbon monoxide measurement in exhaled air (COex). Of the 90 patients, 61.1% were male; average age 51.1 ± 12.2yo.
Results: The main causes for hospitalization were cancer (23.3%), cardiovascular diseases (21.1%) and respiratory diseases (14.4%). The degree of nicotine dependence was elevated in 43.4% and withdrawal symptoms were present in 58.9%. The average COex initial approach was 4.8 ± 4.5ppm, correlated positively with the Fagerstrom score (r = 0.244, p = 0.02) and negatively with days without ourdoor activities (r = -0.294, p = 0.006). After 6 months follow-up, 40.7% patients continued abstinent (Bi = 9 & I = 24) and 59.3% had relapsed (Bi = 31 and I = 17). The final COex average was 0.72ppm. In logistic regression analysis, it was observed that the moderate/severe craving (p = 0.0001) was an independent predictor for relapse, with a relative risk of 0.95 (95% CI: 1.5 to 10.7). When comparing the two cognitive behavioural therapy strategies, it was found that fewer if patients relapsed in comparison with Bi patients (p = 0.001).
Conclusions: The intensive approach was more effective in the treatment of hospitalized patients and only the degree of craving was a significant risk factor for relapse. The inclusion of an innovative technique of cognitive behavioural therapy, easy access and low cost such as the presentation of an educational video proved to be effective in reducing relapse rates in the long term.

INTERVENTIONS IN CARDIOVASCULAR PREVENTION

P5140 | BEDSIDE
Cocoa flavanols improve vascular health: a randomized placebo-controlled study double masked trail in healthy middle-aged subjects
R. Sansone, A. Rodriguez-Mateos, D. Schuler, G. Kuhnle, J. Spencer, Department of Cardiology, Pneumology and Angiology, Duesseldorf, Germany
Background: Cocoa flavanols (CF) increase endothelial function and decrease blood pressure in patients with cardiovascular disease or subjects at increased cardiovascular risk.
Aim: We investigated the primary preventive potential of a dietary CF intervention on vascular health as determined by endothelial function, the Framingham risk and vascular age in healthy middle-aged individuals.
Methods: In a randomized, placebo-controlled, double-masked, parallel-group dietary intervention trial, 100 middle-aged (35-60 yrs) male (n=50) and female individuals. Furthermore, the subjects blood pressure, total and LDL cholesterol allowing the calculation of the Framingham risk scores and pulse wave velocity (PWV) to estimate vascular age.
Results: Following 1 month of daily CF intake, FMD improved in healthy male and female individuals. The subjects blood pressure, total and LDL cholesterol decreased while HDL cholesterol increased leading to decrease in 10 year Framingham risk to develop coronary heart disease (-32%) or cardiovascular disease (-34%) and to develop a myocardial infarction (-22%). The increase in HDL cholesterol decreased the development of coronary heart disease (-34%) or cardiovascular disease (-43%). PWV velocity significantly decreased (-0.34 m/s, equivalent to 3.5 years of vascular age).
Conclusions: Increasing dietary cocoa flavanol intake improved the most important cardiovascular surrogate parameters providing solid data that underscore the primary preventive potential of dietary flavanols to maintain vascular health.

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risk group. These results suggest that ARBs may decrease the occurrence of ma-
linant tumors, especially in those at high risk of cancer.

P5143 | SPOTLIGHT
Artificial neural network modeling using clinical and knowledge features predicts salt reduction behavior
H. Ismae1, G. Sak2, J. Fatallah1, M.M. Almedawar1, S. Bou Zein Eddine1, L. Al-Shaar1, D. Al Harith1, T. Garabedian1, L. Nasreddine1, I. Elhaij2 on behalf of Vascular Medicine Program.1 American University of Beirut Medical Center, Dept. of Internal Medicine, Division of Cardiology, Beirut, 2American University of Beirut AUB, Dept. of Electrical & Computer Engineering, Beirut, 3American University of Beirut Medical Center, Vascular Medicine Program, Beirut, *American University of Beirut AUB, Dept. of Nutrition & Food Sciences, Beirut, Lebanon
Purpose: High dietary salt intake is accountable for up to 30% of the prevalence of hypertension. Hypertension in turn is a significant risk factor for cardiovascular events. The Institute of Medicine (IOM) recommends a salt intake of less than 6g/day/person. Predicting behaviors regarding salt intake habits is vital to guide and focus interventions and increase their effectiveness. We aim to develop an Artificial Neural Network (ANN) statistical based tool that predicts behavior from key knowledge and attitude questions along with clinical data in a high cardiovascular risk population.
Methods: We collected knowledge, attitude and behavior (KAB) data on 115 high risk patients (Coronary Care unit) (mean age: 60.63 SD 15.39 years). A behavior score (BS) was calculated by giving a weight to every answer for the behavior questions from 1 to 4 (unfavorable to favorable) and adding all the weights together. We classified patients into either Favorable Behavior (BS>31), Less Favorable Behavior (between 26 and 31) or Unfavorable Behavior (BS<26) for reporting salt intake. The statistical model has been implemented in a R-based program.
Results: ANN based model achieved an accuracy of 62% CI (58%–67%) using clinical and knowledge questions only; The statistical model has been implemented in a R-based program.

P5144 | BEDSIDE
Dual antiplatelet therapy in stable patients with coronary artery disease: determinants and impact on prognosis, insights from the corona study
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Background: The impact of prolonged DAPT in stable CAD patients is debated. Our aims were (1) to assess the proportion of stable coronary artery disease (CAD) patients under dual antiplatelet therapy (DAPT) in real life conditions, (2) to determine the determinants of DAPT prescription and (3) to compare outcomes of patients under DAPT versus those under monotherapy (MAPT).
Methods: Altogether, 3691 patients with stable CAD for at least 1 year (median time of 4 years) were divided in 2 groups according to their antiplatelet therapy regimen at inclusion: patients under MAPT (n=2823) were compared to those under DAPT (n=824).

Conclusions: Our study reports for the first time that the proportion of patients with stable CAD under long-term DAPT in a contemporary practice is high and around 20%. The major determinants of long-term DAPT were a shorter delay since the last coronary event, markers for a more diffuse atherosclerosis, DES implantation, and markers for a lower risk of bleeding. Of note and even so no increase in major bleeding was observed, our results do not support the prescription of prolonged DAPT.

P5145 | BENCH
A novel potent and selective PPARalpha agonist, K-877, ameliorates the atherogenic profile of fasting and postprandial hypertriglyceridemia in mice
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Fasting and postprandial hypertriglyceridemia (PHTG) is caused by the impaired metabolism of TG-rich lipoproteins and their remnant lipoproteins. Since remnant lipoproteins including VLDL remnants and chyomicron remnants are highly thrombogenic, many treatments for improving impaired metabolism of remnant lipoproteins have been investigated in order to prevent atherosclerotic cardiovascular events. In the current study, we have investigated the effect of a potent and selective peroxisome proliferator-activated receptor alpha (PPARalpha) agonist, K-877, on postprandial metabolism of remnant lipoproteins.

Figure 1

K-877 may ameliorate fasting and postprandial hypertriglyceridemia by enhancing LPL activity and reducing weight gain.
was monitored, and the dose of febuxostat was adjusted to maintain the serum UA level <6.0 mg/dL throughout the course of the study. In the febuxostat group, the plasma renin activity (PRA), plasma aldosterone concentration (PAC), and serum UA level significantly decreased by 33% (p < 0.05), 14% (p < 0.05), and 23% (p < 0.0001), respectively. The estimated glomerular filtration rate significantly increased by 6.0% (p < 0.05). None of these changes was observed in the control group. Significant positive correlations were observed between the change in the serum UA level, and the changes in both the PRA and the PAC.

**Conclusion:** These results suggest that febuxostat might not only reduce the serum UA level, but may also improve cardio-renal interaction. These preliminary findings require confirmation in larger clinical trials.

**P5147 | BEDSIDE**

Weight loss and reduction of waist size in 362 hypogonadal men with obesity grades I to III upon long-term treatment with testosterone undecanoate (TU): observational data from two registry studies

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**Introduction:** Numerous studies have reported inverse associations between testosterone and obesity. Obesity seems to have a greater impact on the decline of testosterone with advancing age than age itself.

**Methods:** From two prospective, cumulative registry studies of 561 hypogonadal men and 362 men with obesity grade I (BMI 30–34.9), grade II (BMI 35–39.9) and grade III (BMI ≥ 40 kg/m²) were selected. All men received TU injections for up to 6 years. Measures were taken at each three-monthly visit.

**Results:** Grade I (n=185, mean age: 58.4±8.0 years): Weight (kg) decreased by 6.0% (p < 0.05) from 89.34±16.7 to 83.62±16.7. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline was -12.55±0.44 kg, percent change from baseline -12.29±5.76%. Waist circumference (cm) decreased from 107.01±7.57 to 97.09±6.95. These changes were statistically significant for five years compared to the previous year and approached significance at the end of six vs. five years. The mean change from baseline was 107.01±7.57 to 97.09±6.95. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline was -9.24±0.3 cm. BMI (kg/m²) decreased from 32.51±1.39 to 28.63±1.92, mean change from baseline -3.99±0.14 kg/m². Grade II (n=131, mean age: 60.5±5.6 years): Weight (kg) decreased by 6.2% (p < 0.05) from 112.02±18.99 to 106.48±15.74. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline was -20.67±0.51 kg, percent change from baseline -17.03±0.52%. Waist circumference (cm) decreased from 114.23±7.51 to 108.52±6.5. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline was -12.29±0.33 cm. BMI (kg/m²) decreased from 37.39±1.46 to 31.05±2.02, mean change from baseline -6.58±0.16 kg/m².

Grade III (n=46, mean age: 60.3±5.4 years): Weight (kg) decreased from 129.02±5.67 to 103.33±4.17. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline - 27.15±0.74 kg, percent change from baseline -20.99±3.16%. Waist circumference (cm) decreased from 116.41±5.69 to 106.48±4.91. These changes were statistically significant for all six years compared to the previous year. Mean change from baseline was -12.44±0.36 cm. BMI (kg/m²) decreased from 41.93±1.5 to 33.62±1.58, mean change from baseline -8.79±0.23 kg/m².

**Conclusions:** All changes were more pronounced with increasing obesity grade. All changes were statistically more pronounced with increasing obesity grade and approached significance at the full observation period. TRT seems to be an effective approach to achieve sustained weight loss in obese hypogonadal men, thereby potentially reducing cardiometabolic risk.

**PS148 | BENCH**

High-dose intravenous N-acetylcysteine prevention of contrast media-induced nephropathy in heart failure: CASIS-HF-A multicenter prospective controlled trial

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**Background:** Contrast media-induced nephropathy (CIN) is one of the major complications in patients who undergo coronary angiography and percutaneous coronary intervention (PCI). Reduced left ventricular systolic function is an established risk factor for the development of CIN. We investigated the efficacy of prophylactic-intravenous high-dose N-acetylcysteine (NAC) for the prevention of CIN in patients with heart failure who were undergoing coronary angiography and/or PCI.

**Methods:** A total of 134 patients with heart failure were randomized into 2 groups: 68 patients were assigned to NAC plus saline infusion (NAC group: intravenous bolus of 1200 mg of NAC twice daily for 7 days). The rate of CIN was significantly lower in the NAC group than in the control group (0.005 [0.10 to 0.10] mg/dL vs 0.04 [0.04 to 0.10]), respectively, (P=0.032). The incidence of CIN was lower in the NAC group than in the control group (7% vs 9.1%), but the difference was not statistically significant (P=0.528) (Fig. 1).

**Conclusion:** The results of this study suggest that use of intravenous high-dose NAC before coronary procedures may decrease SCR levels in patients with heart failure.

**INTERVENTIONS AND OUTCOMES IN CARDIOVASCULAR PREVENTION**

**P5150 | BEDSIDE**

Impact of depressive symptoms on lifestyle management in post-ACS patients

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**Purpose:** To study the impact of depressive symptoms on lifestyle related risk factors for coronary artery disease.

**Methods:** We performed a substudy in RESPONSE, a multicenter randomised clinical trial. Patients (18-80 years) were included within 8 weeks after an ACS. Patients were randomised to a nurse coordinated prevention program (NCPP) in addition to usual care (intervention) or usual care alone (control). The intervention consisted of 4 visits within six months, and focused on guideline based risk factor management through medication and lifestyle modification. In a sub study, a subset of patients were screened for depressive symptoms using Beck’s depression inventory (BDI) questionnaire at baseline and 12 months. Patients with a BDI score of ten or more were classified as having depressive symptoms. Lifestyle related risk factors were (self reported) smoking, overweight and lack of physical activity.

**Results:** A total of 735 participants were randomised in the main study, 164 of these were screened for depressive symptoms using BDI. Twenty-two patients (13.4%) were classified as depressive (11 in the intervention group) and 116 as non-depressive (55 in the intervention group) Lifestyle risk factors were highly prevalent (table), with significantly more smoking and physical inactivity among patients with depressive symptoms. Improvement of lifestyle related risk factors was significantly less among patients with depressive symptoms (table), with no impact of the NCPP compared to control.

**P5151 | SPOTLIGHT**

The healthstart trial: improving depressive symptoms and cardiovascular disease risk in the most physically and mentally unhealthy area in the United States

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**Purpose:** Appalachian Kentucky has the highest rate of mentally and physically...
unhealthy days in the America. The prevalence of multiple co-morbid cardiovascular disease (CVD) risk factors is higher among individuals with depressive symptoms living in Appalachia. Our purpose was to determine the effect on depressive symptoms and other CVD risk factors of a self-care CVD risk reduction intervention that included depression management for Appalachians living in a socioeconomically distressed area at high risk for both depression and CVD.

Methods: We enrolled 425 adults (76% women; mean age 58±16yrs) with two or more CVD risk factors and randomized them to an immediate intervention group or a wait-list control group. The intervention consisted of a 12-week self-care risk reduction program focused on addressing environmental and individual barriers to CVD risk reduction. The program included self-care strategies aimed at preventing or reducing depressive symptoms with the ultimate goal of improving heart healthy behaviors. The program targeted lifestyle change with behavioral intervention; drug therapy was not included.

Results: Depression scores were unchanged during the non-intervention wait-list period, but decreased significantly in both groups (p<0.001) after the intervention; 18.5% of participants had depressive symptoms prior to the intervention and that was reduced to 7.6% after the intervention (41% reduction in depression). With regard to CVD risk factors, during the wait list control period there were no changes. Following the intervention, these changes were seen: 1) low density lipoprotein (LDL) decreased from a pre-intervention level of 110.5±34.5 mg/dL to 95.8±32.6 mg/dL (p<0.01); 2) high density lipoprotein (HDL) increased from 34.5±13.2 mg/dL to 39.8±12.9 mg/dL (p=0.03) and in women, increased from 49.6±15.1 mg/dL to a post-intervention level of 55.7±15.0 (p<0.001); 3) total cholesterol decreased from 190±38 mg/dL to 183±36 mg/dL (p<0.001); 4) pre-intervention, 21% of participants engaged in moderate activity for 30 minutes per day at least 4 days a week, while post-intervention 60% did (p<0.001); 5) body mass index pre-intervention was 32.6±7.7 and went down to a post-intervention level of 28.4±7.9 (p<0.001). Depression reduction was associated with enhanced CVD risk reduction.

Conclusions: A self-care approach to CVD risk reduction that includes depression prevention and management is effective in a rural population living in a socioeconomically distressed area at high risk for both depression and CVD.

Conclusion: CVD risk reduction.

Methods: The model was a state transmission Markov model. The focus was detection and treatment of long QT syndrome (LQTS) and hypertrophic cardiomyopathy (HCM). The arm was the presence or absence of the screening program. A 60% decrease in sudden cardiac death in subjects over 5 to 17 years old was reported between pre- and post-examination periods, preventing death rate was assumed as 60% by the presence of the screening. Prevalence of HCM and LQTS was determined using the data of the screening system. HCM was diagnosed when left ventricular wall thickness was ≥13 mm. LQTS was diagnosed by HRS/EHRA/APHRS Consensus Statement. Five HCM patients of 337,720 six-year-old subjects (1,875,544) were diagnosed and 16 patients of 322,610 twelve-year-old subjects (1,201,163) were diagnosed in 5 areas; prevalence of HCM was estimated to be 1/888,000 and 1/200,000 in 6- and 12-year-old subjects, respectively. Nine patients out of 27,482 six-year-olds and 23 of 28,885 twelve-year-olds were diagnosed as LQTS: prevalence of LQTS was estimated to be 1/3,000 and 1/1,250 in 6- and 12-year-old subjects, respectively. The data for 15-year-olds were not present; prevalence of HCM was estimated to be the same as 12-year-olds. Screening of LQTS patients at high school was estimated to be 0, because prevalence of 1/1,250 was higher than that of 1/200 in healthy live births in Italy. The precision parameters of the examination (sensitivity, specificity, etc) were referred to a previous work. For cost parameters, Japanese medical fee data in 2013 were used.

Results: The life-years saved by the screening system was 66,879 [person-years], and the cost was $232,000,000. Incremental cost-effectiveness ratio (ICER) was $3,481/person-years, which was less than $4,100.

Methods: The cost-effectiveness of the electrocardiogram screening program was firstly estimated as $3,481 per person-years ($1≈102 yen). The reasons for a low ICER may be a low prevalence of HCM in children and adolescents and low medical costs.

Conclusion: By showing that ideal CV health status had a three-fold increased prevention, our findings can contribute to the promotion of primordial prevention of CVD disease.
Q1:30.1% vs Q4:32.7% respectively, P <0.05). The 24-hour BP control was lower in hypertensives with greater variability (Q1:31.9% vs Q4:15.8%, P <0.01). Subjects in the highest quartile of CV showed higher total cholesterol and glycaemia in those in the lowest one (Q1:106.2 ± 35.5 mg/dl vs Q4:109.8 ± 39.1 mg/dl respectively, P <0.05). Glomerular filtration rate was higher in subjects in the lowest quartile of CV than in those in the highest one (Q1:75.9 ± 24.4 mL/min/1.73m² vs Q4:71.9 ± 22.0 mL/min/1.73m², P <0.01). The prevalence of TDD was similar among quartiles of CV, while the cardiovascular risk progressively increased from the lowest to the highest quartile of CV (Q1:66.8% vs Q4:71.8%).

Conclusions: In the hypertensive population of the BP-CARE study the increase in BP variability is associated with an increase in cardiovascular risk, an unfavorable glucose and lipid profile and a poorer 24-hour BP control.

P5155 | BEDSIDE
Nocturnal respiratory rate predicts non-sudden cardiac death after acute myocardial infarction

Background: The aim of this study was to develop an algorithm to derive the mean respiratory rate from ECG recordings and to evaluate the power of nocturnal respiratory rate to predict cardiac mortality in survivors of acute myocardial infarction (MI).

Methods: In a cohort of 1538 survivors of acute MI, mean respiratory rate during a nocturnal 6-hour period was determined from Holter recordings. Our algorithm to detect the respiratory rate in an ECG signal based on three parameters (1) QRS amplitudes in individual ECG leads (2) QRS vectors between pairs of ECG leads (3) RR intervals. The respiratory rate > 18.6/min was considered abnormal. Outcome measures were cardiac death (CD), sudden cardiac death (SCD) and non-sudden cardiac death (N-SCD) at 5 years.

Results: During a follow-up of 5 years, 146 deaths were observed (82 CD, 43 SCD, and 39 N-SCD). In univariable Cox proportional hazards analysis, abnormal respiratory rate was significantly associated with all-cause mortality, CD, SCD and N-SCD (hazard ratios 3.21 (2.32-4.44), 4.63 (2.99-7.19), 3.13 (1.72-5.69), and 7.40 (3.74-14.59), respectively). In a multivariable Cox analysis which also included left ventricular ejection fraction (LVEF), diabetes mellitus, GRACE score, and COPD, respiratory rate remained significantly associated with N-SCD (hazard ratio 4.56 (2.91-7.43)), but not with SCD. Combination of increased respiratory rate with reduced LVEF identified MI survivors substantially more likely to suffer from N-SCD rather than CD (Figure).

Conclusion: The nocturnal respiratory rate calculated from Holter ECGs predicts N-SCD in survivors of acute MI.

P5156 | BEDSIDE
Exercise gas exchange response in diabetes: analysis from the EURO(pean) EX(ercise) population-based study
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Background: Diabetes mellitus (DM) is a risk condition that may determine exercise limitation and reduced oxygen consumption (VO2). Diabetic subjects functional characterization with cardiopulmonary exercise testing (CPET) may help to better define cardiovascular (CV) risk and to improve the timing of therapeutic interventions.

Methods: 373 asymptomatic subjects (mean age 59 ±14 years; male 48%; BMI 28 ±6 kg/m²) with different CV risk factors (hypertension 64%, dyslipidemia 48%, smoking 20%, diabetes 14%) underwent a maximal CPET with personalized ramp protocol.

Results: The population was divided into two groups according to the presence of diabetes (Table). Diabetic subjects (n=32) showed a significant lower VO2 (16.3 ±4.3 vs 20.7 ±7.3 ml/kg/min) and O2 pulse (10.2 ±3.2 vs 11.3 ±3.9 ml/beat) at peak exercise, a steeper VE/VCO2 slope (27.2 ±3.5 vs 25.5 ±3.8) and a reduced heart rate recovery HRR (12 ±6.5 vs 17 ±11.5 bpm). A significant difference in the VE/VCO2 slope and peak O2 pulse between the two population was maintained when a correction for confounding factors (BMI, age, gender, prevalence of dyslipidemia and hypertension) was applied.

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>No DM (n=32)</th>
<th>DM (n=52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>58 ±14</td>
<td>67 ±10</td>
<td>0.0000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.6 ±5.5</td>
<td>28.9 ±5.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Peak VO2 (mL/min/kg)</td>
<td>20.7 ±3.3</td>
<td>16.3 ±4.3</td>
<td>0.0000</td>
</tr>
<tr>
<td>VE/VCO2 slope</td>
<td>25.5 ±3.8</td>
<td>27.2 ±3.5</td>
<td>0.002</td>
</tr>
<tr>
<td>HRR (bpm)</td>
<td>17 ±11.5</td>
<td>12.4 ±6.5</td>
<td>0.0000</td>
</tr>
<tr>
<td>VO2 at anaerobic threshold (mL/min/kg)</td>
<td>15 ±5.4</td>
<td>13 ±3.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak O2 pulse (mL/beat)</td>
<td>11.3 ±3.9</td>
<td>10.2 ±3.2</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Conclusions: Asymptomatic DM subjects with normal left ventricular function compared to non-diabetics show an increased VE/VCO2 slope and a reduced peak O2 pulse as a typical phenotype. These findings suggest that a lower increase in cardiac output at peak exercise may play a role. Whether assessment of these variables may improve the risk-related definition and a timely metabolic control in this patients seems to be worth of further investigation.

P5157 | BEDSIDE
Metabolic syndrome has similar explanatory ability in predicting 10-year CVD events as the cluster of risk factors: the attica study
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Background: Whether the metabolic syndrome is a cluster of risk factors without any additive explanatory ability in predicting future cardiovascular disease (CVD) events has been debated by several investigators. We sought to evaluate whether the metabolic syndrome can better predict future CVD events than the cluster of the common CVD risk factors.

Methods: From May 2001 to December 2002, 1514 men and 1528 women (>18 y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011-12 the 10-year follow-up was performed in 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria. Metabolic syndrome was defined according to NCEP ATPIII classification (2005).

Results: The 10-year CVD incidence was 14.3% in men and 9% in women (p<0.001). Multi-adjusted analysis after controlling for age, sex, physical activity, smoking, and dietary habits, revealed that presence of the metabolic syndrome was associated with 1.57-times higher risk of developing a CVD event (95% CI 1.17-2.12). A model that contained the aforementioned set of covariates, as well as the individual features of the syndrome, revealed that only high glucose levels (i.e., >110 mg/dl) were associated with CVD risk; whereas, all other features of the syndrome did not show any significance. Classification ability as regards the cases, as compared with the analytical model (i.e., 18.5% vs. 15.5%); Moreover the C-statistic (a measure of the predictive accuracy of a model, ranged between 0-1) was equal to 0.804 for the first model that included the metabolic syndrome and equal to 0.808 for the model that included the cluster of the features of the syndrome (p<0.001).

Conclusion: Our data suggest that the accuracy of the metabolic syndrome in predicting 10-year CVD events was similar to the accuracy of the cluster of the common CVD risk factors; whereas, metabolic syndrome as a single feature seems to have better predicting ability in correctly identifying future CVD events, while the cluster of the components has better classification ability as regards non-events.

P5158 | BEDSIDE
Warfarin discontinuation in patients with unprovoked venous thromboembolism: a large US insurance database analysis
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Purpose: The mainstay of venous thromboembolism (VTE) treatment is anticoagulation, and guidelines recommend therapy for 3 months or longer. This study examined warfarin therapy discontinuation and its risk factors among patients with unprovoked VTE in the US clinical practice setting.

Methods: Adult patients with VTE were identified from the Truven Health Mar-
ketScan insurance database, the largest US claims database. Index date was defined as the date of first VTE diagnosis between 07/01/2006 – 12/31/2011. Patients were required to 1) have ≥2 outpatient VTE diagnosis claims within a 3-week window; 2) have no VTE diagnosis in the 6 months prior to index date; 3) receive warfarin therapy within 10 days of index diagnosis; and 4) have continuous health plan enrollment for 6 months prior and 12 months after index date. VTE was considered as unprovoked if patients did not have reversible provoking risk factors in the 6 months prior and did not have cancer diagnosis or chemotheraphy within the 3 months of index date. Warfarin was considered as discontinued if a patient did not have a prescription refilled within 45 days after the ending date of last prescription. Discontinuation rates of warfarin therapy and adjusted hazard ratios (HRs) via multivariate Cox regression were reported.

Results: Of 21,163 eligible patients, 15,483 were diagnosed with deep vein thrombosis (DVT) only (73.1%), 5,027 with pulmonary embolism (PE) only (23.7%), and 673 with both DVT and PE (3.2%). The average duration of warfarin therapy was 5.2 months (SD=3.0). During 1 year follow-up, 21.4% patients discontinued warfarin within 3 months, 42.8% within 6 months, and 70.1% within 12 months. PE versus DVT (HR=0.77), paroxysmal atrial fibrillation (HR=0.73) and thrombophilia (HR=0.62), and age ≥40 years (HR=0.86) were associated with reduced risk warfarin discontinuation (p<0.05). Alcohol abuse/dependence (HR=1.36), history of cancer (HR=1.13), bleeding (HR=1.07), and catheter ablation (HR=1.10) in the 6 months prior to index date was significantly associated with increased risk for warfarin discontinuation (p<0.05).

Conclusions: In the US clinical practice setting, nearly one out of four patients with unprovoked VTE discontinued warfarin therapy within 3 months, and 3 out of 4 patients discontinued therapy within 1 year. Multiple demographic and clinical factors are associated with warfarin therapy discontinuation.

PS159 | BEDSIDE
Infective endocarditis before and after the 2007 endocarditis prevention guidelines: a population-based study from Qatar (2002-2012)
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Objectives: The 2007 American Heart Association guidelines for infective endocarditis (IE) prevention markedly restricted the use of antibiotic prophylaxis in certain at-risk patients undergoing dental and other invasive procedures. How that affected the incidence of IE in the developing countries has never been reported. The aim of the current study is to determine if the incidence of IE has changed following adoption of the 2007 guidelines in a real-world population in a Middle Eastern Country.

Methods: Retrospective analysis of all patients hospitalized with IE in the State of Qatar from 2002 through 2012 was made. Incidence rates per population number per year were compared in the years 2002-2006 (5-years before the guidelines) and 2008-2012 (5-years after the guidelines) with patients hospitalized in the year 2007 excluded to allow time for distribution and application of the guidelines.

Results: We identified 45 cases with IE in Qatar over the 11-year study period 2002-2012. The incidence rate (per 100 000 person-years) during the time interval of 2002–2006 was 3.1 (95% confidence interval, 1.95–4.40), while during the time interval 2008–2012, the incidence rate was 0.9 (95% confidence interval, 0.5–1.4). (P=0.01).

Conclusions: We report a significantly lower incidence of IE following the release of the 2007 IE guidelines in Qatar. Our study represents the first population-based study from a developing country that confirms the safety and effectiveness of these guidelines in IE prevention.

PS161 | BEDSIDE
Differences in symptom presentation in STEMI patients, with or without a previous history of hypertension; a survey report from the SymTime study group
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Introduction: A variety of factors have been associated with prolonged care seeking behaviour in STEMI patients. Specifically, older age, female gender and different co-morbidities have been found to explain prolonged pre-hospital delay times. However, conflicting data still exist due to the impact of a previous history of hypertension on delay times. We hypothesised that acute symptoms will differ in patients with a previous history of hypertension compared to non-hypertensive STEMI patients.

Methods: SymTime is a Swedish multicentre observational study where STEMI patients admitted to the CCU fulfilled in a validated Swedish questionnaire within 24h from admission. The questionnaire measures how patients with MI describe different symptoms and actions in the pre-hospital phase.

Result: In total, 281 non-hypertensive (53%) and 245 hypertensive (47%) STEMI patients were included (mean age 64±11 and mean age 67±8, respectively). There were significant differences in symptom presentation; chest pain (85% vs. 92%, p<0.05, respectively), pain in jaw or teeth were more common in hypertensive patients compared non-hypertensive patients (16% vs. 10%, p<0.05, respectively) and shoulder (23% vs. 16%, p<0.05, respectively), and feeling generally ill (20% vs. 11%, p<0.05, respectively). After age adjustment, non-hypertensive patients had 1.9 times higher odds (OR 1.94, 95% CI 1.1-3.38) of having chest pain compared to hypertensive patients.

Conclusion: STEMI patients with a history of hypertension, as well as non-hypertensive patients, experience chest pain as the predominantly symptom in the acute phase, but in comparison between groups chest pain is more seldom presented in the hypertensive group.

PS162 | BEDSIDE
Role of nursing information to reduce state anxiety before coronary angiography or PTCA
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Purpose: Patients waiting to undergo a coronary angiography and/or a percutaneous transluminal coronary angioplasty (PTCA), experience high levels of anxiety which present some characteristics typical of this kind of procedure. In cardiological patients it can be dangerous to underestimate the problem of anxiety. Symptoms and feelings associated with anxiety are significant and often unrecognised. Studies have demonstrated that it worsens the outcome, increasing morbidity and mortality; the aim of this study is to assess if additional nursing information can reduce the level of anxiety felt by patients before undergoing a coronary angiography or a PTCA. The objectives of the study are to: 1) Assess the level of anxiety in people waiting for a coronary angiography or a PTCA; 2) Assess how and in what measure anxiety is modulated; 3) Assess how nursing information influences the state of the patient’s anxiety.

Method: Epidemic prospective study, descriptive report, carried out on a sample of 62 patients admitted in an Italian hospital. All the patients had been informed and prepared for the procedure according to standard means (informed consent, talk with a cardiologist), moreover 29 patients received additional nursing information. The following exclusion from the study criteria was applied: age <18, unsuitable operation, patients undergoing therapy with anxiolytics, antidepressants, antipsycogeners and neuroleptics. The data was collected using STAI (State Trait Anxiety Index). For the general comparison of the score of the two samples (the Informed and the Non-informed) parametric tests (ANOVA and Student’s T test) were chosen since the conditions of normality and homoscedasticity of the distribution had been verified. All the analyses were carried out with a level of significance of a = 5.

Results: The results confirm that being subject to such a procedure causes anxiety; females are more anxious than males (p=0.028). Age (p=0.06), education (p=0.82), being accompanied by the usual caregiver (p=0.31) and previous admittance in Cardiopathy (p=0.07) are not associated with a reduction in anxiety. A reduction in anxiety is associated with previous experience of PTCA (p=0.03) and the presence of additional nursing information (p=0.00). The latter is considered more efficient in reducing anxiety than previous clinical experience (p=0.00).

Conclusions: Nursing information and the way it is modulated are shown to be important variables in significantly reducing anxiety and contributes to making the patient feel more considered as a whole person, aiding the acquisition of a greater control in the events relating to the management of his/her health.

PS163 | BEDSIDE
Transitioning towards recovery following ACS (NSTEMI/UA)
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Purpose: The purpose of this study was to investigate the experiences of women with a primary presentation of NSTEMI/UA, in the six to eight week timeframe, after discharge from hospital. The aim was to provide insight in an Irish context and to focus on the mediating impact of a newly-diagnosed disease on their lives. There is increased survival and morbidity across the acute coronary syn-
drome (ACS) continuum. However more adverse outcomes have been reported for women and their needs in rehabilitation have not always been recognised. There is a rising rate of non ST elevated myocardial infarction (NSTEMI) in Ireland; yet there is a dearth of information about women’s experiences following NSTEMI and Unstable Angina (UA).

Methods: A naturalistic case study design guided this study. A within-case analysis followed by a cross-case analysis provided meticulous knowledge of each case. Within-methods triangulation captured the depth and breadth of the experiences of thirty women. Data, derived through interviews and participant diaries, were analysed using modified analytic induction which allowed the emergence of theoretical insights.

Results: The women’s narratives revealed divergent and yet dominant constructions of disbelief about the onset of ACS (NSTEMI/UA), along with a period of disorientation during the initial discharge from hospital. The power of the woman’s voices to articulate their experiences provides new insight in an Irish context. A number of women had transitioned towards recovery and cardiac rehabilitation was reported positively by those who were attending. However, a critical interpretation of a low rate of referral to cardiac rehabilitation suggests careful consideration is needed in relation to the provision of cardiac rehabilitation programmes and secondary prevention initiatives to meet the needs of women.

Conclusions: This study creates a platform for a wider discourse on the needs of women following NSTEMI and UA. Women may benefit from gender-specific approaches and targeted interventions to facilitate recovery and adaptation to living with CHD.

P5164 | BEDSIDE
Women’s hearts - fixed and healthy after PCI?
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Purpose: To explore and describe the experiences of women with ischemic heart disease (angina pectoris and myocardial infarction) after Percutaneous Coronary Intervention (PCI). Furthermore, the study examined changes in daily life affected by the PCI and how women relate to heart-healthy lifestyle.

Methods: Data were collected through qualitative interviews in the respondents’ home by using a semi-structured interview-guide reflecting a promotion of health perceptions and the International Classification of Function (ICF) model and adherence to heart-healthy lifestyle approach in terms of the Health Belief Model. The interviews lasted for 1-1.5 hours. The data were analyzed in four steps with Malterud’s modified version systematic text condensation (STC), based on Giorgi’s phenomenological model of qualitative data analysis.

Results: A purposive sample of nine women aged 55-64 were interviewed in 2003. The women were characterized by living alone, low education, incapacitated, sick leave and additional diseases. Risk factors were identified as smoking (n=4), diabetes (n=1), high blood pressure (n=2) and heritance (n=5). Data analysis revealed four main categories: 1. “Experiences in the days before PCI” meaning trivializing cardiac symptoms, undertreated and underdiagnosed. 2. “Experiences in the post-PCI” representing reactions of joy, appreciation of life and laibility, consciousness in avoiding stress and focusing boundaries, and 4. “Compliance with heart-healthy lifestyle” in terms of concerning hereditary, symptom management and side effects of medications. Individual risk factors were given little attention, no one stopped smoking and the level of physical activity was generally low. Diet, however, was to a certain degree adjusted to heart friendly advice and recommendations.

Conclusion: PCI was experienced as a quick and uncomplicated treatment which made the women feeling repaired and “fixed”. Being free from symptoms after PCI challenges the understanding of ischemic heart disease as a chronic illness. In all, lifestyle was only to a limited extent changed after PCI and the women lived largely as before. Individual health promoting approaches and systematic use of assessment tools, including socio-demographic data and risk assessment factors, may strengthen the focus on women’s resources as well as opportunities and needs, to comply with recommendations on heart-healthy lifestyle.

P5165 | BEDSIDE
Impact of percutaneous coronary intervention for chronic total occlusion in patients with hypertension
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Background: Hypertension is known to be associated with increased adverse clinical outcomes in coronary artery diseases (CAD) patients (pts). The impact of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) in pts with hypertension is not clear. We compared the 12-month clinical outcomes of pts treated by PCI with optimal medical therapy (OMT) for CTO lesions in pts with hypertension.

Methods: A total of 413 consecutive CTO pts with hypertension divided into 2 groups; one group underwent PCI (PCI group; n=171) and the other group was treated with OMT (OMT group; n=242). Major clinical outcomes were compared between the two groups up to 12 months.

Results: At baseline, the OMT group had higher prevalence of elderly, stroke, peripheral vascular disease, congestive heart failure, left main disease, failed CTO procedure, multi-vessel disease, multi-vessel CTO, RCA-CTO lesion, and more abundant collaterals (>grade 2), whereas the PCI group had higher prevalence of prior PTCA, current smoker and LAD-CTO lesion. Clinical outcomes at 12 months were similar between the 2 groups except higher TLR and lower trend of mortality in the PCI group (Table). After baseline adjustment by multivariate analysis, there was no difference in 12-month mortality in both groups.

Conclusions: In our study, mechanical recannalization by PCI for CTO lesions in pts with hypertension as compared with OMT seems to have no definite benefit in reducing 12-month mortality. Long-term follow up with larger study population will be necessary for further clarification.

P5166 | BEDSIDE
Groin dressing post cardiac catheterization: traditional pressure vs transparent film
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Purpose of the study: To determine the efficacy of using a small transparent non pressure dressing compared with the traditional controlled pressure dressing applied to the femoral artery puncture wound site to maintain haemostasis following cardiac catheterization procedures.

Methods: Design: An experimental design, Randomized Controlled Trial (RCT). A total of 413 consecutive CTO pts with hypertension divided into 2 groups; one group underwent PCI (PCI group; n=171) and the other group was treated with OMT (OMT group; n=242). Major clinical outcomes were compared between the two groups up to 12 months.

Conclusions: In our study, mechanical recannalization by PCI for CTO lesions in pts with hypertension as compared with OMT seems to have no definite benefit in reducing 12-month mortality. Long-term follow up with larger study population will be necessary for further clarification.

Conclusions: In our study, mechanical recannalization by PCI for CTO lesions in pts with hypertension as compared with OMT seems to have no definite benefit in reducing 12-month mortality. Long-term follow up with larger study population will be necessary for further clarification.
ease of observation of the groin puncture site after the procedure. Five instruments were used for data collection: 1) Demographic and medical data sheet, 2) Hematoma Formation and Bleeding Scale, 3) Skin Integrity Scale, 4) Patient Discomfort and Pain Scale and 5) Nurses Ease of Assessment Scale.

**Results:** There were no significant differences in base line characteristics and medical data between the two groups. 100% in Transparent Film Dressing (TFD) group vs 55% in pressure dressing group reported feeling very comfortable (p value of 0.003). Hematoma formation was equal in the two dressing groups with no incidence of bleeding complications. Nurses rated the ease of assessing the granulation tissue significantly higher for TFD than for pressure dressing (p value of 0.001).

**Conclusion:** Dressing of the puncture site after cardiac catheterization with TFD was more comfortable than the conventional pressure dressing without any difference in hematoma or bleeding complications. So TFD can be used safely and comfortably after achieving hemostasis.

**P5158 | BEDSIDE**

**It’s always a good time: a mixed methods study explaining the results of a heart failure self-care skill-building intervention**

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**Objective:** Most of the day to day care for heart failure (HF) is done by the patient at home and requires consistent adherence to complex treatment regimens and vigilance to symptom management. This process of HF self-care requires skill in establishing and maintaining self-care in cardiac patients. The purpose of this mixed method study was to test the efficacy of a skill-building self-care intervention on HF self-care, knowledge and health-related quality of life (HRQL) at 1- and 3-months and used qualitative data to explain the mechanism of intervention effectiveness.

**Methods:** Using a randomized control trial design, an ethnically diverse sample (n=75) of patients with HF (53% female; 32% Hispanic, 27% Black; mean age 69.9±10 years) was randomized to the intervention group (IG) or a wait-list control group (CG). A protocol-driven intervention focused on HF self-care skill development delivered in small groups by a health educator. Data were analyzed using mixed (between-within subjects) ANOVA. Intervention sessions were audio-taped and transcribed verbatim. Qualitative data were analyzed using content thematic analysis in order to gain insight into the mechanism of effectiveness of the intervention.

**Results:** Although there was a significant improvement in self-care maintenance (F=8.33, P=0.006), self-care management (F=7.30, P=0.01) and knowledge (F=4.8, P=0.001) in the IG compared to the CG, there was no improvement in HRQL. The qualitative data revealed that for many the intervention led to an increased awareness of their condition and that they need further training in these areas.

**Conclusions:** The skill-building intervention improved self-care and knowledge and facilitated ongoing self-care in those who may feel otherwise burdened.

**P5157 | BEDSIDE**

**Do we ask the fear of dying in patients hospitalized for acute coronary syndromes?**

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**Objectives:** Although guidelines recommend the assessment of psychological factors in patients admitted to hospital with acute coronary syndromes (ACS), the screening of posttraumatic stress disorder (PTSD) and fear of dying after acute coronary syndrome is not systematically done in clinical practice. Assessing fear of dying at hospitalization might be a pragmatic approach to identify patients at risk of developing PTSD. We aimed to assess the prevalence of fear of dying in patients hospitalized with a diagnosis of ACS in a Cardiology University Clinic from February to June 2012. At baseline, we collected data on fear of dying, feeling of helplessness, anxiety and coping capacities. One month after discharge, we measured PTSD using the posttraumatic stress scale. Using logistic regression, we estimated age and gender adjusted odds ratios (OR) and 95% confidence intervals (CI) of the associations between baseline psychological factors and the occurrence of PTSD.

**Results:** 24 patients (26.7%) developed PTSD one month after the ACS event. PTSD was more frequently diagnosed in patients who developed PTSD compared significantly greater fear of dying (adjusted OR 3.78, 95% CI 1.39-10.31) and helplessness (OR 4.29, 95% CI 1.50-12.22) at the index hospitalization. The fear of dying was associated with high degree of severe anxiety (P=0.002) and maladaptive coping capacities (P value=0.056).

**Conclusion:** The fear of dying during the hospitalization is associated with the occurrence of PTSD in patients with ACS. A simple question about fear of dying might be useful to identify patients at higher risk for PTSD. Further studies are needed to assess the impact of interventions based on improving coping strategies in those patients.

**IMAGING IN HYPERTENSION**

**P5172 | BEDSIDE**

**Determination of blood pressure limits combined with non-invasive cardiac computed tomographic findings to obtain good long-term prognosis for major adverse cardiovascular events**

H. Takaoka, N. Funabashi, K. Ozawa, Y. Kobayashi. Chiba University School of Medicine, Chiba, Japan

**Purpose:** To determine blood pressure (BP) indicative of good long term prognosis for major adverse cardiovascular events (MACE), we performed cardiac computed tomography (CT) on patients to evaluate coronary arteries, followed their average of systolic and mean BP during the periods and sought the relationship between BP and CT findings of coronary arteries for the occurrence of MACE... Further studies are needed to assess the impact of interventions based on improving coping strategies in those patients.
the average of systolic and mean BP during the period revealed best cutoff points of 137 and 105 mmHg for NCP (with and without CP), and 132 and 105 mmHg for CP (with and without NCP), respectively, to differentiate subjects with and without MACE. Kaplan Meier analysis and log rank test revealed nearly significant differences between subjects with NCP (with and without CP) with an average of 1 systolic BP < 137 and > 137 mmHg, and mean BP > 135 and 105 mmHg (both P = 0.055); and significant differences between subjects with CP (with and without NCP) with average of 1 systolic BP < 132 and > 132 mmHg and 2) mean BP < 105 and > 105 mmHg (both P < 0.001).

Conclusions: Ascending aorta dilation is already present in one third of newly diagnosed EH patients. Older age, male gender, high alcohol intake and BMI are independent predictors of this condition, with increased heart rate to possess beneficial effects, probable due to diminished stroke volume and cyclic aortic expansion.

P5175 | BEDSIDE
Clinical impact and characteristics of coronary artery tortuosity
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Introduction: In the heart coronary tortuosity (CT) is often observed during coronary angiography (CA). Sometimes it is described in patients with Angina (AP) undergoing CA that turn out to have no coronary arteriosclerosis. In this population CT is often associated with reversible myocardial perfusion defects and a smaller coronary reserve. However, the etiology and clinical impact of CT are still undetermined.
Methods: To address this issue we evaluated 177 consecutive patients who were admitted to a cardiological center between 2000 and 2007 for further evaluation of dyspnea or AP by CA, which however did not reveal any evidence of coronary artery disease or structural heart disease. For a quantitative analysis of CT in coronary angiograms a tortuosity index (TI=total length of coronary/ shortest length of coronary artery) was calculated. A correlation of TI with patients’ characteristics and hemodynamic parameters was performed. To further assess symptomatic and pathophysiological correlations we analyzed the severity of TI in subgroups: AP (n=113) vs. non-AP (n=64) and hypertensive patients (HP) (n=90) vs. non-HP (n=87).
Results: No difference in CT severity between AP vs. non-AP was found. However, more pronounced CT was observed in HP in univariate analysis we found a positive correlation of CT with age (r=0.26, height (r=0.21), number of antihypertensive agents (r=0.27), left ventricular systolic pressure (r=0.31), aortic systolic pressure (r=0.29) and aortic mean pressure (r=0.23). CT severity did not correlate with severity of NYHA class.
Conclusion: Our results suggest that CT may be a manifestation of arterial hypertension. However, it is not associated with cardiac symptoms like AP or dyspnea.

P5176 | BEDSIDE
Association of cystatin C with global left ventricular longitudinal strain in hypertensive patients
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Purpose: Hypertension is one of the most common entities leading to cardiac dysfunction. The impact of abnormal renal function on left ventricular (LV) function in patients with hypertension is not fully understood. We tested the hypothesis that cystatin C is associated with subclinical systolic abnormalities of LV function assessed by speckle-tracking global longitudinal strain (GLS) in hypertension.
Methods: The study population consisted of 90 hypertensive patients without history of diabetes mellitus, coronary heart disease or heart failure and 20 age-matched controls. LV structure and function were assessed by conventional echocardiography and two-dimensional speckle-tracking imaging. We measured possible biomarkers of renal and LV conditions included serum cystatin C, urinary albumin-creatinine ratio (ACR), and plasma B-type natriuretic peptide (BNP).
Results: In the hypertensive group, mean GLS was significantly reduced (-18.5±2.7% versus -20.3±1.7%, p<0.01) and mean cystatin C level was increased (2.7±1.5 vs. 2.0±1.1 mg/L, p<0.01). GLS significantly correlated with LV mass index, LV systolic diameter, interventricular septum thickness, and posterior wall thickness (r=-0.321, r=0.328, r=-0.336 and r=0.387, p<0.01: respectively). Serum cystatin C levels were categorized into quartiles (quartile I, 0.66 to 0.84 mg/L; quartile II, 0.85 to 0.94 mg/L; quartile III, 0.95 to 1.00 mg/L; quartile IV, 1.01 to 1.82 mg/L). Age was higher and GLS was reduced in the highest quartile compared with the lowest quartile of cystatin C levels (69±8 years versus 59±11 years, p<0.01; 17.5±2.4% versus 20.9±1.7%, p<0.01, respectively). In multiple regression analysis adjusting for age, ACR, BNP, systolic blood pressure and diastolic blood pressure, cystatin C levels and LV mass index remained significantly associated with GLS (β = 0.246, p<0.05; β = 0.258, p<0.01, respectively).
Conclusion: Increased levels of cystatin C were associated to reduced GLS. This suggests that impaired renal function is associated with subclinical systolic abnormalities of LV function in hypertension.

P5179 | BEDSIDE
Reduced coronary flow reserve is related with impaired Endothelial Glycocalyx in low cardiovascular risk patients with newly diagnosed arterial hypertension
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Background: Aortic stiffness and coronary flow reserve are considered valuable indicators of subclinical damage in hypertensive patients. The aim is to evaluate the relationship between coronary flow reserve, endothelial glyocalyx and aortic stiffness in patients with newly diagnosed arterial hypertension.

Methods: We studied 58 patients with newly diagnosed and never treated essential hypertension (mean age 48±10 years, 40 males). We performed carotid-femoral artery pulse wave velocity (PWV) in order to evaluate aortic stiffness. Since PWV<10 m/sec was considered as normal, patients were divided in Group A (PWV<10 m/sec, n=15, mean age 46±7 years) and Group B (PWV≥10 m/sec, n=43, mean age 49±10 years). Coronary microcirculation (CFR) was estimated by echocardiology. Increased perfusion boundary region (PBR) of the sublingual arterial microvessels (ranged from 5-25 micrometers) using Sideview Darkfield imaging (Mroscosan, Glycocheck) was measured as a non-invasive accurate index of reduced endothelial glyocalyx thickness.

Results: No significant differences were found within groups regarding age, BMI, smoking habit, PWV, PBR (ranged from 5-25 micrometers) and CFR. However, Group A had increased systolic and diastolic blood pressure and pulse pressure in office and 24h ABPM measurements. In Group A, CFR was related with PBR<25 (r=0.60, p<0.01), PBR10-19 (r=0.81, p<0.01) and PBR20-25 (r=0.56, p<0.05). No such relationship was shown in Group B patients.

Conclusions: This is the first study showing an existing relationship between reduced coronary flow reserve and endothelial dysfunction, represented by endothelial glyocalyx thickness, in low cardiovascular risk patients. This relationship which may separate patients with intermediate cardiovascular risk, is lost in patients with more severe atherosclerosis as expressed by higher blood pressure levels and impaired aortic stiffness. Further studies are needed to confirm our results and establish endothelial glyocalyx measurement as a valuable tool in cardiovascular risk evaluation.

P5180 | BEDSIDE
New inflammatory markers in preeclampsia: echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio
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Purpose: Increased epicardial fat thickness (EFT) has been proposed as a new cardiometabolic risk factor. The neutrophil/lymphocyte ratio (NLR) has predictive prognostic value in several cardiovascular diseases. The aim of this study was to explore the association between EFT and NLR in patients with preeclampsia.

Methods: 108 pregnant patients with a mean age of 30.6±6.3 years were included in the study. Patients were divided into 2 groups based upon the presence of preeclampsia. All participants underwent transthoracic echocardiography imaging and complete blood counts were measured by an automated hematology analyzer. Statistical analysis was performed using the Chi-square, Mann-Whitney U, correlation and logistic regression tests, and ROC analysis.

Results: The mean EFT value of the preeclampsia group was significantly higher than the control group (6.9±0.6 vs 5.6±0.6, p<0.001), respectively, and the NLR value of the preeclampsia group was also significantly higher than the control group (7.3±3.5 vs 3.1±1.1, p<0.001). Multivariate analysis showed that increased levels of NLR and echocardiographic EFT are independent predictors of preeclampsia. In the receiver operating characteristic analysis, a level of EFT≥6.2 mm and NLR≥4:1 predicted the presence of preeclampsia with 77.8% sensitivity, 79.6% specificity and 83.3% sensitivity, 81.5% specificity, respectively.

Table 1. Multivariate logistic regression analysis to assess predictors of preeclampsia

<table>
<thead>
<tr>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFT</td>
<td>12.340</td>
<td>2.193-69.530</td>
</tr>
<tr>
<td>NLR</td>
<td>2.740</td>
<td>1.354-5.544</td>
</tr>
<tr>
<td>MPV</td>
<td>1.596</td>
<td>0.734-3.471</td>
</tr>
<tr>
<td>TTV</td>
<td>1.157</td>
<td>0.599-3.340</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>1.011</td>
<td>0.997-1.025</td>
</tr>
<tr>
<td>LVMI</td>
<td>0.985</td>
<td>0.949-1.023</td>
</tr>
</tbody>
</table>

Conclusions: Unlike many other inflammatory markers and bioassets, NLR and echocardiographic EFT are inexpensive and readily available biomarkers that may be useful for risk stratification in patients with preeclampsia.

P5178 | BEDSIDE
The prognostic value of oxygen kinetics during early recovery after exercise in hypertensive patients with impaired coronary flow reserve
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Purpose: The period of early recovery after exercise is characterized by a rapid payback of the oxygen debt incurred during exercise which in turn reflects normal circulatory function. Hypertension may be accompanied by impaired coronary microcirculation. We hypothesized that oxygen consumption (VO2) during exercise as well as its decline during the first minute of recovery after exercise will be impaired in hypertensive patients with reduced coronary flow reserve.

Methods: Eighty (80) non-diabetic, recently diagnosed and well-controlled hypertensive patients (mean age 51±11 years, 55 men) underwent a ramp symptom-limited cardiopulmonary exercise test (CPET) on a bicycle ergometer. We evaluated exercise parameters (work load, O2 pulse and VE/VO2 slope) as well as oxygen kinetics during exercise (peak oxygen consumption [peak VO2]) and early recovery period (slope of VO2 decline during the first minute of recovery, VO2rec). Coronary flow reserve, which was estimated before CPET, was measured by means of color-coded Doppler echocardiography at the distal tract of the left ascending coronary artery after adenosine infusion (140 mg/kg/min). The study group was divided according to CFR values to group A (n=57, normal CFR>2) and group B (n=23, impaired CFR<2).

Results: No significant differences were found between groups regarding age, body mass index and systolic and diastolic blood pressure at rest. All patients completed successfully the exercise test without ECG signs or symptoms of myocardial ischemia. Regarding total population, VO2rec was strongly related with peak VO2 (r=0.72, p<0.001), work load (r=0.70, p<0.001), O2 pulse (r=0.70, p<0.001) and VE/VO2 slope (r=0.20, p<0.05). We found that patients in group B had lower work load (146±46 vs 122±38 watts, p<0.05), peak VO2 (205±30 vs 1798±455 ml/min, p<0.05) while VO2rec was significantly lower (816±374 vs 634±288, p<0.001).

Conclusions: Hypertensive patients with impaired coronary microcirculation exhibit impaired peak exercise parameters (work load, oxygen consumption and oxygen recovery). Cardiopulmonary exercise test may be a useful tool in cardiovascular risk estimation in hypertensive population.
Dipeptidyl peptidase 4 inhibition ameliorates hypertension via normalizing preload through the RAAS axis

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Purpose: DPP4 inhibitors have attracted rising attention regarding their pleiotropic effects on cardiovascular system. Several reports suggested vasorelaxant effects of DPP4 inhibition, namely, anti-hypertensive effect of incretine GLP-1 (Nut Med 2013) or link between DPP4 and angiotensin-converting enzyme (ACE) regarding angiotedema (Hypertension 2009), however, its role in hypertension remains uncertain.

Methods: Spontaneously hypertensive rats (SHR; 10 w/o male) and its counter-part Wistar-Kyoto (WKY) were treated with moxaglizone (10.1 mg/kg/day) in a period of 4 wks (SHR-TEN and WKY-TEN or vehicle (CON). Cardiac function and blood pressure was analyzed using echocardiogram and cardiac catheterization. Molecular mechanisms were examined in each heart, aorta, and blood specimen.

Results: SHR-CON exhibited increase in heart and body weight (BW) ratio, which was attenuated by TEN. Of note, TEN reduced lung weight and BW exclusively to SHR with concomitant normalization of its elevated BNP level, suggesting TEN may reduce preload via ameliorated pulmonary congestion. Systolic and diastolic blood pressure (SBP and DBP) were higher in SHR-CON (in mmHg; 201±16 and 134±15) than WKY-CON (105±6 and 78±4). TEN reduced both SBP and DBP of SHR (141±17 and 96±6). In contrast, TEN had no effects on BP of WKY. TEN attenuated cardiac hypertrophy of SHR-CON. There was no difference in ejection fraction and LV diameter among all groups. Maximum dp/dt (max dp/dt) of SHR-CON was elevated (in mmHg/sec; 1045±353) compared to WKY-CON (5739±599), which was reduced by TEN (SHR-TEN; 8033±656) without affecting heart rate, consistently suggesting TEN reduced preload in SHR (because the determinants of max dp/dt are heart rate and preload). Minimum dp/dt was elevated in SHR-CON (in mmHg/sec; 313±97) compared to WKY-CON, which was ameliorated by TEN; however, there was no difference in other diastolic indices. DPP4 activity was 1.5-fold higher in SHR-CON than WKY-CON, which was suppressed by TEN. Circulating angiotensin 2 (AT2) receptor was higher in SHR-CON compared to WKY-CON. In contrast, TEN modulated ACE activity in vitro. In SHR, the major occurrence of “pathological genotype” TT and T allele of polymorphism G894T of eNOS gene were observed significantly more often than WKY (45.5% vs 38.6%) and without the metabolic syndrome (62.4% and 44.1%) respectively, and without the metabolic syndrome (62.4% and 44.1%) respectively, and without the metabolic syndrome (62.4% and 44.1%) respectively, and without the metabolic syndrome (62.4% and 44.1%) respectively, and without the metabolic syndrome (62.4% and 44.1%) respectively,

Conclusions: DPP4 inhibition with TEN ameliorates pathological hypertension and metabolic syndrome. These findings could represent a novel link between DPP4 and RAAS pathway.
Risk genes of hypertension: results from Kaunas cohort study in Lithuania

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Purpose: Clinical and experimental studies have demonstrated a major role of the renin-angiotensin system (RAS) in hypertension. Polymorphisms of angiotensinogen (AGT rs699), angiotensin II type 1 receptor (AGTR1, rs1856), and angiotensin converting enzyme (ACE, rs4340) genes have been extensively studied in association with hypertension, however, findings are conflicting. Among new identified loci for blood pressure and hypertension there are genes encoding adrenomedullin (ADM, rs12258967), a plasma membrane calcium/calmodulin dependent ATPase (ABT2B1, rs2681472) and a beta-2 subunit of voltage-gated calcium channel (CACNB2, rs12259867). The objective of the present study was to assess the contribution of gene polymorphisms to blood pressure (BP) in the Kaunas cohort study.

Methods: Study subjects were participants of Kaunas cohort study started in 1977. At the time of the baseline survey the participants were 12-13 years age old. A total of 507 subjects (64.4% of eligible sample) participated in the 35-year follow-up in 2012 being 48-49 years old. Health examination included measurements of BP, anthropometric parameters and interview about health behaviours. Single nucleotide polymorphisms (rs699, rs15186, rs7129220, rs12259867, rs2681472, rs4340) were analyzed by real-time and conventional polymerase chain reactions.

Results: Mean values of systolic BP were highest in boys with AGT TT genotype. In girls, the CACNB2 GG genotype carriers had a significantly lower level of diastolic BP, while ADM AA genotype was positively related both to systolic and diastolic BP in girls. After adjustment for BMI, alcohol consumption, salt intake and physical activity, the odds ratios (OR) of having hypertension in middle age women with AGT TT genotypes were higher compared to AGT MM genotype carriers (OR≈2.31; 95% confidence interval: 1.01-5.29).

Conclusions: The associations between analysed gene polymorphism and blood pressure differ by gender in Kaunas cohort study.
chronic thromboembolic pulmonary hypertension

P5191 | BEDSIDE
External validation of a simple non-invasive algorithm to rule out chronic thromboembolic pulmonary hypertension after acute pulmonary embolism

Purpose: International guidelines do not provide clear recommendations on medical follow-up after acute pulmonary embolism (PE) including screening programs for chronic thromboembolic pulmonary hypertension (CTEPH). We aimed to externally validate the performance of the non-invasive “CTEPH rule-out criteria” (Thromb Res 2011,128:21-6) to exclude CTEPH in the long-term course of PE based on a normal NT-proBNP level (below age- and gender-adjusted threshold) and the absence of 3 specific ECG characteristics.

Methods: 134 consecutive patients with acute PE underwent echocardiography 6 months after the PE diagnosis. The non-invasive CTEPH rule-out criteria were used to categorize patients as either “pulmonary hypertension (PH) unlikely” or “PH possible/likely” according to the ESC guideline. The latter patients underwent further (invasive) diagnostic procedures. NT-proBNP, high-sensitive troponin T (hsTnT), and ECGs, all assessed at the day of echocardiography, were evaluated post-hoc.

Results: Sixty-three patients (47%) scored none of the criteria, of whom 61 had a normal echo (97%). Twenty-five patients (19%) were categorized by echo as “PH possible/likely”; of those, 6 were diagnosed with CTEPH. The sensitivity of the CTEPH rule-out criteria to exclude CTEPH was 100%, and to exclude echocardiographic defined “PH possible/likely” 92% (23 of 25 patients identified); 2 asymptomatic patients with elevated estimated systolic pulmonary artery pressures of 36 mmHg and 38 mmHg, respectively, who remained echocardiographic clean after 12 months, were considered to be “false negatives” as the predefined ECG criteria were not met.

Conclusions: In this external validation cohort, we confirmed the excellent diagnostic accuracy and reproducibility of the CTEPH rule-out criteria. When applied as first test in a CTEPH screening program, echocardiographic examination could have been avoided in half of our patients.

P5192 | BEDSIDE
Phenprocoumon dose requirements and genetic polymorphisms in chronic thromboembolic pulmonary hypertension

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by large fibrotic thrombi in the pulmonary arteries, likely originating from pulmonary embolism. Inadequate anticoagulation is one of the suspected mechanisms of disease in CTEPH. Taking into consideration the phenprocoumon pharmacokinetics and the dose–response relation in cancer patients with CTEPH, we sought to determine if CTEPH patients on phenprocoumon oral anticoagulation for at least 6 months, compared with PAH patients, VKORC1 (-1639, -3730) and CYP2C9 (2, *3) single nucleotide polymorphisms (SNPs) were determined by polymerase chain reaction (PCR).

Results: In 72 patients (46 CTEPH, 26 PAH), mean treatment duration was over 51.7±44.7 months, and mean age was 63.3±12.2 years (63% female). Mean dose of phenprocoumon per week was 15.8 mg (4.5 mg to 42 mg). The mean ratio of weekly phenprocoumon dose and INR levels showed statistically significant differences between CTEPH (mean ratio 6.58±3.3) and PAH (mean ratio 4.87±1.7; P=0.013). Patients with CTEPH and VKORC1 -1639 GG homozygous wild type required significantly higher phenprocoumon doses compared with VKORC1 -1639 AA homozygous mutants (P<0.05). No statistically significant difference was found between the two subsets of CYP2C9 (2, *3).

Conclusions: CTEPH patients require more phenprocoumon in relation to INR levels than PAH patients. Unmet phenprocoumon dosing requirements may be one mechanism of disease in CTEPH.

P5193 | BEDSIDE
Percutaneous transluminal pulmonary angioplasty ameliorates metabolic and renal dysfunctions associated with hemodynamic improvement in patients with chronic thromboembolic pulmonary hypertension

Background: Metabolic impairment, such as insulin resistance and dyslipidemia, has been reported to be associated with development of pulmonary hypertension. Recently, we have reported that percutaneous transluminal pulmonary angioplasty (PTPA) markedly improves pulmonary hemodynamics and midterm prognosis of patients with chronic thromboembolic pulmonary hypertension (CTEPH). In this study, we tested our hypothesis that PTPA is effective to improve metabolic and renal impairments in CTEPH patients.

Methods and results: From March 2012 to May 2013, we examined serum levels of various markers (fatty acids fraction, glycated hemoglobin, insulin and immunoreactive insulin) in 51 CTEPH patients, and calculated the homeostatic model assessment of insulin resistance (HOMA-IR) using samples from non-diabetic patients. Renal function was assessed by estimation of glomerular filtration rate (eGFR) and urinary albumin to creatinine ratio (U/A-Cr). We also evaluated cardiac fatty acid and glucose metabolic state by [133I]-BMIPP SPECT and [18F]-FDG PET. In 27 out of the 51 patients, the measurements were repeated after PTPA. Among the 51 patients, 4 had WHO functional class IV, 7 had 6 minute walk distance <300m, and 13 had cardiac index (CI) <2.0 l/min/m2. Enhanced [123I]-BMIPP and [18F]-FDG accumulation in the right ventricular (RV) free wall was noted in 14. The mean value of eicosapentaenoic acid to arachidonic acid (EPA/AA) ratio was 0.42. Regarding glucose metabolism, mean HOMA-IR was 3.6 and insulin resistance (defined as an HOMA-IR >2.5) was noted in 22 out of 51 (54%). Regarding renal function, mean eGFR was 63.4±3.0 ml/min/m2 and U/A-Cr ratio was 77.1±35.5 mg/gCr. Chronic kidney disease (CKD) in stage 3 or more was noted in 25 patients (49%). We performed PTPA (2±1.6 sessions) in 27 patients (57±15 years, 22 female). PTPA markedly improved pulmonary vascular resistance (-143±45[SD] dynes sec cm-5, P<0.001), mean pulmonary arterial pressure (3.6±1.8 mmHg, P<0.03), mean right atrial pressure (1.6±0.8 mmHg, P<0.03), and heart rate (3±2mm/min, P<0.03). [123I]-BMIPP and [18F]-FDG uptake in the RV free wall was also decreased after PTPA. Surprisingly, PTPA significantly improved body mass index (BMI) (0.46±0.20 kg/m2, P=0.048), EPA (22.6±7.8 mg/gCr, P<0.01) and EPA/AA (0.12±0.04, P<0.02). PTPA also significantly improved eGFR (5.2±1.2 ml/min/m2, P<0.001) associated with reduction in microalbuminuria (-68.5±56.3 mg/gCr, P<0.05).

Conclusions: These results indicate that metabolic and renal dysfunctions are commonly present in CTEPH patients, for which PTPA is highly effective, associated with improvement of pulmonary hemodynamics.

P5194 | BEDSIDE
A gradual improvement without functional restenosis one year after percutaneous transluminal pulmonary angioplasty for chronic thromboembolic pulmonary hypertension

Aims: Percutaneous transluminal pulmonary angioplasty (PTPA) has been demonstrated to be effective for treatment of chronic thromboembolic pulmonary hypertension (CTEPH). However, the course of improvement and functional restenosis in PTPA has not been clarified yet.

Methods: Among 103 patients with CTEPH (average age: 62±11 years old, male/female: 9/5, the number of PTPA per patient: 3.6±1.6, post-endarterectomy: 6) who underwent PTPA from January the first 2009 to December 31st 2013, 38 completed the follow-up right heart catheterization both at 6 months and 12 months after the final PTPA. Hemodynamic parameters including mean pulmonary arterial pressure (PAP) and pulmonary vascular resistance (PVR) at baseline and final PTPA, and at 6 and 12 months after the final PTPA were compared.

Results: PAP and PVR significantly improved in the course (baseline vs. final PTPA: PAP: 42.7±9.8 vs. 27.3±7.9 vs. 21.8±4.3 vs. 19.9±4.0 mmHg, P<0.01, PVR: 10.2±1.5 vs. 5.1±2.8 vs. 3.1±1.3 vs. 2.9±1.6 wood unit; p<0.01, at 6 months vs. 12 months: no significant change).

Conclusions: Hemodynamic parameters improved gradually during course of a year and did not deteriorate one year after the angioplasty, meaning no functional restenosis.
Short-term impact of balloon pulmonary angioplasty on exercise capacity and ventilatory inefficiency in patients with inoperable chronic thromboembolic pulmonary hypertension


Purpose: We have previously demonstrated that ventilatory inefficiency improves in early-phase, while exercise capacity increases continuously toward the late-phase after pulmonary endarterectomy (PEA) in chronic thromboembolic pulmonary hypertension (CTEPH). Recently, balloon pulmonary angioplasty (BPA) has been reported to improve hemodynamics and functional capacity, with an ac- ceptable safety profile. CTEPH patients who underwent BPA at our hospital, however, is little known about the detailed, short-term effects of BPA on exercise capacity and ventilatory efficiency in patients with inoperable CTEPH. Thus, the aim of the present study was to determine short-term impact of BPA on exercise capacity and ventilatory efficiency, relative to hemodynamic improvements, in patients with inoperable CTEPH, using cardipulmonary exercise testing (CPX).

Methods: We enrolled 19 consecutive patients (mean age, 66±9 years; 13 women) with inoperable CTEPH who underwent a series of BPA (3±1.5 procedures) between March 2013 and February 2014 and whose recordings of CPX were performed before the first BPA and at a mean of 3.6±4.4 weeks after the final BPA.

Results: At baseline, peak oxygen uptake (peak VO2, 59.7% of predicted) was modestly reduced with the consequent decrease in the ventilatory response to carbon dioxide production (VE/VCO2 slope), reflecting reduced exercise tolerance with impaired ventilatory efficiency in inoperable CTEPH. BPA markedly attenuated mean pulmonary arterial pressure (mPAP, 35±10 to 23±5 mmHg), cardiac index, mean right atrial pressure, and total pulmonary resistance (863±313 to 466±159 mmHg/sec/cm5) (all P<0.01), without death or major complications including severe reperfusion pulmonary edema. Furthermore, BPA significantly improved World Health Organization functional class, brain natriuretic peptide levels (126±166 to 28±11 pg/ml), and 6 minute walk distance (269±292 vs. 91±0.05 m, both P<0.05). After BPA, peak VO2 (15±2.3 to 17±3.2 m/kg/min), VE/VCO2 slope (45±8 to 40±10), peak work load (WR), and ∆VO2/WR all significantly improved (all P<0.05). Changes in VE/VCO2 slope significantly correlated with those in mPAP (R=0.46, P<0.01), although the correlation between peak VO2 and mPAP did not reach statistical significance (R=0.41, P=0.08).

Conclusions: These results suggest that BPA could ameliorate both impaired exercise capacity and ventilatory inefficiency during exercise in short-term, safely by ameliorating hemodynamic abnormalities in patients with inoperable CTEPH.

P5198 | BEDSIDE

Pulmonary endarterectomy in a country without pulmonary circumscription: the favorable impact of a cross-border system of care


Purpose: Pulmonary endarterectomy (PEA) is the treatment of choice for Chronic Thromboembolic Pulmonary Hypertension (CTEPH) and can be curative. PEA is not routinely available in Portugal but the patient is fully reimbursed by the Portuguese National Health Service if surgery is performed abroad. We aimed to assess treatment options and outcomes for patients with CTEPH in a country where there is limited access to PEA, namely if there are any barriers to foreign treatment.

Methods: We performed a multicenter, retrospective analysis of 140 patients diagnosed with CTEPH in six pulmonary hypertension centers in Portugal during the last 10 years. Surgical status (operated vs. non-operated) was available for all patients; the remaining clinical and follow-up data was available for 87 patients.

Results: The mean age of CTEPH patients was 57±15 years, with a female preponderance (68%). Surgery was performed in 43 patients (31%), consisting of 42 PEA and 1 heart-lung transplantation due to concomitant severe left ventricular dysfunction. PEA mortality rate was 7.1%. Although patients submitted to PEA were significantly younger (50±15 vs. 61±12 years, P<0.001), their functional capacity as assessed by NYHA class (NYHA class II or IV 84% vs. 69%, P<0.05) or 6-minute walking test (356±86 vs. 366±119 m, P=0.966) was similar to patients not submitted to PEA. No differences were also found regarding pulmonary vascular resistance (11±6.4 ν 7 WU, P=0.535) however, 6MWD increased significantly more when patients were submitted to PEA than when treated with pulmonary vasodilators (+110 m vs. 3 m, P<0.001). At presentation to the expert center, 23% of patients were already treated with selective pulmonary vasodilators. Half of patients submitted to PEA did not require any pulmonary vasodilator after surgery, whereas 12% required double or triple combination in 75% of patients. Only 7% of patients not submitted to PEA were on pulmonary vasodilators (39 single, 24 double and 9 triple combination therapy), most commonly an endothelin receptor antagonist, followed by sildenafil and prostanoids.

Conclusion: In CTEPH patients, exercise measures of RV function and hemodynamics reflect exercise capacity and ventilatory efficiency better than resting measures.
P5190 | BEDSIDE
Usefulness of optical coherence tomography imaging in chronic thromboembolic pulmonary hypertension
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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by unresolved thromboemboli in the pulmonary arteries (PA). We have previously noticed the usefulness of optical coherence tomography (OCT) to diagnose CTEPH, which is an interferometer-based imaging modality with a high resolution. In the present study, in order to develop an effective and safe treatment for inoperable CTEPH, we examined the effectiveness of percutaneous transluminal pulmonary angioplasty (PTPA) combined with OCT evaluation.

Methods: From July 2009 to December 2013, we prospectively enrolled 48 consecutively patients with inoperable CTEPH (41±11 [SD yrs.], 77% females). After optimal medical treatment, we performed PTPA in a step-wise manner until mean pulmonary artery pressure (PAP) reached the level of less than 30 mmHg.

Results: We performed 279 OCT examinations in order to observe the target lesions for PTPA, which clearly showed meshwork (85%), wall thrombus (10%), and slit (5%). We also performed a total of 232 PTPA procedures, which resulted in significant improvement of mean PAP (41.1±10.4 to 25.7±5.4 mmHg, P<0.001) and pulmonary vascular resistance (738±345 to 283±97 dyn sec cm⁻⁵, P<0.001) in all patients. OCT showed that PTPA enlarged the lumen diameter (63±90%) increase. Furthermore, 3D-OCT imaging more clearly revealed that PTPA destroyed the typical flaps and webs and shifted them to the pulmonary artery walls (Figure). The complication of PTPA was mild to moderate hemoptysis in 16 out of the 48 patients, which was successfully managed with oxygen and non-invasive positive pressure ventilation without intubation.

Conclusion: OCT-guided PTPA combined with medical treatment markedly ameliorates pulmonary hemodynamics of patients with inoperable CTEPH.

P5200 | BEDSIDE
The efficacy and safety of the balloon pulmonary angioplasty (BPA) for inoperable chronic thromboembolic pulmonary hypertension (CTEPH) - preliminary results
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Purpose: The purpose of this study was to assess safety and benefits of the BPA procedure. Hemodynamic measures and functional NYHA class, before and after BPA, were compared within the group of patients undergoing BPA (group A). Comparison of outcomes between the group A and the historical control group on targeted PAH therapy (silodinilfen, bosentan, treprostinil, riociguat) was also performed.

Methods: From 36 patients (aged 62.2±14.66; 20 females) diagnosed with CTEPH between 2001 and 2013, who were disqualified from pulmonary endarterectomy (PEA) due to distal localization of thrombi, 8 patients (aged 56.5±17.4; 6 females) were found suitable for BPA. The remaining 28 patients (aged 63.85±13.7; 14 females) who received optimal medical therapy for at least 3 months served as control group (group B). The total of 11 BPA procedures were performed in group A. Overall 34 segmental pulmonary arteries have undergone angioplasty. For each patient in group A, a right heart catheterization (RHC) was performed directly before and after each BPA procedure. In group B results from RHC performed at baseline and after at least 3 months of targeted therapy were compared. Baseline and follow-up functional capacity (NYHA class) and hemodynamic measures including pulmonary vascular resistance (PVR), mean pulmonary artery pressure (mPAP), cardiac index (CI), cardiac output (CO) and mean right atrial pressure (mRAP) were recorded.

Results: Comparisons within the group A, before and after BPA, showed significant decrease in PVR (11.0±6.0 vs 9.1±5.6 mm Hg; p=0.042) and mPAP (52.9±15.19 mm Hg vs 48.1±12.92 mm Hg; p=0.021) and improvement of at least one NYHA functional class in group A vs group B (50% pts vs 3.6% pts; p=0.005). No improvement of hemodynamic measures or NYHA class was noticed within the follow-up period for patients from group B. There were no deaths in group undergoing BPA, but several complications occurred including hemoptysis (n=3), dyspnea (n=3), reperfusion pulmonary injury (n=2), desaturation (n=3), atrial arrhythmia (n=1) and subcutaneous hematoma (n=1).

Conclusion: Despite mild complications, in selected CTEPH patients, BPA may offer an additional option for patients not suitable for PEA. It provides early significant improvement of functional NYHA class and reduction of PVR and mPAP. More information on early and long term results is required.

P5201 | BEDSIDE
The forkhead transcription factor FoxO3a regulates NK cell function - role in CVB3 myocarditis
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Background: Despite mild complications, in selected CTEPH patients, BPA may offer an additional option for patients not suitable for PEA. It provides early significant improvement of functional NYHA class and reduction of PVR and mPAP. More information on early and long term results is required.

Conclusion: OCT-guided PTPA combined with medical treatment markedly ameliorates pulmonary hemodynamics of patients with inoperable CTEPH.

P5202 | BENCH
The forkhead transcription factor FoxO3a regulates NK cell function - role in CVB3 myocarditis
C. Skurk¹, M. Loebe², L. Holzhauser³, A. Jenke¹, K. Savalits¹, W. Poller¹, C. Schütze¹, Y. Hori¹, P. Haussinger², H. Masuda³, K. Tajiri¹, S. Sakai¹, T. Kimura¹, T. Machino-Ohtsuka¹, N. Murakoshi¹, D. Xu⁴, Z. Wang⁴, A. Salo¹, T. Miyachi¹, K. Aomura¹, University of Tsukuba, Cardiovascular Division, Faculty of Medicine, Tsukuba, Japan

Background: FoxO3a is a transcription factor involved in cell metabolism, survival and immunity. For several years FoxO3a has been postulated as an association with longevity and differential outcomes in inflammatory disease have recently been reported. However, mechanistic insight into FOXO3a effects is still limited. Here, we investigated the role of FoxO3a on NK cell responses and its effects in pathogen-induced viral myocarditis.

Methods: The effects of FoxO3a viral load and inflammation were investigated a murine model of Coxsackie B3 (CVB3) myocarditis in WT and FoxO3a deficient mice. FoxO3a dependent regulation of CVB3 replication was determined in cell culture in vitro. Functional characterization of NK cells was performed by surface marker expression, cytotoxic assay and IFNγ expression.

Results: FoxO3a−/− mice were characterized by significantly reduced inflammation, lower viral titers and attenuated expression of pro-inflammatory cytokines in cardiac tissue associated with decreased tissue injury compared to wild-type littersmates 7 days post infection. Interestingly, viral titers were attenuated in FoxO3a−/− mice at day 3 while IFNγ and NKp46 expression were significantly up-regulated in cardiac tissue suggesting early viral control by enhanced innate immune responses. Interestingly, FoxO3a gene transfer in vitro significantly inhibited post-entry CVB3 replication without regulating adhesion or cellular entry. In line with accelerated viral clearance, NKp46+ splenic NK cells of FoxO3a−/− mice exhibited a superior functional status ex vivo determined by enhanced expression of the activation marker CD69, higher frequencies of differentiated CD11b/CD27 effector NK cells and increased cytotoxicity compared to NK cells of WT littermates. Moreover, miRNA-155 expression, recently reported to be essential in NK cell activation and IFNγ expression, was significantly elevated in FoxO3a−/− NK cells while its inhibition led to diminished production of IFNγ in FoxO3a−/− mice. In line with our murine data, our studies showed that heterozygous or homozygous for the longevity-associated FoxO3a SNPs rs9402039a/rs12212067 exhibited significantly reduced cytotoxic degradation of NK cells.

Conclusion: Taken together our results implicate FoxO3a in regulation of NK cell activation, differentiation and function and suggest that FoxO3a plays an important role in the innate immune response to viral infection. Thus, enhanced FoxO3a activity may be protective for diseases associated with chronic inflammation such as cancer and cardiovascular disease but disadvantageous to control viral infection.

P5203 | BENCH
The role of endothelin in the myocardial inflammation: experimental study using the endothelin antagonist SB209670
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Background: Myocarditis and subsequent dilated cardiomyopathy are major causes of heart failure in young adults. Experimental autoimmune myocarditis (EAM) is a mouse model of post-infectious myocarditis and inflammatory cardiomyopathy. The pathological role of endothelin (ET) in myocarditis has not been elucidated.

Methods: EAM was induced by immunization of cardiac myosin peptide with complete Freund’s adjuvant on days 0 and 7 in BALB/c mice. An ETA/ETB dual receptor antagonist, SB209670, was administered by a continuous infusion from a subcutaneous pump for 2 weeks.

Results: An increase in the heart-to-body weight ratio was observed in SB209670-treated mice compared with vehicle-treated mice. The heart pathology in SB209670-treated mice was remarkable for gross inflammatory infiltration, in contrast to the lesser inflammation in the hearts of vehicle-treated mice. We found that an ET blockade decreased the number of Foxp3 regulatory T cells in the heart. The ET blockade also inhibited the expression of the suppressor of cytokine signaling 3 that plays a key role in the negative regulation of both TGF-β (a cytokine that promotes collagen deposition) and T-cell mediated inflammation.

Conclusion: The ET receptor antagonist exacerbated autoimmune myocarditis in mice. Our novel findings may suggest that ET plays an important role in the regulation of inflammation in myocarditis.
P5204 | BEDSIDE
Changes in clinical, biochemical and echocardiographic parameters and their correlations with immunohistological features in patients with inflammatory cardiomyopathy
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Background: Patients with inflammatory cardiomyopathy have a variable degree of improvement in clinical and echocardiographic parameters with standard heart failure therapy. Aim: To correlate changes in clinical, echocardiographic and laboratory parameters with changes in the number of inflammatory cells in endomyocardial biopsy (EMB) samples in 6-month follow-up.

Patients and methods: We evaluated 40 patients with biopsy proven myocarditis and impaired left ventricular function (left ventricle ejection fraction – LVEF <40%) who had <12 months heart failure symptoms. Myocarditis was defined as presence of >14 leukocytes/mm² and/or >7 lymphocytes/mm² in baseline EMB. EMB, echocardiography and clinical evaluation were repeated after 6 months of standard heart failure therapy.

Results: LVEF improved from 25.8±9.2% to 42.1±2.8% (p<0.001), left ventricle end-systolic volume (LVESV) and left ventricle end-diastolic volume (LVEDV) decreased from 158±61 to 111±58 ml and from 211±69 to 178±63 ml. NYHA class decreased from 2.6±0.5 to 1.6±0.6; NTproBNP from 299±3273 to 851±1835 µg/ml (all p<0.001). In EMB observation was decreased in the number of infiltrating leukocytes (LCA+) from 23±15 cells/mm² to 13±18 cells/mm² and decrease in the number of infiltrating T lymphocytes (CD3+) from 7±5 cells/mm² to 3±1 cells/mm². The number of CD3+ cells significantly correlated with change in LVEF (R = -0.43; p=0.006), LVEDV (R = 0.39; p=0.012), NYHA classification (R=0.35; p=0.025), NTproBNP (R=0.33; p=0.045). Decrease in the number of CD3+ cells correlated with the change of systolic and diastolic diameter of left ventricle (R= -0.33; p=0.038 and R = -0.45; p=0.003), and with change in LVEDV (R = -0.43; p=0.006).

Conclusion: Improvements in clinical status, LV function and NTproBNP levels correlate with decrease in number of infiltrating inflammatory cells. This observation suggests that contemporary guideline-based treatment of heart failure is effective therapeutic approach in patients with biopsy-proven inflammatory cardiomyopathy.

Acknowledgments: This study was supported by a Grant from IGA MH CR NT14087-3/2013.

P5205 | BEDSIDE
Determinants of myocarditis recurrence: single experience in a tertiary referral center

Introduction: Myocarditis (MC) is an under-diagnosed inflammatory cardiac disease, frequently with a benign curse, but potentially lethal. Little is known about factors related with its recurrence. Our aim was to assess the incidence and determinants of new episodes of MC in our population.

Methods: We included 72 patients (pts) consecutively admitted from 2007 to 2013. Cardiac magnetic resonance (CMR) was performed during hospitalization for MC diagnosis.

Results: 56 (78%) patients were men, mean age of 33±10 years. Acute chest pain was the main inaugural symptom (92%) and fever at admission was detected in 44 (71%). A viral prodrome was frequent (69%). Tropinin I elevation was found in all patients (mean peak level of 22±33 ng/ml). Mean BNP, C-reactive protein values at admission were 176±336 pg/ml and 79±76 mg/dl, respectively. An abnormal ECG was present in 54 (75%) pts. Moderate to severe left ventricular (LV) systolic dysfunction (ejection fraction <45%) was present at admission in 13 pts (18%). CMR was displayed at 4±2 days after admission and mean LV systolic function was 59±8%, myocardial oedema was present in 58% and late gadolinium enhancement (LGE) in 92%. Mean hospitalization time was 9±3 days. 61 patients (54 male, mean age 33.5±1.9 years) were included. T wave inversion was found in 20 patients (33%), ST segment depression in 7 patients (11%) and ST segment elevation in 39 patients (64%). We identified a statisticaly significant association between ST segment elevation location and necrosis location (Fisher’s exact test: p=0.023). This association was particularly strong for the anterior location (x²=6.46 p=0.011). We did not find a statistically significant association between ST segment elevation and necrosis, or any other association was found between other ECG and CMR changes.

Conclusions: ST segment elevation correlated topographically with necrosis, but not oedema, in patients with acute myocarditis. The remaining ECG changes exhibited no topographical correlation with myocardial injury. Considering that myocardial lesions in acute myocarditis are often mesoparietal and/or subepicardial, it is possible that ST segment elevation may translate non-subendocardial myocardial injury, in addition to transmural lesions as seen in ST segment elevation myocardial infarction.

P5206 | BEDSIDE
ST segment elevation in acute myocarditis: a new paradigm?

Background: Acute myocarditis often displays electrocardiographic changes (ECG), yet their significance is not well established. Considering that cardiac magnetic resonance (CMR) can detect the location, extension and type of injury in acute myocarditis, it is possible that it can contribute a better understanding of the ECG changes observed in this disease.

Purpose: To correlate the observed ECG changes in patients with acute myocarditis with the type and distribution of myocardial lesions as assessed by CMR.

Methods: Prospective observational study of consecutive patients with the diagnosis of acute myocarditis confirmed by CMR. All patients underwent ECG evaluation on admission and repeatedly during hospital stay. The following ECG changes were analysed: T wave inversion, ST segment depression and ST segment elevation. CMR analysis comprised the presence of T2 hyperintensity (edema) and late gadolinium enchancement (necrosis). For topographical analysis using both ECG and CMR changes, the following locations were considered: anterior (anterior wall and anterior septum), lateral (lateral and posterior walls) and inferior (inferior wall and inferior septum). To analyze the association between the topographic location of ECG and CMR changes, we used the Chi-Square test and Fisher’s exact test.

Results: 61 patients (54 male, mean age 33.5±11.8 years) were included. T wave inversion was found in 20 patients (33%), ST segment depression in 7 patients (11%) and ST segment elevation in 39 patients (64%). We identified a statisticaly significant association between ST segment elevation location and necrosis location (Fisher’s exact test: p=0.023). This association was particularly strong for the anterior location (x²=6.46 p=0.011). We did not find a statisticaly significant association between ST segment elevation and necrosis, or any other association was found between other ECG and CMR changes.

Conclusions: ST segment elevation correlated topographically with necrosis, but not oedema, in patients with acute myocarditis. The remaining ECG changes exhibited no topographical correlation with myocardial injury. Considering that myocardial lesions in acute myocarditis are often mesoparietal and/or subepicardial, it is possible that ST segment elevation may translate non-subendocardial myocardial injury, in addition to transmural lesions as seen in ST segment elevation myocardial infarction.

P5207 | BENCH
Peramivir ameliorate murine myocarditis associated with influenza A virus H1N1pdm
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Purpose: Severe influenza sometimes causes myocarditis. We previously reported that fifteen fulminant myocarditis patients associated with influenza A virus H1N1pdm were seen in the 2009/2010 season in Japan. To analyze effects of peramivir, one of neuraminidase inhibitor, on influenza A virus myocarditis, we investigated pathological roles of cytokines in murine myocarditis associated with influenza A virus H1N1pdm.

Methods: 8-week-old male BALB/c mice were infected intra-nasally with influenza A virus H1N1pdm, and divided into 2 groups: group C; injected with saline, group P: treated with peramivir. Histological study, echocardiogram and quantitative analysis of viral RNA and mRNA of inflammatory cytokines and adhesion-molecules were performed.

Results: There were no significant difference in survival rate (C: 80%, P: 100%) on day 14, and heart/body weight ratio on day 8. LVdV in group P was significantly smaller than that in group C on day 8. FS of group P (52.2%, p=0.0001) was significantly higher than FS of group C (26.6%) on day 8. Histological study showed localized myocarditis with lymphocyte infiltration, and myocarditis lesions were found in perivascula area or myocarditis was associated with pericarditis. Myocarditis lesions of group P were smaller than that of group C. Viral replication in heart and lung was suppressed in group P. Expression of mRNA of inflammatory cytokines and adhesion-molecules was suppressed in group P.

Discussion: Peramivir suppressed viral replication, and also probably improved cardiac function with suppression of cytokines and adhesion-molecules. Conclusion: Peramivir ameliorate murine myocarditis associated with influenza A virus H1N1pdm through suppression of viral replication.

UCG
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Methods: Fifteen patients with AFM aged 3-17 years (AFM group), fourteen patients with dilated cardiomyopathy (DCM) aged 6-14 years (DCM group) and 20 controls aged 3-12 years (Control group) were evaluated from June 2010 to February 2014. All images were acquired using STIR, early gadolinium enhancement (EGE) and late gadolinium enhancement (LGE). Physical examination, plasma cTNT and NT-proBNP, viral PCR in blood, electrocardiogram (ECG) and transthoracic echocardiography were performed in all children.

Results: Typical clinical, ECG and echocardiographic presentations were identified in the AFM group and DCM group. Of fifteen patients with AFM, all had acute heart failure and eight suffered from Adams-Stokes attacks. Nine patients with AFM underwent CMR within two weeks and the others after one month. Ten of fifteen patients with AFM had LGE imaging. There was significant difference between AFM group (67%) and DCM group (14%) (P < 0.05). All the controls had normal CMR. Ten of seven patients with AFM had abnormal CMR with sensitivity of 73%, specificity of 100%, positive predictive value of 100% and negative predictive value of 83%, when compared with their clinical findings. Of fifteen patients with AFM, one had abnormal T2WI signals in intraventricular septum (IVS), eight had regional myocardial thinning (including anterior wall, lateral wall, posterior wall and apex of LV and IVS), four had regional myocardial thickening in IVS, four had small pericardial effusions. Using viral PCR in blood, all fifteen patients with AFM had viral infections including Epstein-Barr virus (EBV) (10/15), cytomegalovirus, human herpes virus and adenoviruses. Of the eight patients with AFM and normal CMR, five had abnormal CMR. In DCM group, we found significant dilated cardiac chambers and reduced LV function. The hypersensitive cTNT level in the AFM group were significantly higher than that in the DCM group (P < 0.05). There was no difference in NT-proBNP level between the AFM group and DCM group (P > 0.05). Eight of ten patients with ST-T changes mimicking myocardial infarction had LGE on the same area of myocardial damage. Six patients underwent CMR during both acute phase and recovery phase, three patients recovered completely and three patients improved.

Conclusions: CMR is a safe and useful technique for diagnosis and follow-up in children with AFM.

P5210 | BEDSIDE
The diagnostic value of cardiac magnetic resonance in children with acute fulminant myocarditis
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Objectives: To assess the role of cardiac magnetic resonance (CMR) in children with acute fulminant myocarditis (AFM).

Methods: Nineteen patients with suspected myocarditis and preserved LVEF were enrolled.
were examined; they underwent CMR and echocardiography the same day. In patients with DE we calculated the percentage using the 2 standard deviation (SD) method. A complete echocardiographic examination was performed in all patients. LV function was studied by EF calculated by Simpson’s method and by an off-line complete speckle tracking analysis, including LV longitudinal, radial, circumferential and torsion.

Results: Twelve patients showed DE with non-ischemic pattern. These patients presented a significantly lower apical-radial strain (26.8% vs 32.5%, p < 0.0001) and a lower LV apical rotation (6.4 deg vs 7.4 deg, p = 0.01) compared to subjects without DE. Among patients with DE we found significant correlations between DE percentage and total cardiac apical strain (R -0.77; p<0.0002) and basal (R -0.35; p<0.01) radial strain, LV torsion (R -0.28; p<0.01) and LV apical (R 0.36; p<0.01) and basal (R -0.20; p<0.05) rotation. No significant correlation was found with longitudinal strain and the percentage of DE.

Conclusions: In patients with myocarditis and preserved LVEF, LV apical-radial strain and LV apical rotation correlate with the presence and the percentage of DE.

### PS216 | BEDSIDE

**NT-proBNP: an important prognostic marker in familial amyloid polyneuropathy**

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**Purpose:** Cardiac involvement in familial amyloid polyneuropathy (FAP) V30M-ATTR is characterized by progressive myocardial amyloid infiltration, but heart failure is rare, even in advanced forms of the disease. NT-proBNP is a biomarker of cardiac dysfunction and a strong prognostic predictor in other forms of systemic amyloidosis. However its prognostic value in FAP is not well known. The aim of this study is to examine the prognostic value of NT-proBNP in FAP V30M-ATTR.

**Methods:** Prospective observational study of V30M-ATTR patients who underwent annual clinical evaluation and periodic serum NT-proBNP measurements. The prognostic value of NT-proBNP was evaluated by multivariate Cox logistic regression analysis (adjusted for age) and Kaplan-Meier survival analysis.

**Results:** We studied 155 (45±15 years, 56.6% female) FAP V30M-ATTR patients. During a median follow-up of 27 months, 374 periodic determinations of serum NT-proBNP were conducted. The median serum level of NT-proBNP was 84 (42-157) ppm/L and increased progressively with age (R: 0.37; P<0.001; Rho: 0.30; P<0.001) and the duration of symptoms (R: 0.18; P=0.017; Rho: 0.22; P=0.004).

The risk of death progressively increased with NT-proBNP concentration [hazard ratio (HR): 4.43, 95% CI 1.22-16.06, P=0.024]. Thus, patients in the 3rd tertile distribution of NT-proBNP (>118 ppm/L) had a significant increased risk of death (HR: 44.7, 95% CI 9.25-216.0, P<0.001).

**Conclusion:** Despite the fact that the levels of NT-proBNP are substantially lower in FAP V30M-ATTR than in other forms of amyloidosis, this biomarker is still an important predictor of mortality and should be integrated in the evaluation and follow-up of these patients.

### PS217 | BEDSIDE

**Elevated pulmonary artery systolic pressure predicts poorer survival in constrictive pericarditis**

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**Purpose:** Pulmonary artery systolic pressure (PASP) of more than 50 mmHg is considered atypical of constrictive pericarditis (CP). We investigated the prevalence and correlates of elevated PASP in CP and its impact on survival.

**Methods:** We reviewed 417 patients with a surgically confirmed diagnosis of CP from January 1985 to October 2006, who underwent preoperative evaluation of PASP by transthoracic echocardiography, cardiac catheterization, or both. Patients were categorized into those with PASP ≥50 mmHg by at least one test (Group II; n=139) and those without (Group I; n=278).
Results: PASP > 50 mmHg was present in 33% of patients. Group II patients were more often female (odds ratio [OR] 2.29, p=0.002) and more likely to have systemic hypertension (OR 1.69, p=0.035), pulmonary disease (OR 2.23, p=0.005), prior cardiovascular surgery (OR 2.17, p=0.002), significant mitral regurgitation (OR 2.85, p=0.003) or tricuspid regurgitation (OR 2.71, p=0.001). Perioperative mortality (within 30 days of surgery) was 3% and 14% in Groups I and II respectively (p<0.001). Overall survival was poorer in Group II (p<0.001 by log-rank test) (Fig. 1).

Conclusion: PASP is elevated beyond 50 mmHg in a third of patients with CP. Patients with elevated PASP have poorer perioperative and long-term survival.

P5218 | BEDSIDE
Matrix metalloprotease activity in patients with cardiac AL amyloidosis and in human cardiac fibroblasts exposed to cardiotoxic amyloidogenic light chains

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Introduction: Cardiac fibroblasts represent the majority of cardiac cells within the myocardial wall. Among the many factors that modulate extracellular matrix (ECM) homeostasis, matrix metalloproteinases (MMPs) and MMP specific inhibitors (TIMPs) play an important role. In cardiac AL amyloidosis, amyloid fibril deposition has been shown to result in disruption of myocardial ECM.

Aim: To measure serum MMP and TIMP concentration in cardiac AL patients and to test the hypothesis that light chain (LC) - induced cardiotoxicity is associated with changes in fibroblast-derived MMP activity.

Methods: Serum MMP-2, MMP-9, TIMP-1 and TIMP-2 (ELISA) and MMP-2/ MMP-9 gelatinolytic activity (zymography) were assessed in 31 consecutive untreated AL patients with predominant cardiac involvement and in 18 MGUS patients (as a control group). In a parallel experiment, primary fibroblast cell cultures (HCF) derived from normal human myocardial explants were grown in DMEM serum, supplemented with 10% FCS. After seeding (5x10^4 cells/cm^2), cells were grown to confluence. Medium was then removed and fresh DMEM containing cardiac AL LCs or MGUS LCs derived from 3 MGUS patients (MG-LCs) (100 mg/ml for both) was added for 24 hours.

Results: When compared with MGUS, cardiac AL was associated with higher serum MMP2 (142.2±16.7 vs. 121.9±33.5 for both), TIMP2 (39.5±22.2 vs. 27.8±15.6) and TIMP-2/2 (24.4±7.5 vs. 20.7±11.9) concentrations (ng/ml/mg protein; p<0.05 for all comparisons). In HCF, incubation with cardiotoxic LCs was associated with significantly higher MMP-2 and MMP-9 activities, when compared with MG-LCs (5.27±0.70 vs. 3.91±0.25, and 4.77±0.61 vs. 3.93±0.23 OD mm^2/mg protein; p<0.05 for both).

Conclusions: Cardiac AL patients show an increased and sustained stimulus to ECM degradation. Exposure to cardiotoxic amyloidogenic light chains increases cardiac fibroblast-derived MMP activity. In vivo, this may cause extracellular matrix degradation, further contributing to the development and maintenance of amyloid-induced cardiac damage.

P5219 | BEDSIDE
Minimally Invasive Strategy For Resection Of Primary Cardiac Tumors: The Leipzig Experience

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Objectives: Here we report our single center experience using the minimally invasive right-sided thoracotomy approach (MIC) in resecting intracardiac tumors.

Methods: Between 1994 and 2010, 252 patients underwent evaluation and treatment of primary cardiac tumors at our institution. Of these, 108 patients underwent minimally invasive surgery through a right mini-antero-lateral thoracotomy. The follow-up was 95% complete with a mean follow-up of 10±5 years.

Results: Seventy four patients (68.5%) were diagnosed with myxomas (mean age 65.1±13 years). In-hospital mortality (HM) was 1.3% (n=1) and was due to non-cardiac causes. Late mortality was 6.8% (n=5). Postoperative morbidity in the form of reoperation for bleeding, arrhythmia and pericardial effusion was 10.8% (n=8), 14.8% (n=11) and 9.5% (n=6) respectively. No recurrent tumors have been diagnosed at follow-up. None of the 31 patients (28.7%) diagnosed as benign non-myxomas (mean age 63.1±16 years) died after surgery. However, one patient (3.2%) died within four years due to non-cardiac causes. Six patients (19.3%) required reoperation for bleeding, 5 (16.1%) developed arrhythmias and 3 (9.6%) developed pericardial effusion. Of the 3 patients diagnosed with a malignant tumor (mean age 63±16), one patient died within 30 days after surgery. The other two patients required a reoperation at 8 and 14 months after the primary operation because of aggressive tumor recurrence. Within our entire cohort of 108 patients, no patient required conversion from right antero-lateral mini-thoracotomy to sternotomy.

Conclusion: Surgical resection, when possible, is the treatment of choice for all primary cardiac tumors. Minimally invasive surgical approach can be routinely applied with excellent surgical results. However, the entity of tumor formation affects the long-term prognosis.

P5220 | BEDSIDE
Colchicine for the prevention of pericarditis: systematic review and meta-analysis

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Aims: The purpose of this study was to investigate and summarize available evidence on the efficacy and safety of colchicine for pericarditis prevention. Disease recurrence is the major and most common complication of pericarditis and its prevention may reduce morbidity and management costs. Colchicine has been intensively studied in the last decade for pericarditis prevention.

Methods: Controlled clinical studies were searched in several databases and were included provided they focused on the pharmacologic primary or secondary prevention of pericarditis. We performed a meta-analysis including studies primary outcome, adverse events, and drug withdrawal.

Results: From the initial sample of 175 citations, 7 controlled clinical trials were finally included (1275 patients): 5 studies were double-blind randomised controlled trials (RCT), and 2 studies were open-label RCTs. Trials followed patients for a mean of 19 months. Meta-analytic pooling showed that colchicine use was associated with a reduced risk of pericarditis during follow-up (OR= 0.33 [0.25-0.44], p for effect<0.001, p for heterogeneity=0.98, I2=0%) either for primary or secondary prevention without a significant higher risk of adverse events compared with placebo (OR= 1.28 95% CI 0.84-1.93), but more cases of drug withdrawals (OR= 1.64 95% CI 1.04-2.58). Gastrointestinal intolerance is the most frequent side effect (mean incidence 8%), but no severe adverse events were recorded.

Conclusions: Colchicine is safe and efficacious for the primary and secondary prevention of pericarditis. Gastrointestinal intolerance is responsible for an increased risk of drug withdrawal, mainly due to diarhoea.

P5221 | BEDSIDE
Survival after alcohol septal ablation in hypertrophic obstructive cardiomyopathy: results from a consecutive patient cohort

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Alcohol septal ablation (PTSSA) is an effective treatment for hypertrophic obstructive cardiomyopathy, however the long-term effects still remain a matter of anxiety. We examined survival of consecutive patients (pts) treated in a referral center.

We followed 111 consecutive pts (53±15 years; 59% men) who underwent septal ablation at our institution between 2005 and 2006. Only 1 target septal branch was occluded in each PTSSA attempt regardless of immediate haemodynamic result. Follow-up was at 3 months after PTSSA and at yearly intervals thereafter. 67 (60%) pts had concomitant hypertension, 13 (12%) had coronary artery disease and 15 (14%) had atrial fibrillation. 17 (15%) pts had a device (7 pacemaker, 10 ICD) implanted before first PTSSA while 12/94 (13%) and 13/94 (14%) received a pacemaker or an ICD after PTSMA respectively. All ICDs were implanted with excellent surgical results. However, the entity of tumor formation affects the long-term prognosis.
for primary prevention of sudden death based on risk stratification. 3 (3%) pts had unsuccessful myectomy before PTSMA, 3 (3%) had myectomy at follow-up because of technically futile (no suitable septal branch after contrast echocardiography testing) or partially effective PTSMA, while 1 pt had myectomy both before (unsuccessful) and after (successful) inadequate haemodynamic effect of PTSMA. 18 (16%) had a PTSMA before and 19 (17%) underwent a 2nd PTSMA after the index procedure. 90 (81%) had procedural success with at least 80% gradient reduction without complications. 99 (89%) were treated for pure subaortic, 4 (4%) for midventricular and 8 (7%) for combined subaortic and midventricular obstruction. The intra-ventricular gradient before first treatment was significantly reduced at last follow-up from 66±39 mmHg to 14±17 mmHg at Rest (p<0.0001) and from 108±50 mmHg to 26±29 mmHg afterValsalva (p<0.00001). Over a follow-up of 5.2±3.2 years after first PTSMA, survival free of all mortality was 99%. Total of 5 deaths: 3 of possible cardiac cause (1 sudden death of a 36-year-old male 20 months after 2nd PTSMA, 2 of unknown cause: 67-year-old female 45 months after PTSMA and 78-year-old female 74 months after PTSMA) and 2 noncardiac (69-year-old female with sepsis, 67-year-old female with cancer). For the endpoint of documented sudden cardiac death, unknown cause of death, the incidence per 100 person-year-follow up was 0.5. PTSMA in an unselected patient cohort treated in a referral center is associated with favourable long-term survival without increased risk of sudden cardiac death.

The need for repeated procedures is probably related to our conservative wait-and-see approach with occlusion of only one septal branch at every attempt.

P5222 | BEDSIDE
Feasibility of multimodality treatment for cardiac sarcomas
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Background: Cardiac sarcomas (CS) have a dismal prognosis. Multimodality treatment (MMT) with surgery, radiation (RT) +/- chemo (CT) therapy improves event-free survival of soft tissue sarcomas, but cardiac CS is considered at high risk. Modern RT techniques as Intensity Modulated RT (IMRT) and Tomotherapy (TOMO) concentrate radiation to the tumor volume with limited involvement of surrounding structures.

Purpose: We report our experience with MMT (using IMRT/TOMO) in 22 patients (pts) (14 males, 8 females, aged 22-72, median 44) with high-grade, 5 low-intermediate grade CS (five with local relapse after surgery) seen at our Institutes over 20 years.

Methods: The therapeutic approach was: a) anthracycline CT and/or IMRT/TOMO in resected CS with margin infiltration; b) CT + RT in unresectable CS, followed by surgery if feasible after mass reduction. RT was used in 15 pts, CT in 19. Cardiac evaluation and echocardiograms were obtained before and every 3 months during CT, before and weekly during RT, every 3 months after ending therapy for 2 years, and then yearly.

Results: Of 22 pts, 13 are dead (1 of pulmonary embolism; 12 of metastases), 2 had local relapse at last follow-up (at 15 and 20 months) and have been lost thereafter, 7 are alive to 103 months after starting treatment (of which 5 free of tumor, 2 still on treatment). Early toxicity during CT/RT were paroxysmal atrial fibrillation (AF) in 3 pts (reverted by amiodarone), acute pericarditis in 1. Late toxicity were: localized hypokinesia with globally normal ejection fraction (EF) in 2 pts, mild EF reduction in 2, recurrent AF in 2, and constrictive pericarditis in one.

Type of treatments and outcome

<table>
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<th>Treatment</th>
<th>Total</th>
<th>Dead/lost</th>
<th>Alive</th>
<th>Free of tumor</th>
<th>Survival (months)</th>
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<tr>
<td>Surgery + postoperative C/RT</td>
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<td>4</td>
<td>5</td>
<td>4</td>
<td>2-61 (mean 23, median 18)</td>
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<td>1</td>
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<td>12-138 (mean 54, median 34)</td>
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<td>3</td>
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</table>

Conclusions: A patient-tailored MMT including CT and/or RT was safe, with good local disease control. Five out 22 (23%)patients are currently alive, free of disease, at a median of 25 month follow-up and without significant late cardiac adverse effects.

P5223 | BEDSIDE
How are patients with acute pericarditis managed in the emergency room? A real-life study
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Purpose: Most published series of pericarditis are issued from patients treated in cardiology departments, but data on their management in emergency departments (ED) are scarce. We aimed to describe the characteristics and outcomes of patients diagnosed for acute pericarditis (AP) in our ED within a tertiary care university hospital and to compare the management to the 2004 ESC guidelines (2004-GL).

Methods: We retrospectively retrieved all the patients diagnosed for acute pericarditis in our ED from 01/2011 to 06/2013. Data were collected from medical records and through a questionnaire sent to the referring physician to assess the outcome.

Results: During the study period we identified 150 patients (age 41.5±16.2 years, 66% males) of whom 42.5% consulted within the first 6 hours after the episode to determine those patients meeting the 2004-GL criteria for the diagnosis of AP were met only in 47.6% of cases. An increased (>5mmHg) C-reactive protein (CRP) was present in 51.3% of patients. CRP levels were significantly higher in patients meeting the diagnostic criteria when symptoms were present for ≥24 hrs.和 vs. <24 hrs (p<0.001). In 49% of cases, ECG was compatible with the diagnosis of AP. An echocardiography was performed during the stay in ED in 77.3% of patients, showing a pericardial effusion in 26% of cases. Patients were hospitalized in 27.3% of cases. Aspirin was the most often prescribed (84%). Eleven different therapeutic regimens were encountered. Colchicine alone or in association with aspirin was proposed in 30% of patients and was significantly associated with a medical history of pericarditis (63% with- vs. 25% without history of AP, p<0.001). The duration of drug therapy was longer for colchicine than for other and cardiac treatment. Cardiac manifestation included right-sided endocardial fibrosis and valve dysfunction. Valve replacement is the only definitive treatment. Although surgical mortality has been reported around 20%, superior outcomes together with more effective oncologic therapies have extended overall survival. With a median survival of 16 months (IQR11-25). Four patients (36%) were NYHA class >II. Median peak levels of serum lactate dehydrogenase, Chromogranin A, and urinary 5-HIAA were 920ng/ml (IQR608-2328), 2527ng (IQR138-4400), and 159mg/L (IQR6-732) respectively. Median peak levels of Chromogranin A were found to be higher than normal in all patients (p<0.001). Chromogranin A and urinary 5-HIAA were found to be effective predictive factors for recurrent CHD (49.4% vs. 48.5%, p=0.004). Echocardiographic analysis revealed moderate prosthetic dysfunction in 5 (21%) patients of which 4 (16%) had moderate to severe RV dysfunction. Among these, 2 patients underwent reoperative surgery with mechanical valves, 2 received percutaneous balloon valvuloplasty, and 1 was deemed inoperable due to severe tumor burden. Reintervention was successful in all patients.

Conclusion: Recurrence of CHD might be high despite maximized antitumor therapy and is expected to increase due to improved survival. Reintervention in the absence of a near demise is feasible and has excellent outcomes. However, a multidisciplinary approach is mandatory to proceed with appropriate decision making and prosthesis selection. Novel therapies such as tryptophan hydroxylase inhibitors might potentially play a key role in a near future to control tumor activity and avoid recurrent CHD.
Conclusions: Heart rate recovery (HRR), defined as the rate of decline in the heart rate immediately following the cessation of exercise, is influenced by autonomic function. The myocardial bridge (MB) is an anomaly characterized by a typical intramyocardial route of a segment of one of the major coronary arteries. The aim of the present study was to assess HRR in patients with MB.

Methods: A total of 87 patients with MB were selected from our medical records between January 2012 to December 2013. All patients with MB had a positive exercise stress test. Presence of MB detected by coronary computed tomography angiography in all patients. We compared the clinical and exercise test data of these patients with 73 volunteers matched for age and sex. All exercise stress tests were treadmill stress tests using the Bruce protocol and were symptom limited or pushed to 90% of maximal heart rate in the absence of symptoms. HRR indices were calculated by subtracting first, second, and third minute heart rates from the rate obtained during stress testing and designated as HRR1, HRR2, and HRR3.

Results: Patients with MB and control group were similar with respect to age (32.1±8.5 vs. 32.0±9.7 years) and left ventricular ejection fraction (62.0±3.0% vs. 61.9±3.1%). Mean HRR (29.6±11.6 vs. 35.8±10.4, P<0.001) and HRR2 values (52.7±13.5 vs. 60.0±13.2, P<0.040) were significantly lower in patients with MB than the control group. In addition, HRR1 was more lower in patients with left anterior descending (LAD) coronary artery MB than patients with non-LAD coronary artery MB (29.6±11.6 vs. 34.1±8.8, P<0.045).

Conclusions: Patients with MB has lower HRR indices with respect to normal subjects. The HRR index is more impaired in patients with LAD coronary artery MB. These findings are implying the presence of cardiac autonomic dysfunction in patients with MB, especially in LAD involvement.

P5225 | BEDSIDE
Diagnostic accuracy of quantitative PCR (xpert MTB/RIF) for tuberculosis pericarditis compared to adenosine deaminase and unstimulated interferon-gamma in a high burden setting: a prospective study
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Purpose: Current tools for rapid, accurate diagnosis of tuberculous pericarditis (TP) are sub-optimal.
Methods: We evaluated the diagnostic utility of the Xpert-MTB/RIF assay, unstimulated interferon-gamma (uIFN-γ), and adenosine-deaminase (ADA) using peri-cardial fluid (PF) from 151 suspected TBP patients. Mycobacterium tuberculosis culture and intramyocardial route of sarcomeric (11 mutations) or desmosomal (3 mutations) or lamin A/C (1 mutation) genes were frequent genes for a given phenotype. Fifteen mutations have been identified in sarcolimic (11 mutations) or desmosomal (3 mutations) or lamin A/C (1 mutation) genes.

The identification of these mutations had significant impact: assessing right diagnostic threshold, (HRR<10% or LVH), modifying the appropriate diagnosis in another case (HCM and not DCM), confirming a genetic disease even in the absence of affected relatives in the family, providing guidance for genetic counseling and predictive genetic testing in relatives in all situations. Technical, ethical and legal issues may however be encountered and will be discussed.

This study is one of rare series of post-mortem molecular testing after SCD. Our findings suggest the feasibility, molecular efficiency and the clinical benefit of the approach in order to improve the management of families. Postmortem molecular testing must take its place in the strategy of family care after SCD, even if a cardiac cause for the SCD is not detected.

P5229 | BEDSIDE
Arrhythmogenic right ventricular cardiomyopathy (ARVC): genetic profile and arrhythmogenicity
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Purpose: ARVC is mainly a disease of the desmosomes, although there are also other non-desmosomal types of the disease. We investigated the correlation between arrhythmic profile and the presence of a desmosomal mutation (Dm) in our cohort of ARVC patients (pts).

Methods: Thirty-six consecutive ARVC-pts (26 males, 72.2%) were prospectively evaluated and divided into two groups (I&II) based on the identification of a pathogenic Dsm. Analyzed genes were Plakophilin, Desmplakin, Desmoeglin, Desmocollin and Plakoglobin. During a 106.7±64.9 months f/u, SCID, history of aborted SCD, appropriate implantable cardioverter-defibrillator (ICD) activation and syncopal episodes were considered as malignant arrhythmic events. Anti-arrhythmic medication did not differ between the two groups (amiodarone, sotalol).

Results: Pathogenic Dsm were found in 26/36 pts (72.2%) diagnosed with ARVC (group I). No Dsm were identified in the 10/36 (27.8%) pts (group II).

Mean age at diagnosis was similar between the two groups (38.0±20.0 group I vs. 33.7±14.2 group II, P=0.543). Group I had a mean f/u of 90.7±49.3 months, whereas group II pts were followed-up for 148.2±83.5 months (P=0.015). In 8 out of 18 mutation-positive families (44.4%) the disease was familial with at least an affected member, whereas in none of mutation-negative families there was evidence of affected relatives (P<0.025).

During f/u malignant arrhythmic events occurred more often in group I pts as compared with those of group II (76.9% versus 40%, P=0.045) despite the fact that group II had longer f/u period (Table 1).

Table 1. Major arrhythmic events during follow-up

<table>
<thead>
<tr>
<th>Event</th>
<th>Group I (n=26)</th>
<th>Group II (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCD</td>
<td>4</td>
<td>1</td>
<td>0.571</td>
</tr>
<tr>
<td>Aborted Sudden Death</td>
<td>1</td>
<td>1</td>
<td>0.844</td>
</tr>
<tr>
<td>Appropriate ICD activation</td>
<td>6</td>
<td>0</td>
<td>0.157</td>
</tr>
<tr>
<td>Clinical sustained VT with syncope</td>
<td>9</td>
<td>2</td>
<td>0.023</td>
</tr>
</tbody>
</table>

SCD: sudden cardiac death; VT: ventricular tachycardia.

Conclusions: During a long-term f/u, ARVC pts with DsMs had a higher probability for severe and potentially life-threatening arrhythmic events. On the contrary, Dsm-negative pts had a rather mild arrhythmic profile despite the longer f/u.

P5230 | BEDSIDE
Increased circulating mesenchymal stem cells in patients with hypertrophic cardiomyopathy: correlation with left ventricular mass index
Purpose: Stem and progenitor cells are implicated in ventricular remodelling and have great clinical significance in the pathophysiology of heart failure. However, there are limited data regarding the involvement of mesenchymal stem cells (MSCs) in the pathogenesis of left ventricular hypertrophy (LVH). The aim of this study is to investigate MSCs circulation in patients with hypertrophic cardiomyopathy (HCM).

Pericardial and myocardial diseases / Cardiomyopathies – I 923
Methods: We included 22 patients with HCM (12 males, aged 54±12 years) and 13 healthy individuals (8 males, aged 53±14 years). All subjects underwent a complete echocardiographic study. In addition, peripheral blood samples from all participants were immunostained with antibodies against the cell surface markers CD34, CD45 and CD90. Using flow cytometry, we measured MSCs as a population of CD45-/CD34-/CD90+ and CD45-/CD34-/CD105+ cells and also as a population of CD45-/CD34-/CD90+ cells. The resulting counts were translated into the % percentage of MSCs in the total cell number of peripheral blood.

Results: Patients with HCM were shown to have increased circulating MSCs compared to healthy individuals and this is correlated with the severity of LVH. Our findings contribute to the understanding of pathogenesis of HCM and might offer a future therapeutic target.

P5231 | BEDSIDE
Fragmented QRS as a prognostic tool for predicting cardiac events in hypertrophic cardiomyopathy
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Background: Hypertrophic cardiomyopathy (HCM) is a primary disorder of the myocardium that can cause fatal cardiac events. Fragmented QRS complexes (fQRS) on a 12-lead electrocardiogram reflect intraventricular conduction delay and have been demonstrated to be a prognostic marker in coronary artery disease. The aim of this study was to assess whether fQRS could predict cardiac events in HCM patients.

Methods: Ninety-four HCM patients registered in Left Ventricular Hypertrophy Multicenter Registration Study in Japan from September 2008 to March 2010 were prospectively investigated. fQRS was defined by the presence of various RSR' patterns in at least two contiguous leads corresponding to a major coronary artery territory. Composite cardiac events (CCE) was defined as the occurrence of cardiac death, combined ventricular tachycardia/ventricular fibrillation, new onset atrial fibrillation and heart failure with hospitalization.

Results: Median follow-up duration was 4.6 years (interquartile range [IQR], 4.1 to 4.8 years). Mean age was 58±17 years, and 56 patients (60%) were male. fQRS was detected in 31 patients (33%). The cumulative survival of CCE at 4 years was 72.0%. In multivariate analysis, fQRS was significantly associated with CCE (adjusted HR [95% CI], 2.5 [1.01–6.4], P=0.047). At 4 years, the CCE-free survival was significantly lower in fQRS (+) group compared to fQRS (-) group (55.5% vs. 80.0%, P=0.02).

Conclusion: These findings suggest that fQRS could be a non-invasive prognostic tool for predicting cardiac events in HCM patients.

P5232 | BEDSIDE
Hypertrophic cardiomyopathy in a large cohort of MYBPC3 c.927-2A->G founder mutation carriers
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Purpose: Most hypertrophic cardiomyopathy (HCM) cohort studies are characterized by great heterogeneity of sarcomeric protein gene mutations. The aim of this study was to determine the penetrance and clinical disease expression in a large cohort of patients and relatives carrying the MYBPC3 c.927-2A->G founder mutation, arising more than 500 years ago.

Methods: The initial study population comprised 76 probands carrying the MYBPC3 c.927-2A->G. Additionally, 223 first degree relatives accepted to undergo genetic testing and clinical evaluation, including echocardiography.

Results: Out of 223 family members, 95 c.927-2A->G mutation carriers were identified, of whom 47 (50%) were clinically affected with left ventricular hypertrophy (LVH) ≥13 mm. The penetrance was age related (34% <40 years versus 61% ≥40 years, p=0.009) and greater in males (67%) than females (35%, p=0.001). Gender specific, cumulative age related penetrance is shown in Figure 1. Neither males nor females were affected until age 17 and by age ≥80, more than 90% of individuals were affected. The degree of LVH among the relatives ranged from 13 mm to 28 mm, none had left ventricular outflow tract gradient ≥30 mmHg at rest. The pattern of septal hypertrophy was reverse curve in 67% of patients, neutral in 21%, apical in 5.8%, and 3.5% had sigmoid septum.

Conclusions: HCM related to the MYBPC3 c.927-2A->G founder mutation is mainly late onset and shows gender specific penetrance. Other genetic or environmental factors must play an important role.

P5233 | BEDSIDE
Genotype-phenotype correlation in desmosomal gene related ARVC
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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a primary heart muscle disorder, mostly caused by mutations in genes encoding desmosomal proteins. The purpose of this study was to compare disease penetrance, phenotypic expression and lifetime arrhythmic risk between groups of desmocollin-2 (DSC2), plakophilin-2 (PKP2) and plakoglobin (JUP) mutation carriers.

Methods: The study population included 96 consecutive mutations carriers of DSC2 (n=28), PKP2 (n=38) and JUP homozygous (n=30). Serial clinical work-up consisting of history, physical examination, echocardiography and electrocardiography was performed. Clinical characteristics were recorded and compared between the 3 groups using chi-square and Kruskal-Wallis tests for categorical and continuous variables respectively. To determine the cumulative survival from the first major arrhythmic event (sustained ventricular tachycardia, sudden cardiac death) during lifetime, Kaplan-Meier curves were constructed and compared using the log-rank test.

Results: Penetrance and expressivity was the highest in JUP and the lowest in DSC-2 mutations (Table). Thirty-nine mutation carriers experienced the arrhythmic outcome. DSC-2 mutation carriers had a better lifetime cumulative event-free survival as compared to PKP-2 carriers and JUP homozygous carriers (p=0.022 and 0.003, respectively), whereas no difference was found between the later (p=0.55).

Clinical characteristics by genotype

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DSC-2 (n=28)</th>
<th>PKP-2 (n=38)</th>
<th>JUP (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43±18</td>
<td>42±18</td>
<td>41±20</td>
<td>0.155</td>
</tr>
<tr>
<td>Gender: male</td>
<td>14 (50)</td>
<td>24 (63)</td>
<td>16 (53)</td>
<td>0.53</td>
</tr>
<tr>
<td>Definite ARVC</td>
<td>11 (39)</td>
<td>28 (74)</td>
<td>29 (97)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Reappraisal abnormalities</td>
<td>6 (21)</td>
<td>26 (68)</td>
<td>22 (73)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Degeneration abnormalities</td>
<td>16 (57)</td>
<td>21 (55)</td>
<td>28 (93)</td>
<td>0.001</td>
</tr>
<tr>
<td>Right ventricular dysfunction</td>
<td>9 (32)</td>
<td>17 (46)</td>
<td>27 (90)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Left ventricular dysfunction</td>
<td>4 (14)</td>
<td>6 (21)</td>
<td>5 (14)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Values are reported as n (%) and means ±SD for categorical and continuous variables respectively.

Conclusions: Desmosomal gene related ARVC shows a gene-specific disease phenotype. JUP homozygocity was associated with higher penetrance and disease expressivity, however provided similar risk with PKP-2 heterozygocity. DSC-2 mutations were associated with lower disease penetrance, expressivity and arrhythmic risk.
Long-term outcome of percutaneous septal ablation for symptomatic hypertrophic obstructive cardiomyopathy

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Background and methods: We analyzed the long-term outcome of 575 consecutive patients (pts), mean age 56.1 ± 14.7 years treated with percutaneous septal ablation (PTLSMA) for symptomatic hypertrophic obstructive cardiomyopathy (HOCM). Data were acquired by outpatient examination in our institution or by phone contact with the pts’ local cardiologist. Pts who could not be traced neither personally nor via their home physician or their health insurance company were considered “lost” to follow-up.

Results: In-hospital mortality was 0.9% (5 pts.). Mean CK rise was 506U/l (reference:<80). A DDD-pacemaker (DDD-PM) had to be implanted in 44 pts. 7.5% (p<0.01) for procedure-related AV conduction problems. Follow-up was 97% complete (n=556). During follow-up (65.5±3 [range:0.1-204] months), 62 pts. (11%) died of these 28 (5%) from non-cardiac, and 34 (6%) from cardiovascular causes. Overall survival was 93% at 5 years, and 90% at 10 years. A re-intervention for significant residual or recurrent outflow obstruction was necessary in 51 pts. (9%). The latter cases included, at their last follow-up visit 518 pts. (90%) were in functional class I or II. The most frequent problem was atrial fibrillation in 63 pts. (11%).

Conclusions: During long-term follow up following PTLSMA, a persistent clinical improvement of symptoms was observed. A second intervention (surgical or catheter-based) was needed in about 10%. The survival rates observed in this cohort compares favorably to the natural disease course in symptomatic HOCM, and seem to be equivalent to post-myectomy data.

High incidence of subclinical atrial fibrillation in patients with hypertrophic cardiomyopathy


Purpose: In patients with hypertrophic cardiomyopathy (HCM) atrial fibrillation (AF) is an important prognostic parameter and often causes cardiac decompensation. Incidence of subclinical atrial fibrillation in HCM is unknown. Moreover, it remains unclear whether parameters like septal hypertrophy, obstruction of left ventricular outflow tract (LVOT) or diastolic dysfunction contribute to higher incidence of AF. In a single centre study we evaluate the incidence of AF in patients with HCM and de novo implantation of pacemakers and implantable cardioverter defibrillators (ICD).

Methods: Over a period of 26 months 44 patients with HCM (25 with LVOT obstruction ≥30 mmHg) received ICDS (4 TV, 33 DDD, 1 subcutaneous ICD, 30 primary prophylaxis), pacemakers (5 DDD) or event recorder (1). To detect AF device interrogation was performed by analysing atrial high rate episodes.

Results: In 30 HCM-patients (68%) AF could be detected. In 13 patients AF was detected only by device interrogation. During follow-up (337.4±263 days) in a total of 17 patients newly diagnosed AF was detected only by the use of AF. In 3 patients inadequate shock delivery was seen due to supraventricular tachycardia occurred in 6 patients (23%) suffered from thromboemolic event vs 1 patient without documentation of AF but diagnosed coagulopathy (p<0.01).

In 3 ICD patients inadequate shock delivery was seen due to supraventricular tachycardia. None of them had AF before. ICD therapy due to ventricular tachycardia occurred in 6 patients (24%).

Conclusion: Interrogation of cardiac devices revealed a much higher incidence (68%) of AF in HCM patients as anticipated. According to a high rate of thromboembolic events (23%) in patients with AF early detection and treatment of AF in HCM patients should be addressed more thoroughly.
PS239 | BEDSIDE
Ventricular fibrillation post alcohol septal ablation in hypertrophic obstructive cardiomyopathy: A complication caused by dislocation of the temporary pacemaker?
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Introduction: Ventricular tachyarrhythmias are well-known complications after a transcoronary alcohol septal ablation therapy (TASH) in hypertrophic obstructive cardiomyopathy. Due to the risk of total heart block a temporary pacemaker (TPM) back-up is recommended after TASH for at least 24 h after the intervention. Dislocation of the TPM resulting in an undersensing that may cause ventricular fibrillation is a well known complication in the treatment of acute bradycardia in general.
Methods: We performed a retrospective analysis for the occurrence of post procedural ventricular tachyarrhythmias (day 1-8) of all patients treated by TASH in our center during the period 2008-2013. The monitoring attack ECG’s were evaluated.
Results: A total of 389 Patients were analyzed. In 6 patients (2.1%) post procedural ventricular tachyarrhythmias occurred. In 6 cases the arrhythmia was induced by a clear R on T phenomenon caused by a dislocation of the TPM with loss of sensing. All patients had a pacemaker (ASA) in a large cohort from a tertiary medical center and were all treated by a fast external defibrillation and inactivation of the TPM. The inactivation of the pacemaker is crucial because of otherwise frequent recurrent reinduction of ventricular fibrillation. The other cases were a sustained ventricular tachycardia with spontaneous termination and a case with spontaneous ventricular fibrillation and effective therapy by an ICD implanted pre TASH.
Conclusion: The occurrence of ventricular tachyarrhythmias after TASH is rare. In most of the cases a dislocation of the TPM with loss of sensing was the reason for the arrhythmia. Therefore, an accurate positioning of the TPM and a proper post procedural ECG monitoring with rapid inactivation of a dislocated TPM are essential.

PS240 | BEDSIDE
Long-term outcome after septal alcohol ablation in symptomatic patients with obstructive cardiomyopathy: a single center experience
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Purpose: Alcohol septal ablation (ASA) is now considered to be an alternative to surgical myectomy in patients with symptomatic hypertrophic obstructive cardiomyopathy (HOCM) despite optimal medical treatment. Although its short and mid-term efficacy has been established, few results are available on its long-term outcome. The aim of this study was to analyze the long-term effect of echo-guided septal alcohol ablation (ASA) in a large cohort from a tertiary medical center.
Methods: 210 patients (56.6% male, 57.1 ± 10.0 years) underwent transcatheter alcohol septal ablation therapy in hypertrophic obstructive cardiomyopathy between November 1999 and May 2013. Follow-up was performed by phone, mailing or e-mailing to the patients or referring cardiologist with parameters including new pacemaker implantation (PM), new intra-cardiac defibrillator (ICD), Re-intervention by alcohol septal ablation or surgical myectomy, NYHA functional class, medications after hospital discharge and death (cardiac and non cardiac).
Results: Alcohol septal ablation (ASA) was echo-guided in all patients and was performed via the radial route in 69.1% of cases. Procedural success rate was 92.8%. In-hospital events were observed in 16/210 cases: coronary dissection successfully treated by stenting in 1 case, ventricular fibrillation in 1 case, ventricular tachycardia in 2 cases, transient ischemic attack TIA in 2 cases, acute pulmonary edema in 2 cases, hepatic cytolysis in 1 case, transfusion in 3 cases, fever in 2 cases and death in 2 cases (0.9%). Mean follow-up time was 5.14 years, survival rate was 95% at 1 year, 90% at 5 years and 85% at 8 years, which did not differ from the survival rate of the same age general French population. After discharge from hospital, all-cause mortality rate was 1.75% per year, and cardiac-related mortality was 0.55% per year. Age (p=0.005, OR 1.07, 95% CI 1.021-1.121) and procedural septal thickness (p=0.015, OR 2.095 95% CI 1.038-4.079) were the only independent predictors of cardiac mortality.
Re-intervention was performed for recurrence of symptoms in 9.6% of patients: surgical myectomy in 2.03% and repeated septal alcoholisation in 7.6%. Median re-intervention was performed for recurrence of symptoms in 9.6% of patients: surgical myectomy in 2.03% and repeated septal alcoholisation in 7.6%. Median re-intervention was performed for recurrence of symptoms in 9.6% of patients: surgical myectomy in 2.03% and repeated septal alcoholisation in 7.6%.
Conclusion: Alcohol septal ablation (ASA) is a safe and useful technique with good long-term efficacy.

PS241 | BEDSIDE
The role of metalloproteinases in the variants of the hypertrophic cardiomyopathy formation
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Purpose: To examine the role of matrix metalloproteinase system on the clinical course and prognosis of hypertrophic cardiomyopathy (HCM).
Methods: 196 patients (98 men, 78 women) with hypertrophic cardiomyopathy were subjected, mean age was 47.1±10.0 years. The duration of the observation - 7.66±0.36 (from 3 to 28 years). 55.4% of patients had a progressive course (PC) of the disease, stable course (SC) was observed in 35.5%, 9.1% had atrial fibrillation (AF), sudden cardiac death (SCD) was registered in 0.5%. The course was seen in 2.7% and 0.5% had the end-stage type (EST). All patients were investigated according standard cardiac algorithm and genotyping of gene MMP-3 polymorphisms. Biological markers (MMP-3, TIMP-1, TIMP-2, collagen-I) were identified in 40 patients with HCM and 39 controls.
Results: The allelic variant 6A/5A MMP-3-1171 was associated with pronounced hypertrophy of the interventricular septum (p=0.074) in patients with HCM. TIMP-1 values in HCM patients (835±73.31) were reduced compared with those in the control group (804±1±28.1; ng/ml; p=0.001). The concentration of the marker MMP-3 of patients with left ventricular hypertrophy of the LV myocardium was 2.44±0.11 fold higher than in control group (p=0.014). An inverse correlation were found between MMP-3 and index posterior wall thickness of the left ventricle (r=-0.313; p=0.049), and the asymmetry coefficient (r=-0.337; p=0.047). For genotype 6A/5A MMP-3-1171 was characterized by an increase in the level of TIMP-1, for the other genotypes decrease its concentration (p=0.008).
Conclusions: The MMP-3 and TIMP-1 concentration in patients with HCM has a predictive significance. However, the definition and the diagnostic tool for optimal management of the disease needs to be identified.

PS242 | BEDSIDE
Assessment of left atrial function in hypertrophic cardiomyopathy and left ventricular hypertrophy in athletes
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Background: Hypertrophic cardiomyopathy (HCM) is the first cause of sudden death, and its frequency is probably more 1/500. Differenciating this condition from the nonpathological “left ventricular hypertrophy” remains a challenge. The development of pathological left ventricular hypertrophy (LVH) is associated with left atrial (LA) dilatation and dysfunction. LA strain and strain rate by two-dimensional (2D) speckle tracking are novel indices of LA function and might contribute to differentiate pathological from physiological pathological LVH undiagnosed HCM.
Methods: We evaluated 70 patients with nonobstructive HCM, 40 athletes and 40 healthy controls matched for age, gender, and body surface area. All patients underwent a transthoracic echocardiogram with evaluation of LA strain: s-wave (LASS) and strain rate: s-wave (LASRs) and a-wave (LASRa). LA volume; LA mass index, LA volume index, and ejection fraction were comparable between patients with HCM and athletes’ group. Left ventricular volumes and stroke volume were higher in athletes, likely for the mitral pick velocity of the early diastolic wave (E) and E/A ratio. HCM group has higher E/e’ ratio (9.4±1.5 vs 6.7±1.8, p=0.002) Patients with HCM had a significantly lower LA Ss (19.8±8.8% vs 32±7.3%, P<0.01), LASRs (0.55±0.25 s-1 vs 1.2±0.25 s-1, P<0.01), and LASRsA (-0.7±0.1 s-1 vs -1.1±0.3 s-1, P<0.01). Among hypertrophic subjects, independent predictors of hypertrophy related to HCM were LASs and E/e’ ratio.
Conclusions: LA myocardial deformation is significantly impaired in patients with HCM compared to athletes and healthy controls. LA strain and strain rate assessed by 2D speckle tracking should be incorporated in the evaluation of trained athletes with LVH and LA dilatation.

PS243 | BEDSIDE
Cardiac magnetic resonance can detect cardiac involvement in systemic sclerosis even in patients without any abnormalities in screening tests -Comparison with serological tests and other imaging-
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Background: The early diagnosis of cardiac involvement in systemic sclerosis (SSc) has a predictive significance. However, the definition and the diagnostic tool remain unclear. We assessed the values of cardiac magnetic resonance (CMR) for the early diagnosis by comparing with traditional screening tests.
Methods: Forty five SSC patients (56.3±14.2 years, 5/40 male/female, 16/29 diffuse/limited type, mean disease duration; 98.5 months) underwent CMR and
screening tests: serological test, 12-lead ECG and echocardiography. The abnormal CMR measures were defined from normal ranges (means±2SD) in age- and gender-matched controls by previous papers.

Results: (1) Thirty patients had some abnormalities in screening tests. The serological test identified 12 patients with NT-proBNP>125 pg/ml and 13 troponin I>0.015 ng/ml. The 12-lead ECG showed 3 atrial fibrillation, 2 ventricular tachycardia, 3 atrio-ventricular block, 6 bundle branch blocks, 1 abnormal Q wave, and 6/3 electrical LV/RV hypertrophy. The echocardiography revealed 4 low LVEF, 3 asynergy, 1 LV hypertrophy, 5 LV diastolic dysfunction, and 3 pulmonary arterial hypertension. (2) Twenty five patients had some CMR abnormalities including 9 late gadolinium enhancement (LGE), 3 asynergy, 6 LV wall thinning, 3/1 LV/RV hypertrophy, 4/3 LV/RV dilatation, and 13/10 LVEF/RVEF; (3) Nine of 15 patients (60%), who showed no abnormalities in screening tests or Medsger Severity Index=0, demonstrated some CMR abnormalities (Figure).

Conclusions: CMR abnormalities were frequently identified in patients with SSc. CMR is useful for LV/RV early systolic dysfunction and myocardial fibrosis which could not be detected by screening tests. Clinicians should examine CMR for the early diagnosis of cardiac involvement in addition to screening tests.

PS244 | BEDSIDE

Serum MMP-9 as a quantitative biomarker for myocardial fibrosis in patients with hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiovascular disease and associated with an increased risk of sudden cardiac death (SCD). Myocardial fibrosis is one fundamental pathogenic substrate for cardiac arrhythmias. Therefore late gadolinium enhancement (LGE) shown by contrast cardiac magnetic resonance imaging (CMR) is an important risk factor of SCD as well as the occurrence of syncpeces and ventricular tachycardias (VTs). Certain matrix metalloproteinases (MMPs) can impact on collagen turnover and are therefore relevant to myocardial fibrosis. These serum biomarkers were correlated with the amount of myocardial LGE and the occurrence of cardiac syncpeces and VTs in HCM patients.

Methods: 54 HCM patients (age 55.9±14.3 yrs, 27 women) were investigated by CMR. After injection of 0.2 ml/kg gadolinium the amount of fibrotic tissue was assessed in percentage of the total myocardial mass of each patient. A myocardial signal intensity >2 standard deviations above remote myocardium was regarded as LGE. Serum concentrations of MMP-9, MMP-2 and its corresponding tissue inhibitor TIMP-1 were measured using ELISA-Assays (Amersham Pharmacia Biotec®). Linear regression models were used for statistical analysis.

Results: The mean MMP-9 concentration was 53.7±34.9 ng/ml. Those nine patients (16.7%) without LGE in CMR had a lower MMP-9 value (29.6±14.2 ng/ml), than patients positive for LGE (59.6±36.2 ng/ml, p=0.01). The mean fraction of fibrosis was 13.3±10.3% in these 45 patients and in each patient showing fibrosis MMP-9 was enhanced compared to healthy controls. Hence, an increased value of MMP-9 is highly sensitive (92%; 95%-CI [73; 99]) for the occurrence of myocardial fibrosis (23% specificity; 95%-CI [10; 42]). With a mean increase of 6.3g (95%-CI [5.8; 6.8]) of fibrosis per ten units of MMP-9 (p<0.001), this association was stronger in women than in men (2.7g (95%-CI [0.4; 4.5]) 10 units MMP-9; p=0.023) and was also a gender dependent predictor for the occurrence of syncpeces and VTs. While the MMP-9/TIMP-1 ratio also positively correlated with the amount of fibrosis, myocardial fibrosis could be detected for MMP-2 or TIMP-1 alone. All effects were adjusted for age, sex and myocardial mass.

Conclusion: Serum MMP-9 levels are associated with the amount of myocardial fibrosis detected by LGE in cardiac MRI in HCM patients. Hence, MMP-9 is an easily to obtain serum biomarker, which seems to be suitable for predicting myocardial fibrosis and possibly SCD risk factors such as syncpeces and VTs especially in women with HCM.

PS245 | BEDSIDE

Impact of latent obstruction on exercise tolerance in hypertrophic cardiomyopathy

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Background and aims: Reduced exercise tolerance is variably present in hypertrophic cardiomyopathy (HCM). We sought to evaluate the impact of exercise induced obstruction on exercise performance and the determinants of functional capacity in this subgroup.

Methods: The study sample included 144 HCM patients with normal ejection fraction (mean age: 51±14, males 63%), enrolled from 2007 to 2012 with a complete clinical assessment, including rest and stress echocardiography and cardipulmonary exercise test (CPET) with impedance cardiography. Results: At baseline 41 patients had an obstruction at rest (28%; group 1), 33 (23%) presented a latent obstruction (group 2) while 70 (49%) were non obstructive (group 3). Patients with rest obstruction showed a reduced peak VO2, in comparison with the other two subgroups (group 1: 22.4±7.7 ml/kg/min; group 2: 28.9±11.7 ml/kg/min; group 3: 32.8±10.5 ml/kg/min, p=0.005). VE/VO2 slope was similar in the three subgroups (group 1: 30.7±6.7; group 2: 28.2±5.8; group 3: 28.3±6.0, p=0.17) as well as peak CI (group 1: 9.6±3.2 vs. group 2:11.1±4.5 vs. group 3: 10.3±3.5 l/min/m², p=0.29). In the latent subgroup the main determinants of peak VO2 at a multivariate analysis were age (<0.06, p=0.001) and relative wall thickness (<0.39, p=0.03), while neither gradient at stress nor the Δ gradient between rest and stress reached the statistical significance.

Conclusions: Patients with latent obstruction and non-obstructive have a similar exercise tolerance. In patients with exercise induced obstruction the reduction of functional capacity is not related to the peak stress gradient, but to relative wall thickness and age.

PS246 | BEDSIDE

Clinical profile and in-hospital course of patients with Takotsubo cardiomyopathy and right ventricular involvement

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Purpose: Is to describe the prevalence, clinical findings, echocardiographic features and in-hospital course of patients with takotsubo cardiomyopathy (TTC) and right ventricular involvement (RVI).

Methods: The study population consisted of 495 consecutive patients (mean age 69.1±14.2 years, 91% females, 92% with acute non obstructive cardiomyopathy (HCM). We sought to evaluate the impact of exercise induced obstruction on exercise performance and the determinants of functional capacity in this subgroup.

Results: RVI was detected in 53 pts (10.7%) and there are no significant differences in age (mean 68.2±13.9 vs 69.3±11.2 years), and sex prevalence (92% vs 91% female) between the two groups. Chronic obstructive pulmonary disease (23% vs 15%; p=0.006), other non-acute cardiac disease (27 vs 13%; p=0.008) and history of cancer, included previous treatment with chemotherapeutic agent (19 vs 9%; p=0.034) as well as total associated comorbidities were more frequent in group A (1.25 vs 0.89; p=0.032). The association of chest pain with dyspnea was more prevalent in group A (25 vs 5%; p=0.001), whereas isolated chest pain was the most common presenting symptom in patients without RVI (55 vs 74%; p=0.003). Any significant difference concerning the ECG changes at admission was found between the two groups. Left ventricular ejection fraction (35.7±6.8 vs 36.8±7.1%; p=0.036) and E/e’ ratio (11.6±4.1 vs 10.9 ± 3.9; p=0.045) were not significantly different between the two groups. Tricuspid annular plane systolic excursion (16.7±4.3 vs 19.6±4.0 mm; p=0.003) and RV exercise tolerance were lower in group A (27.4±12.7 vs 41.1±4.3; p<0.001) Conversely pulmonary artery systolic pressure was higher (43.7±14.6 vs 39.6±8.9 mmHg; p=0.034) in group A. Moderate to severe mitral regurgitation (36 vs 18%; p=0.02), major adverse events (acute heart failure and cardiac shock) were more frequent in group A (pts 17 vs 4.3%; p=0.01).

Conclusion: Patients with TTC and RVI have a different clinical profile associated with several comorbidities and represent a subset of patients at higher risk of in-hospital complications such as acute heart failure and cardiac shock. Thus additional therapeutic strategies should not be neglected or postponed in this setting.
The study population included 105 desmosomal mutation carriers of plakophilin-2 (n=38), desmocollin-2 (n=28), desmoplakin (n=6), plakoglobin homozygosity (n=30) and digenic heterozygosity (n=3). Serial clinical work-up consisting of history, physical examination, electrocardiography, and echocardiography was performed. Clinical characteristics of each group were recorded and compared between the 2 groups, using the chi-square and Mann-Whitney U tests for categorical and continuous variables, respectively. To determine the cumulative event free survival from the first major arrhythmic event (sustained ventricular tachycardia and sudden cardiac death) during lifetime, Kaplan-Meier curves were constructed, stratified by gender and compared with the log-rank test.

Results: Of the 105 subjects, 56 were male and 49 female. Gender was equally represented as suggested by the chi-square goodness-of-fit test (χ²=0.467, p=0.5). Clinical characteristics and their comparison between males and females are presented in Table 1. Forty-three mutation carriers experienced the arrhythmic outcome. Males exhibited a significantly lower cumulative arrhythmia-free survival (p=0.002) as compared to females.

Clinical characteristics by gender

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Males (n=56)</th>
<th>Females (n=49)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39 ±19</td>
<td>44 ±17</td>
<td>0.22</td>
</tr>
<tr>
<td>Definite ARVC</td>
<td>44 (79)</td>
<td>32 (65)</td>
<td>0.13</td>
</tr>
<tr>
<td>Repolarization abnormalities</td>
<td>34 (61)</td>
<td>23 (47)</td>
<td>0.16</td>
</tr>
<tr>
<td>TAD ≥55 ms</td>
<td>21 (39)</td>
<td>23 (50)</td>
<td>0.68</td>
</tr>
<tr>
<td>Epsilon waves</td>
<td>19 (34)</td>
<td>9 (18)</td>
<td>0.07</td>
</tr>
<tr>
<td>Right ventricular dysfunction</td>
<td>37 (66)</td>
<td>18 (38)</td>
<td>0.004</td>
</tr>
<tr>
<td>Left ventricular dysfunction</td>
<td>18 (32)</td>
<td>10 (21)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Values are reported as n (%), mean ±SD for categorical and continuous variables respectively.

Conclusions: Male carriers of ARVC-associated desmosomal gene mutations developed more frequently right ventricular functional-structural alterations and exhibited higher arrhythmic risk.

PS248 | BEDSIDE
Clinical significance of persistently-increased heart rate despite optimal pharmacotherapy to predict heart failure prognosis independent of improved left ventricular ejection fraction

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Purpose: Increased heart rate (HR) has been known as a poor prognostic factor in heart failure (HF) patients with systolic dysfunction. We thought to clarify whether persistently high HR has also prognostic value in patients with subsequent functional improvement after optimal pharmacotherapy (OPT).

Methods and results: We enrolled 85 consecutive newly-diagnosed non-ischemic dilated cardiomyopathy (ND-DCM) patients with left ventricular ejection fraction (LVEF) <35% and sinus rhythm at baseline. HR and LVEF were serially evaluated for 12 months follow up after OPT. Among baseline variables, multivariate analysis indicated that higher HR was an independent predictor of combined cardiac events (CCEs) including HF hospitalizations and major ventricular arrhythmias (adjusted hazard ratio 1.1, 95% confidence incidence 1.0-1.2, P<0.01). The receiver-operating characteristics curve demonstrated that baseline HR was a significant predictor, with an area under curve of 0.72 for subsequent CCEs and a receiver-operating characteristics curve demonstrated that baseline HR was a significant predictor, with an area under curve of 0.72 for subsequent CCEs and a significant predictor, with an area under curve of 0.72 for subsequent CCEs and a receiver-operating characteristics curve demonstrated that baseline HR was a significant predictor, with an area under curve of 0.72 for subsequent CCEs. The patients were divided into three groups stratified by gender and compared with the log-rank test. Forty-three mutation carriers experienced the arrhythmic outcome. Males exhibited a significantly lower cumulative arrhythmia-free survival (p=0.002) as compared to females.

Conclusions: Male carriers of ARVC-associated desmosomal gene mutations developed more frequently right ventricular functional-structural alterations and exhibited higher arrhythmic risk.

PS249 | BEDSIDE
Three-dimensional myocardial strain patterns in patients with physiological and pathological hypertrophy and preserved left ventricular systolic function: a comparative study

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Purpose: This study aimed to explore the utility of three-dimensional speckle-tracking strain (3DST) to discriminate functional adaptations of the left ventricle (LV) in physiological versus pathological LV hypertrophy (LHV).

Methods: A total number of 286 subjects, including 50 HCM patients (52 ±15 yrs) with preserved ejection fraction (LVEF 67 ±13%) and 211 healthy volunteers (44 ±15 yrs) were examined using Vivid E9 scanner. LV 3D volumes (end-diastolic, EDV, end-systolic, ESV), mass, peak global and segmental strain (longitudinal, 3DL; circumferential, 3DC; radial, 3DR; 3DA) were measured with EchoPac BT12. Global strain dispersion index (DSI) was calculated for all 3D strain parameters as the average of the standard deviation values of segmental strain in all 17 LV segments.

Results: Adequate tracking for global 3D strain analysis was achievable in 248 (87%) datasets (temporal resolution 36.7 vps). HCM pts had significantly lower global and segmental peak 3DL, 3DC, and 3DA compared with athletes and controls (p<0.001 for all), while 3DC was similar among groups (p=0.7). Strain dispersion index (DSI), a measure of regional contractile heterogeneity, was higher in HCM compared with the other groups (Table). On receiver operating characteristics analysis, DSI had the best discriminatory ability among all strain parameters to distinguish HCM from athletes (area under curve, AUC=0.80, p<0.001) or controls (AUC=0.84, p<0.001). However, 3D LV geometry (LV mass/EDV) and indexed LV mass were better suited than DSI to differentiate the athlete’s heart from HCM (AUC 0.98 and 0.95, respectively).

Conclusions: Three-dimensional echocardiography allows a fast and comprehensive characterization of LV geometry and myocardial deformation in subjects with LHV, which may help to differentiate HCM from athlete’s heart. Impairment of 3D longitudinal strain with a high strain dispersion index favor the diagnosis of HCM.

PS251 | BEDSIDE
Extensive overlap of myocardial fibrosis and regional sympathetic nervous dysfunction predicts long-term clinical outcome in patients with idiopathic dilated cardiomyopathy

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Purpose: Myocardial fibrosis detected by late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) and sympathetic nervous dysfunction detected by 123I-metabolin-benzylguanidine (MIBG) are associated with worse outcome in idiopathic dilated cardiomyopathy (IDCM) patients. However, relationship remains unknown. We sought to compare the distribution of LGE and detect locations of MIBG and to investigate the association of them with long-term adverse events.

Methods: We studied 85 IDCM patients (59 ±15 yrs, LVEF 31 ±8%) with positive LGE by CMR. They underwent MIBG, and defect locations in SPECT as area with relative activity >60% of maximum were investigated. Distribution of positive LGE and MIBG defect were distinguished at apical, anterior, septal and lateral regions except for inferior region (due to MIBG image attenuation) and then compared. Heart/nasimium ratio in delayed phase (delayed (H/M) was calculated from planner image. Cardiac death and heart failure hospitalization were defined as events (follow-up 2279±819 days).

Results: LGE distributed mainly in inter-ventricular septum, whereas spread more diffusely into other segments in part. Defect in MIBG was observed in 76 cases (89%). There was no overlap between CMR and MIBG (non overlapping group) in 49 (42%), overlap only at septum (partially overlapping) in 30 (35%), and overlap at spread into other segments (largely overlapping) in 16 (18%) cases, respectively. Among three groups, largely overlapping group was associated with worse outcome (P<0.01) and lowest delayed H/M (P<0.01).

Conclusions: Extensive overlap of myocardial fibrosis and regional sympathetic dysfunction predicts long-term clinical outcome in patients with idiopathic dilated cardiomyopathy.
A founder MYBPC3 frameshift mutation results in HCM with a severe prognosis and high risk of sudden death in middle-aged patients

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Previous studies reported a delayed expression and clinically benign outcome in hypertrophic cardiomyopathy (HCM) patients carrying MYBPC3 mutations. The aim of this study was to evaluate the clinical characteristics, penetrance and prognosis of HCM patients carrying a frequent founder mutation in MYBPC3.

Methods: Study population included 97 HCM probands. All of them were screened for MYBPC3 mutations and 19 were found to have the same frameshift mutation (c.912_913delTT, p.F305PfsX27). Pedigree analysis, including both clinical evaluation and genotyping, was performed. Carriers of the identical mutation were genotyped with 4 microsatellites and 9 SNPs flanking this gene in order to understand if it was a founder mutation. Clinical characteristics and cardiovascular events were compared between the frameshift mutation carriers (Group 1), other MYBPC3 mutation carriers (Group 2) and patients negative for MYBPC3 mutations (Group 0), using univariate and multivariate analyses.

Results: The MYBPC3 frameshifting mutation c.912_913delTT (p.F305PfsX27), found in 19 (19.5%) index cases (14 males and 5 females). Among 81 relatives belonging to 14 apparently unrelated families, 45 (20 males and 25 females) resulted to be mutation carriers and 29 of them (17 males and 12 females) had HCM. Haplotype analysis confirmed a common founder ancestor in these families. Disease penetrance was incomplete (64.4%) and was greater in males than females (85% versus 48%, p=0.008). Eleven (38%) affected mutation carriers were diagnosed between 30 and 40 years old. Probands carrying this frameshift mutation had less maximal hypertrophy at last control (p=0.05) compared to patients with other MYBPC3 mutations (Group 2). During a mean follow-up of 10 years they experienced more frequently non-sustained ventricular tachycardia (p=0.01), underwent ICD implantation (p=0.02) and showed a worse prognosis for sudden cardiac death (SCD) or aborted SCD (p=0.01), underwent ICD implantation (p=0.02) and showed a worse prognosis for sudden cardiac death (SCD) or aborted SCD (p=0.01) compared with Group 0 patients.

Conclusions: The founder MYBPC3 mutation carriers have a high probability to develop the disease between 30 and 40 years of age, with an increased risk if they are men, and they show a significantly reduced survival after the fourth decade of life when compared to patients without MYBPC3 mutations. These findings are of importance to the genetic counseling and therapy, considering the high frequency and poor prognosis associated with this founder mutation.

Corticosteroid therapy might have beneficial effects on long-term clinical outcomes by reduction of HF admission, with retarding progression of left ventricular systolic dysfunction in patients with CS.

Discriminating hereditary transthyretin cardiomyopathy from hypertrophic cardiomyopathy using an echocardiographic and ECG based classification tree

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Purpose: Hereditary transthyretin amyloidosis (ATTR amyloidosis) with cardiac involvement could easily be misdiagnosed as hypertrophic cardiomyopathy (HCM) due to echocardiographic similarities, as both diseases are characterized by increased left ventricular myocardial thickness. The aim of this study was to create a classification tree based on ECG and echocardiography that could identify ATTR amyloidosis patients.

Methods: Thirty-three patients with ATTR amyloidosis and cardiac involvement and 30 patients with diagnosed HCM were included in the study. Retrospective analyses of echocardiographic variables were analysed, including measurements of dimensions, systolic and diastolic left ventricular (LV) function, Voltage, PQ- and QRS duration was analysed from ECG. LV deformation and entropy were measured in order to assess myocardial intrinsic function and texture.

Results: Two classification trees were created, one only based on echocardiographic features accessible in everyday practice. The second tree was based on multimodal features: conventional and advanced echocardiography and ECG. The multimodal tree presented with the highest sensitivity (0.938) and specificity (0.919) and included two branches. QRS voltage <30 mm classified patients as HCM. Subjects with voltage <30 mm were classified as HCM if interventricular septal and posterior wall thickness ratio (IVS/PWT) were >1.6 and as ATTR if IVS/PWT <1.6.

Conclusion: Our study proposes an easy interpretable classification tree for the differentiation between HCM and ATTR amyloidosis, presenting with higher sensitivity and specificity than any single variable associated with ATTR amyloidosis. Our combined echocardiographic and ECG model could increase the ability to identify ATTR cardiac amyloidosis in clinical practice.

Long-term effect of corticosteroid therapy in patients with cardiac sarcoidosis

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Purpose: Cardiac involvement is the worst prognostic determinant in patients with sarcoidosis; however, the long-term effects of corticosteroid therapy on clinical outcomes in patients with cardiac sarcoidosis (CS) remains unclear.

Methods: We examined 86 consecutive patients who were definitively diagnosed as CS during past 35 years in our institution. Patients were divided into two groups based on the presence or absence of corticosteroid therapy at diagnosis.

Results: Corticosteroid therapy was performed in 70 patients. Patients with corticosteroid therapy had lower age and higher incidence of positive findings in gallium scintigram (Ga) at diagnosis than those without. LV ejection fraction (LVEF), angiotensin converting enzyme (ACE) and lysozyme, BNP levels, other cardiovascular medications and therapies were comparable between the two groups. During the follow-up (8.3±5.6 years), corticosteroid therapy was associated with lower long-term adverse events (overall, P=0.005; cardiac death, P=0.076; symptomatic arrhythmias, P=0.91; heart failure (HF) admission, Figure A), and greater % increase in LVEF (7.3±36.0% vs -16.7±34.8%, Figure B). Multivariate analyses showed that corticosteroid therapy (HR 0.41, 95% CI 0.20-0.91, P=0.029) was an independent negative determinant of long-term adverse events among variables including age, gender, baseline LVEF, and positive Ga findings. Subgroup analyses showed corticosteroid therapy was associated with better clinical outcomes in all subgroups (age, gender, baseline LVEF, ACE and lysozyme, BNP levels, finding of Ga).

Heart rate and blood pressure responses to exercise in familial amyloid polyneuropathy - impact on the prognosis


The responses of heart rate (HR) and blood pressure (BP) to exercise reflect cardiac autonomic balance and appear to be attenuated in patients with familial amyloid polyneuropathy (FAP) V30M-TTR, even in the pre-clinical stages of the
Playing the role of a helpful assistant, I can comprehend and convert the text into a plain text representation as follows:

**Objective:** To evaluate the prognostic value of changes in HR and BP during exercise test (ET).

**Methods:** Of the 239 V3OM-TTR mutation carriers followed annually, 155 (42±12 years, 53.5% females) asymptomatic or mildly symptomatic who were able to perform exercise (Bruce protocol) were enrolled. HR and BP were recorded at rest, at each stage of exercise and during recovery. The chronotropic index ([C]; normal > 0.8) and the HR recovery (HRR) at one minute after cessation of exercise (normal > 180 - age in years) were calculated. To examine the risk of death from any cause we used multivariate Cox regression analysis, adjusted for age, and Kaplan-Meier survival analysis.

**Results:** Over a median follow-up of 36 months, the ET was repeated periodically under the patients' physical capacity allowed, for a total of 464 tests. The mean exercise duration was 9.3±2.8 minutes (11.9±4.9 METS). During follow-up, eight patients (5.2%) died. Multivariate Cox regression (backward conditional method) adjusted for age showed that the risk of death increased with baseline systolic BP [Hazard Ratio: 1.09, 95% CI 1.03-1.16, P=0.005] and correlated inversely with baseline diastolic BP [Hazard ratio: 0.88, 95% CI 0.80-0.96, P=0.006]. In addition, the risk was inversely proportional to the peak HR [Hazard ratio: 0.95, 0.93-0.97, P < 0.001] and increased with HR at the 1st minute of recovery [Hazard ratio: 1.07, 95% CI 1.03-1.17, P < 0.001]. In fact, the risk of death was nearly four times higher in individuals with HRR abnormality (Hazard ratio: 3.81, 95% CI 1.15-12.67, P=0.029), whereas CHF had no prognostic value.

**Conclusion:** In asymptomatic or mildly symptomatic patients with V3OM-TTR, the changes in blood pressure induced by exercise have no prognostic value. Only peak HR, HR at the 1st minute of recovery and HRR have prognostic impact.

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**PS526 | BEDSIDE**

What is the optimal duration of pacemaker (PM) backup after TASH in HOCM? Results from a prospective study in 139 patients

T. Lawrenz1, M. Brodsky2, M. Schloesser2, C. Drephal2, H. Kuhn2, C. Stellbirk3.

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2. Urban Hospitals Bielefeld, Bielefeld, Germany

**Background:** Even after an uneventful TASH a total heart block may occur within the first days after the intervention. Therefore, telemetric monitoring is recommended for 7 days. After we identified risk factors (RF) for the total heart block in 2007 we published our approach for the postprocedural pacemaker management: In patients with a retrograde AV nodal block after TASH and at least one additional RF (age > 58 years, QRS-interval > 120ms, intraprocedural total heart block) we recommended to extend the temporary pacemaker period from 24 h up to 7 days.

**Aim of the study:** Prospective examination of this PM-regime under real-life conditions.

**Methods:** Of the 139 consecutive patients we analyzed the risk for total heart block after TASH. Only patients with atypical CHCM and patients who already had a PM or ICD pre TASH were excluded. We examined in particular whether the patients were under PM protection at the time of the occurrence of a post-procedural III^° AV-block or not.

**Results:** (2/139) of the patients experienced a total heart block after TASH (18 within the first 4 days and one patient on day 7 after TASH). According to our regime we treated 71 patients with low risk (0 or 1 RF) with a PM for only 24 h and 68 high-risk patients (retrograde AV block + at least one additional risk factor) who were put on a pacemaker for several days (average 4.8 days). The risk for PM dependency after TASH was more than twice as high in the high-risk group (18%) compared to the low-risk group (7%). During the occurrence of III^° AV-block, 71% of the low-risk and 75% of the high-risk patients were under the protection of the temporary PM. In the other cases a rescue temporary PM could be placed until permanent PM-implantation was performed without complications.

**Conclusion:** For the first time, risk factors for the occurrence of a total heart block after TASH could be confirmed in a prospective study. The risk for III^° AV-block was 2.6 times greater in the high-risk group compared to the low-risk group. Risk stratification and optimization of the duration of PM-backup improves the safety after TASH and increases the rate of patients who are under PM protection when total heart block occurs from 26% to 73%. According to these data we recommended to place a temporary PM for 4 days in patients with high risk for total heart block after TASH. In low-risk patients it appears to be adequate to leave the PM lead for 2 h.

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**PS527 | BEDSIDE**

Usefulness of longitudinal strain to predict major cardiac events in patients with hypertrophic cardiomyopathy

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**Introduction:** Many studies have reported that the presence of fibrosis in left ventricular myocardium (LVM) as late gadolinium enhancement (LGE) on cardiovascular magnetic resonance (CMR) has prognostic value for the occurrence of MACE in HCM patients. Low global longitudinal strain (GLS) values by speckle-tracking (ST) have been related to the presence of fibrosis on CMR in HCM patients. Therefore we speculated that GLS values might independently predict prognosis of HCM patients.

**Methods:** We included 51 HCM patients. 48.1% ICD carrier. Medical records were checked for occurrence of a MACE, including cardiac death, sustained ventricular tachycardia and hospital admission due to cardiac cause. Events were analyzed using Kaplan–Meier curves.

**Results:** Follow-up was completed in 98% of patients with a mean of 39.3±13.7 months. Long S was independently associated with MACE in our HCM cohort (OR curves demonstrated increased amount of cardiovascular events in group 4 were not. ROC curves of GLS revealed AUC of 0.71 (0.54-0.87, p = 0.017) and the best cut off point was -11% (sensitivity 71%, specificity 72%). Kaplan-Meier curves by strain >11% are shown in the picture below.

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**Conclusion:** Speckle tracking derived GLS with a cut-off point of -11% provides useful non invasive information to accurately predict MACE in HCM. This clinically promising parameter might be added to classic risk factors to improve risk stratification in patients with HCM.
Right atrial enlargement is a marker of left ventricle diastolic dysfunction in patients with hypertrophic cardiomyopathy

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Introduction: Left atrial (LA) enlargement is an established marker of poor prognosis in several cardiovascular diseases, including hypertrophic cardiomyopathy (HCM). Recently, right atrial (RA) enlargement has been associated with right diastolic dysfunction. There are no data describing the R and L atria. This study aimed to characterize RA size and function in HCM patients, and to evaluate the specific characteristics of those with increased right atrial volume index (RAVI).

Methods: HCM patients were prospectively enrolled and submitted to a transthoracic echocardiographic examination. Atrial volumes were calculated in ventricular end systole and end diastole, through the Simpson's method and indexed to body surface area. Right atrial ejection fraction (RA EF) was calculated through the formula (major RAVI - minor RAV)/major RAV.

Results: 39 patients, 62.3% men, mean age of 48.7 ± 17.7 years were included. Mean RAVI was 21.8 ± 9.0 ml/m2 and mean RA EF was 48.7 ± 17.6%. Twenty-three patients (46%) met the current guidelines criteria for RA enlargement (RAVI > 21 ml/m2). Patients with increased systolic RAVI were more commonly men (82.6% vs 41.1%, p=0.001), presented the septal asymmetric HCM subtype (82.6 vs 51.8%, p=0.02), had higher systolic LA volume index (LAVI) (48.6 ± 22.5 vs 35.8 ± 13.4 ml/m2, p=0.03) and smaller RA EF (40.6 ± 17.6 vs 50.4 ± 16.1%, p=0.004) and LA EF (38.4 ± 13.4 vs 49.3 ± 10.1%, p=0.006), without significant differences regarding left ventricular (LV) volumes or LV EF. Patients with higher RAVI had lower late transmitral flow velocity (A wave 6.3 ± 2.5 cm/s vs 7.9 ± 1.9 cm/s, p=0.008) and higher E/A ratio (1.7 ± 0.7 vs 1.2 ± 0.5, p=0.009), without significant differences on tissue Doppler velocities or E/E' ratio. Additionally, these patients had higher LAVI (7.7 ± 5.3 vs 5.3 ± 3.9, p=0.03), a new marker of severe left diastolic dysfunction. The groups had similar transmural flow velocity, tricuspid annular systolic excursion, right ventricle tissue Doppler velocities and E/E' ratio. Univariate logistic regression, showed significant association between increased RAVI and A wave (p=0.016), E/A ratio (p=0.017). There are no data describing the R and L atria. This study aimed to characterize RA size and function in HCM patients, and to evaluate the specific characteristics of those with increased right atrial volume index (RAVI).

Conclusions: Increased systolic RAVI is frequent in patients with HCM and it is associated with LV diastolic dysfunction. Presence of septal asymmetric HCM type was the only independent predictor of increased RAVI.

NON-INVASIVE ELECTROPHYSIOLOGY

Magnetocardiographic analysis of ventricular repolarization in hypertrophic cardiomyopathy: the role of heterogeneous repolarization on the occurrence of lethal ventricular tachyarrhythmias


Background: The mechanism for lethal ventricular arrhythmias (VA) in hypertrophic cardiomyopathy (HCM) is poorly understood. Hypertrophy causes heterogeneous repolarization (Rep), increasing arrhythmia vulnerability. The aim of this study was to investigate the specific characteristics of those with increased right atrial volume index (RAVI).

Methods: In 105 HCM patients with QRS > 120ms, we recorded 64-Channel MCGs (1kHz), yielding 2-D maps. On QRS map, we defined heterogeneous Dep characterized by divergent multi-directional LV currents according to our previous study. Current pattern during Rep was analyzed on ST-T (Rep) map. We also 25 normal volunteers and 15 subjects with isolated LBBB (LLBBB) with normal LV function.

Conclusions: Increased systolic RAVI is frequent in patients with HCM and it is associated with LV diastolic dysfunction. Presence of septal asymmetric HCM type was the only independent predictor of increased RAVI.

Regional distribution of T-wave alternans in patients with genotyped long QT syndromes assessed by 24-hour 12-lead electrocardiography: What is the optimum lead?

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Purpose: To elucidate the optimal electrocardiogram (ECG) lead for detecting T-wave alternans (TWA) in patients with genotyped long QT (LQT) syndromes using 12-lead continuous ECG monitoring.

Methods: 24-h 12-lead ECG was recorded in 23 patients (10 male; mean age, 13.8 ± 7.9 years) with congenital LQT syndrome types 1 (LQT1, n=15), 2 (LQT2, n=4), and 3 (LQT3, n=4). Peak TWA was determined by the modified moving average method. TWA in the other 11 leads at the time of peak TWA was also
measured. The lead with the peak TWA values in each patient was termed the “highest lead”. The probability of detecting TWA >40 μV was evaluated in each of the 12 leads.

**Results:** TWA >40 μV was recorded in 78.3% (18/23) of the patients (12/15 in LQT1, 3/4 in LQT2, 3/4 in LQT3). In the whole group, mean TWA was highest in lead V2 (49±1.28 μV) and the second highest in lead V3 (43.7±31.0 μV), which was significantly higher than in the third highest lead V4 (26.1±27.4 μV) (P<0.05). The highest lead was V2 in 9 patients (all LQT1), V3 in 9 patients (4 LQT1, 1 LQT2 and 4 LQT3), V4 in 3 patients (1 LQT1 and 2 LQT2), and II in 2 patients (1 LQT1 and 1 LQT2). The proportion of detecting TDO1: (1 μV was the highest in lead V2 (83.3%). The precordial leads V2-4 could detect 94.4% of the episodes of TWA >40 μV.

**Conclusions:** TWA is regionally specific and more prevalent in the precordial leads, particularly in V2 and 3, in LQT patients. Thus, use of limited ECG leads may lead to underestimation of TWA, which is not only one of the diagnostic criterion of LQT syndrome but also a risk marker for lethal cardiac arrhythmias. The high prevalence of TWA in the precordial leads may provide insights into mechanisms.

**P5264 | BEDSIDE**
The response of the QT interval to standing in children with long QT syndrome

**Background and aims:** Patients with Long QT Syndrome (LQTS) often display paradoxical prolongation of the QT interval in response to an increase in heart rate. Studies in adults have shown that the tachycardia induced by standing can be a useful aid in the investigation and diagnosis of LQTS. However, data on the response of the QT interval to standing in the paediatric LQTS population are limited. This study, therefore, aimed to observe the changes in the QT interval invoked by the action of standing in children with LQTS.

**Methods:** 48 consecutive children from 45 families with LQTS (aged <18 years; median 13.2 years [interquartile range 8.5-15.1]; 49% female), followed up in a specialist tertiary centre for paediatric inherited cardiovascular disease underwent supine-12 lead ECG followed by a second ECG immediately after standing. Corrected QT interval (QTc) was measured in lead II using Bazett’s and Fredericia’s formula. 29 patients from 26 families (60%) had undergone genetic testing (LQT1, 6/10; LQT2, 3/4 in LQT2, 3/4 in LQT3). In the whole group, mean TWA was highest in lead V1 (43±18 μV) followed by Lead V2 (40±14 μV), V3 in 3 patients (1 LQT1 and 2 LQT2), and II in 2 patients (1 LQT1 and 1 LQT2). The proportion of detecting TDO1: (1 μV was the highest in lead V2 (83.3%). The precordial leads V2-4 could detect 94.4% of the episodes of TWA >40 μV.

**Results:** The corrected QT interval (QTc) was 432ms supine vs. 454ms standing (mean increase of 22ms [±50ms]) in lead II. When subdivided by genotype, impairment of the QT response was most pronounced in LQT1 (416ms supine vs. 477ms standing; mean increase of 42ms [±62ms]) compared to LQT2 patients who showed improved QTc shortening (468ms supine vs. 432ms standing; mean decrease 35ms [±19ms]) p<0.002 compared to LQT2 patients. In patients with a diagnosis of LQT3 but a normal QTc at rest, QTc was 407ms supine vs. 443ms standing (mean increase of 35ms [±49ms]).

**Conclusions:** This study shows that the QTc increases in children with LQTS on standing, particularly in LQT1. This may improve diagnostic accuracy in children in whom a diagnosis of LQTS is suspected.

**P5265 | BEDSIDE**
A novel new magnetocardiography-based algorithm for discrimination between ventricular tachyrhythmias originating from right ventricular outflow tract and aortic sinus cusp
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**Background:** Radiofrequency (RF) catheter ablation has been established as an effective and curative therapy for ventricular arrhythmia originating from the outflow tract (OT-VA) in structurally normal hearts. Although there are several reports concerning characteristic 12-lead ECG findings of outflow tract ventricular arrhythmias (OT-VAs), accuracy of the ECG algorithms to predict their origin is sometimes limited. The aim of this study was to develop a magnetocardiography (MCG)-based algorithm using a novel adaptive spatial filter to differentiate VA from aortic sinus cusp (ASC-VA) from VA from right ventricular OT (RVO-VA).

**Methods:** This study consisted of 51 patients (20 men, mean age 49±15 years) who underwent successful catheter ablation for symptomatic diastolic VT or PVCs originating from the outflow tracts. Activation mapping and pace mapping were performed during the clinical arrhythmia. In all patients, surface 12-lead ECGs were recorded during sinus rhythm and during the clinical arrhythmia. Transition zone index is defined as TZ score of VA minus TZ score of sinus beat, where TZ score is graded in 0.5-point increments according to the site of the transition zone in the precordial leads. All patients underwent an MCG during sinus rhythm 1 day before ablation. MCG methodology was described in detail previously. An algorithm was developed by correlating the MCG findings with the successful ablation site. The arrhythmias were classified as RVO-VA or ASC-VA. The following three parameters were obtained from 3-D MCG imaging: 1) depth of the origin of OT-VA in the anteroposterior direction, 2) distance between the earliest atrial activation site, i.e., sinus node, and the origin of OT-VA, and 3) orientation of VA propagation at the QRS peak.

**Results:** The origins of VAs were identified in the RVO (n=41, 80%) and the ASC (n=10, 20%). There were no significant differences with regard to baseline patient characteristics. ROC analyses determined that depth of origin was the most predictable variable for distinguishing between VAs originating from the OT and sinus. This suggests that the depth of origin was significantly higher in lead V1 (43±18 μV) vs. V2 (40±14 μV), V3 in 3 patients (1 LQT1 and 2 LQT2), and II in 2 patients (1 LQT1 and 1 LQT2). The proportion of detecting TDO1: (1 μV was the highest in lead V2 (83.3%). The precordial leads V2-4 could detect 94.4% of the episodes of TWA >40 μV.

**Conclusions:** This novel MCG-based algorithm using an adaptive spatial filter could precisely discriminate ASV-VAs from RVO-VAs.
was elucidate the relation between the manifestation of early repolarization (ER) pattern and J wave and autonomic function using head-up tilt test (HUT).

Methods and results: A total of 191 patients (94.9±12.4 years) underwent HUT using 12-leads electrocardiogram (ECG) and impedance cardiography. If patients didn’t show syncope or presyncope, HUT was repeated under drug loading (adenosine triphosphate, isobutylate diibrite, isoproterenol). At baseline ECG, 17 patients showed ER pattern with J point elevation (<1mm) (ER group) (35.4±2.15 years), 24 showed J wave, notch or slurr of the terminal of the QRS (J group) (51.2±24.0 years) and 17 showed J wave with ER pattern, (J-ER group) (36.9±17.7 years) at least in 2 leads of inferior (II, III, aVF) or lateral (I, V4-6) leads. 133 patients didn’t show any remarkable change which suggests idiopathic ventricular fibrillation (N-group).

Patients in J and J-ER groups showed high positive rate of HUT compared to that idiopathic ventricular fibrillation (N-group). Moreover QT of anterior appearing rhythm was frequently observed in inferior leads compared to lateral leads (36 vs. 12).

Conclusions: Our findings suggest that abnormal autonomic nerve activity is a factor of the manifestation of J wave especially in inferior leads and may link to arrhythmogenicity of J wave syndrome.

P5268 | SPOTLIGHT Prognostic analysis of heart rate variability assessment in familial arrhythmogenic right ventricular cardiomyopathy


Introduction: Familial amyloid polyneuropathy (FAP) V30M-TRR, a rare form of hereditary amyloidosis, is characterized by progressive autonomic neuropathy. The disease is associated with conduction disturbances, increased risk of complications and, in rare cases, sudden death. These events are attributed to autonomous dysfunction. The heart rate variability (HRV) which integrates the balance of sympathetic and parasympathetic tone may be a useful tool for prognostic stratification in these patients.

Aim: To study the prognostic value of heart rate variability analysis assessed by 24 hr Holter monitoring in FAP.

Methods: Prospective observational study of consecutive patients with V30M-TRR mutation. All patients were evaluated annually and underwent 24hr Holter monitoring. To evaluate the predictive value of the mean heart rate (HR), PNN50, PNN30, RMSSD, SDNN, Total Power, VLF, LF, HF and LF/HF ratio in the risk of death, from any cause, multivariate Cox regression analysis with adjustment for age and Kaplan-Meier survival analysis were used.

Results: 223 patients (mean age 44±14 years; 54.3% female) were included. During a median follow-up of 55 months, 777 Holter exams were performed. From a total of 635 exams in sinus rhythm, time and frequency domain analyses of heart rate variability were available in 575 exams. The independent predictors of prognostic value of age, mean HR and VLF. The risk of death increased with age (HR: 1.054; IC 95% 1.026-1.083; P<0.001) and varied inversely with the mean HR (HR: 0.936; IC 95% 0.905-0.968; P<0.001) and VLF (HR: 0.420; IC 95% 0.24-0.723; P=0.002). The risk of mortality differed significantly according to the tertiles distribution of these variables, being twice in patients with VLF -279 ms2 (HR: 2.23, IC 95% 1.34-3.68 P=0.001) and higher in patients with mean HR -75 bpm (HR: 9.39; IC95% 4.70-18.77; P<0.001).

Conclusion: Very Low Frequency and mean HR assessed by 24 hr Holter monitoring in FAP.
Conclusions: A weak tendency to higher R2I2 values in patients with autonomic dysfunction is seen.Combining R2I2 with HRV-i may improve its performance as an SCCD risk marker. These data begin to answer the challenge that R2I2 is a quantification of autonomic dysfunction and raise the possibility that R2I2 could be effective in populations with normal autonomic function.

P5274 | BENCH

Inhibitory effects of prednisolone on the recurrence after atrial fibrillation ablation in a rat model

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Background: We previously reported that transient use of corticosteroids after atrial fibrillation (AF) ablation was effective for preventing AF recurrences. However, the mechanism underlying the suppressive effect of corticosteroids on AF recurrences has not been fully examined.

Methods: Ten-week-old-Wister rats were divided into 3 groups: ablation (A)- group, ablation and steroid (AS)-group, and control (C)-group. Rats in A- and AS- groups underwent right atrial linear ablation with a 2-French transvenous catheter, and rats in C-group underwent catheter insertion without ablation. Rats in AS-group were treated with prednisolone (10mg/kg/day) intragastrically, and rats in A- and C-groups were treated with vehicle from 5 days before the procedure. One week after the procedure, the durations of AF induced by 30-second burst pacing were measured. Atrial structural changes were assessed histologically, and tissue levels of inflammatory cytokines in the atria were measured by multiplex immunoassay.

Results: AF duration was significantly shorter by ablation, and additionally reduced by prednisolone (9.0±5.6 vs.[AS]-group), 10.3±5.0 vs.[A]-group) vs. 4.8±3.3 vs.[AS]-group). Microscopic analysis revealed suppression of ablation-related histological changes (inflammatory cell infiltration and interstitial fibrosis) by prednisolone. The tissue levels of TNF-a, MCP-1, IL-17A, IL-18, and VEGF were significantly enhanced by ablation, and were significantly reduced by prednisolone (Table).
Atrial fibrillation (AF) is the most common cardiac arrhythmia in the human population, with an estimated incidence of 1-2% in young adults but increasing to more than 10% in >80 years patients. Albeit AF is a frequent electrophysiological disorder, to date, the genetic bases of AF remain rather elusive. Point mutations in a large variety of ion channels have been described in familial cases of AF, yet explaining a minority of cases. Recently, genome wide association studies (GWAS) have unraveled risk SNPs highly associated with AF, among which the most significant are located in 4q25 locus. Surprisingly these risk alleles are located in a gene desert, being the closest gene PITX2. Experimental evidences of Ptx2 loss-of-function in mice revealed that this homeodomain (HD)-containing transcription factors plays a pivotal role in atrial electrophysiology. Therefore these data, underscore Ptx2 as a candidate gene for AF. In this context, we have recruited 31 AF patients from the Regional Hospital “Ciudad de Jaén” and 23 controls from the University Hospital of Jaen for genetic analyses of both the risk alleles and PITX2 ORF re-sequencing. Among those patients, we have found two point mutations in the HD of PITX2 and three other mutations in the 5’ untranslated region. A 65 years male patient with recurrent AF displayed both HD mutations, G947A (Q103H) and G1008A (E124Q), which both resulted in a change within a highly conserved amino acid position. Curiously, no 4q25 risk variants were present in this subject. Both PITX2 HD mutations were further followed for functional studies. We generated plasmid constructs with mutated version of each nucleotide variant (MD4 and MD5, respectively) as well as a dominant negative control construct in which the PITX2 HD was lacking (DN). Functional analyses demonstrated PITX2 MD4 and PITX2 MD5 decreased Nppa-luciferase transactivation by 50% and 40%, respectively, in a similar range as PITX2 DN (50%). Co-transactivation with other cardiac-enriched transcription factors, such as Gata4 and Nkx2.5, was similarly impaired, further supporting the pivotal role of these mutations for correct PITX2 function. We are currently evaluating the functional consequence of these mutations in a cardiomyocyte context. Preliminary data suggest that distinct AF-related genes are similarly impaired. In summary, we have identified novel PITX2 mutations in an AF patient, which functionally impairs the transactivating capacity of PITX2.

**P5277 | BENCH**

**Dose-dependent pitx2 loss of function impairs zfhx3, wnt18a and calcium handling: novel links to atrial arrhythmogenesis**

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Atrial fibrillation (AF) is the most common cause of arrhythmogenesis in humans yet the genetic cause of AF remains elusive. Recent genome-wide association studies have revealed that risk variants in four distinct genetic loci (4q25, 1q21, 16q22 and 16q13) which have been associated with AF. Among them, the most significant are 4q25 risk variants, which are located in the vicinity of the PITX2 gene. Given the key developmental role of PITX2 during cardiac development and partially its role in pulmonary vein deployment, it has been postulated that Pitx2 dysfunction might be the molecular link to AF. Experimental evidences in distinct laboratories, including ours, have demonstrated that Pitx2 loss of function predisposes to atrial arrhythmogenesis. However, the molecular mechanisms driven by Pitx2 in this context remain somehow elusive, proposing either embryonic or mature gene expression defects. In order to get further insights into the molecular mechanisms driven by Pitx2 and their putative relation with novel AF GWAS associated genes, we have generated a new Pitx2 conditional mouse line, by intercrossing Sox2Cre and Pitx2loxP mice. Epiblast deletion of Pitx2 leads to the generation of heterozygous and systemic null Pitx2 null mutants, respectively. As expected, embryonic mortality and cardiac defects were similarly observed in Sox2CrePitx2 null mice as those previously reported for Pitx2 knock-out mice. Molecular analyses of the left atrial appendage in heterozygous Sox2CrePitx2 mice (20-30% reduction in Pitx2 expression) and atrial specific NppaCrePitx2 null mice (60-70% reduction in Pitx2 expression) demonstrate that AF associated genes such as Zfhx3, Kcnq3 and Wnt18a are severely impaired while other such as Cavr1, Sypnp20 or Prx1 are not. Surprisingly, beta-adrenergic signaling is not altered in these models whereas multiple calcium handling genes such as Serca2a, calsequestrin, phospholamban are severely impaired in atrial specific NppaCrePitx2 null mice but not in heterozygous Sox2CrePitx2 mice. Functional assessment of cardiac handling further underscores these findings. Importantly, neither Zfhx3 nor Wnt18a gain-of-function or loss-of-function experiments impairs Pitx2 expression, suggesting that Pitx2 is upstream of these genes. Furthermore, these data suggest a dose-dependence relation between Pitx2 expression and the susceptibility to display basal or only inducible electrophysiological defects. We are currently studying the hierarchical between Pitx2, AF GWAS associated genes and calcium handling, as well as to putative involvement of post-transcriptional modulators such as microRNAs.
Prothrombotic potential of Gq signalling in the left atrium

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Heterotrimeric G proteins are membrane-associated proteins that comprise an alpha, beta and gamma subunit and are the intracellular mediators of G-Protein coupled receptor activation (Park et al., 2004; Neer et al., 1994; Salazar et al., 2001). Transgenic overexpression of constitutively active Gq under the control of the heavy chain promotor leads to cardiac hypertrophy, re-expression of foetal genes, diffuse atrial and ventricular fibrosis, atrial fibrillation and ultimately heart failure (Mende et al., 1998, Hirose et al., 2009).

Echocardiographic analysis revealed increased atrial size and reduced atrial function in 16 week old Gq mice prior to the development of compromised ventricular function. Atrial thrombi were found in 33% of Gq mice at 16 wks of age (n=69, but no thrombi were observed in wild type controls (n=43) (p<0.05). Telemetric electrocardiogram recordings (n=6, 15-17 hours recording/mouse) identified very short episodes of paroxysmal AF (on average 32 sec per day) in Gq mice >12 weeks of age. In addition, we found atrial thrombi in 14% of mice without documented AF (n=43), suggesting that enhanced activation of Gq signalling may have a direct prothrombotic effect on atrial cardiac tissue.

We therefore analysed atrial gene expression in search for prothrombotic genes. A Mid Map microarray that contains genes that are activated during Gq signaling was compiled by combining DAVID (Database for Annotation, Visualization and Integrated Discovery) and IPA (Ingenuity Pathway Analysis) analyses of a RNA-seq dataset generated from whole heart from a second transgenic mouse line overexpressing Gq protein (Matkovich et al., 2010). Prothrombotic candidates identified via literature search and linked to Gq were also included in the Mind Map. The expression levels of 20 candidate genes were quantified in the left atria (LA) of 8-14 wk old mice (n=7-15 transgenic and n=9-18 wild type) by RT-PCR. Four candidate genes were found to be significantly upregulated in LA Gq-compared to wild type LA: Tenascin C (TnC, 3.3 fold, p<0.001), von Willebrand Factor (1.7 fold, p<0.006); Trombospondin 1 (2.2 fold, p<0.03) and Serpin peptidase inhibitor C3 (1.7 fold, p<0.03). The expression of these genes was confirmed at the protein level by western blotting. The expression of TnC was associated with increased levels of Gq signalling in LA, which was upregulated in Gq transgenic mouse, indicative of Gq signalling promoting a prothrombotic environment.

Inhibition of aldosteronosynthese CYP11B2 inhibits atrial fibrosis during atrial fibrillation in vivo and in vitro

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Introduction: Earlier studies have suggested that inhibition of aldosteronosynthese CYP11B2 may reduce fibrosis in the left ventricle. The role of CYP11B2 inhibition for structural remodeling during atrial fibrillation (AF) is unknown. Methods and results: Primary neonatal cardiac fibroblasts were stimulated with angiotension II (1µM; 3 hours) and pre-incubated with or without the CYP11B2 specific inhibitor SL 242, SL 242 (1µM; 24 hours) reduced the expression of the pro-fibrotic cytokine connective tissue growth factor (CTGF), the key enzyme of collagen crosslinking lysyl-oxidase (LOX) and the fibrosis regulator microRNA-21 (miR-21) as well as the collagen content, whereas Rac1 expression and activity was unaffected. Lung fibroblastes (V97MZ cells) deficient of endogenous aldosteronsynthase CYP11B2 were transfected with human aldosteronsynthase (CYP11B2) and normalized. Under basal conditions, aldostensynthase activity was unaffected. Lung fibroblastes (V97MZ cells) deficient of endogenous aldosteronsynthase were transfected with human aldosteronsynthase (CYP11B2) and treated with terosamide. These experiments showed that terosamide inhibited aldosteronosynthese CYP11B2 activity by 75±1.8%, most likely through a competitive inhibition of CYP11B2 by binding of terosamide to the heme binding site of CYP11B2 through its nitrogen ring. Mineralocorticoid receptor expression and activity was not altered by terosamide.

In order to test the effect of CYP11B2 inhibition in vivo, transgenic mice with cardiac expression of Gq were used. Rac1 GTPase (Rac1 GTpase) was increased, CYP11B2 development was hampered in Gq mice treated with terosamide (10mg/kg/day) for 8 months. Untreated Rac1 GTpase were characterized by increased atrial fibrosis, increased protein expression of CTGF (257±1.7%), LOX (195±2.4%) and the miR-21 (252±4.3%) compared to wildtypes (WT). Long-term treatment with terosamide prevented fibrosis in Rac1 GTpase as well as the up-regulation of CTGF (62±18%), LOX (124±23%) and miR-21 (68±7%) compared to vehicle, whereas Rac1 expression and activity remained unaffected. Terosamide did not affect blood pressure but reduced the pressure induced atrial fibrosis (38% Rac1-GTpase/Tors vs. 70% Rac1-GTpase). All effects are significant with p<0.05.

Conclusion: Inhibition of aldosteronosynthese (CYP11B2) prevents atrial fibrosis and reduced the prevalence of atrial fibrillation in mice. These effects were mediated through reduced expression of the proibritotic regulators CTGF, LOX and miR-21.
This suggests that alterations in inflammatory T lymphocytes are present in AF, patients. Our aim was to investigate inflammatory mechanisms underlying AF.

Results: We show for the first time that the percentage and number of CD4+CD28null T lymphocytes was quantified by flow cytometry in AF patients, and age, gender and ethnicity matched healthy subjects. IFN-γ and TNF-α levels were quantified by ELISA. The number of CD4+CD28null T cells has a specific expansion of pro-inflammatory CD4+CD28null T lymphocytes that produce inflammatory cytokines IFN-γ and tumor necrosis factor-α (TNF-α), factors that promote fibrosis. Patients with AF have elevated levels of TNF-α, although its cellular source has not been investigated. Furthermore, production of IFN-γ by T cells has been implicated in cardiac inflammation and fibrosis in animal models, whilst no information exists in AF patients.

Background: Intravenous amiodarone has been established as the first-line drug for cardipulmonary resuscitation (CPR) in patients with refractory ventricular arrhythmia (VT/VF). According to the CPG guidelines of the American Heart Association, 300 mg bolus i.v. of amiodarone should be used for the initial dosage. On the other hand, patients with refractory VF who were performed more than two times of automatic external defibrillator (AED) or direct current shock (DC) during CPR by emergency medical service (EMS) or physicians. The endpoint was the successful rate of return of spontaneous circulation (ROSC), admission to the hospital, and 24hrs survival rate.

Conclusion: Low dose intravenous amiodarone resulted in better ROSC, admission and 24hrs survival rates than that of 300mg amiodarone in patients with refractory VF.
 treated by manual defibrillation. The other 2 VF were occurred in patients who were implanted ICD, and treated by appropriate ICD shocks. No patients died during the follow-up period. There are no differences in the characteristics of the patients between those with and without recurrence of lethal arrhythmia and acute myocardial infarction. However, medications for coronary spasm were discontinuated in 25 patients who developed VF and STEMI. The intervals between discontinuation of medications and cardiac events were less than 2 days in all events.

Conclusions: The patients who survived cardiac arrest due to coronary spasm were at high risk for recurrence of severe ischemia and lethal arrhythmia. Discontinuation of medication, even within a few days, was closely associated with the cardiac events. ICD therapy may be beneficial in patients who survived cardiac arrest.

P5289 | BEDSIDE Long-term follow-up of asymptomatic Brugada syndrome

Purpose of the study: To report the follow-up of asymptomatic Brugada syn-
drome in our study the event according to familial history and results of pro-
grammed ventricular stimulation (PVS). The prognosis of asymptomatic BS remains questionable.

Methods: 43 asymptomatic patients, 38 males, 5 females with a type 1 Brugada pattern in ECG underwent study; 20 patients had a family history of sudden death (SD); age varied from 23 to 74 years (mean 46±13). All patients underwent echocardiogra-
phy, exercise testing and Holter monitoring. PVS was performed in all except in 7 patients who refused the study. ICD was implanted in 24 patients (3 patients refused the study). Two asymptomatic patients without familial history of SD, but with inducible VF were treated by hydroquinidine and PVS became negative. Implantable loop recorder was used in 12 patients. Mean follow-up was 6.3±9 years.

Results: At PVS, VF was induced in 16 patients (44%), non-sustained (NS) VF (29.4±11 sec) in 6 patients (17%). PVS remained negative in remaining 14 pa-
tients (39%). During follow-up, 2 patients in whom PVS was not performed died suddenly; 2 patients with ICD had a ventricular fibrillation (VF). Another patient died from unknown death. Prevalence of death was 11.6%. One patient had a NIf VF; VF induction did not predict the occurrence of death or VF (sensitivity 50%, specificity 56%). VF and non-sustained VF induction did not add a benefit for the prediction of arrhythmic event. The risk factors for a serious event were the male gender (no death in women) and the history of familial sudden death (all SD's or VF in patients with familial SD but in 1 of them, SD was debatable (occurring at 70 years).

Conclusions: Prevalence of deaths was high in these young patients without heart disease. PVS has a low sensitivity and specificity (about 50%) for the pre-
diction of a significant clinical event. Only female gender was a factor of good prognosis. Familial history of SD was a significant predictor of major event in our population.

P5290 | SPOTLIGHT
Two novel SCN1B variants (V169M in SCN1B and G266S in SCN1B) increased late sodium current in a Sudden Arrhythmic Death Syndrome Syndrome
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Purpose: A 17-year-old boy suffered from sudden arrhythmic death syndrome. The aim of this study was to elucidate the electrophysiology mechanism of these arrhythmic events.

Methods and results: We obtained DNA from patient and sequenced the cod-
ing region of KCNQ1, KCNH2, SCN5A, SCN1B, RyR2, and GPDL1 genes. Two mutations in SCN1B (V169M and SCN1B2 (G266S) were identified. Chinese hamster ovary (CHO) cells were used to co-express hNav1.5 with either wild-type or mutant Nav1.1 subunits (V169M, G266S or V169M+G266S) to recapitulate the cardiac sodium current (I Na). Whole-cell patch clamp recording showed that V169M channels had depolarizing shifts in steady-state activation, while V169M/ G266S combination turned this activation curve to a small but significant hyper-
polarization, as compared to their respective wild type. Besides, G266S and before the events in all patients. Only female gender was a factor of good prognosis. Familial history of SD was a significant predictor of major event in our population.

P5291 | BEDSIDE
Role of cardiac arrhythmias in sudden cardiac death in renal transplant candidates
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Purpose: The single largest cause of death in renal transplant candidates (RTC) is sudden cardiac death (SCD), accounting for roughly 25%. This study investi-
gated the role of arrhythmic events (AE) diagnosed by implantable loop recorder (ILR) in sudden cardiac death in RTC.

Methods: Prospective observational study performed between June/2009 and January/2011. One hundred consecutive RTC underwent ILR implantation to monitor cardiac rhythm for at least one year, for cardiac arrest, AE were classified in ventricular fibrillation (VF), atrial tachycardia (AT), atrial fibrillation (AF), non-sustained (NSVT) and sustained ventricular tachycardia (SVT). Groups were compared by Mann–Whitney U test, Chi square test or Fisher’s exact test, as appropriate. Multivariable logistic regression models were developed to determine risk predictors of AE and death.

Results: The average age was 59±8.8 years, with predominance of men (65%). Hemodialysis mean time was 53±30 months. Echocardiography characteristics showed left ventricular ejection fraction (LVEF) of 59±10%. During mean follow-
up of 2.9±1.3 years 33% patients died. We were unable to identify the cause of death in 4 (12.1%). The causes of death were sepsis (33.3%), SCD (21.2%), renal complications (12.1%), pulmonary (6.0%) and one of each cause: heart failure, myocardial infarction, stroke, hypovolemic shock and renal transplant complica-
tion. During mean ILR monitoring of 42±127 days, AE was detected in 73% of patients. Bradyarrhythmias were present in 25%, AT/AF in 18%, NSVT in 56% and one patient presented SVT; AE was detected in 71.4% of patients with SCD, 68.1% in non-sCD patients and 73% in survivors, therefore the presence of AE was not associated with SCD (P=0.830). Left ventricular dilatation was independent-
dantly associated with TNRS (OR 2.83 [95%CI 1.01-7.96] P=0.041). The use of hypoglycemic drugs (OR 2.5 [95%CI 1.01-6.19] P=0.047) and PR interval (OR 1.03 [95%CI 1.01-1.06] P=0.017) were independent predictors of death.

Conclusion: Renal transplant candidates had a high incidence of AE and SCD. AE occurred for almost a quarter of the identifiable causes of death, however the AE were not associated with SCD.

P5292 | BENCH
Next-generation sequencing data strengthens the involvement of cardiac structural diseases in Sudden Infant Death Syndrome (SIDS)
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The Sudden Infant Death Syndrome (SIDS) represents the most prevalent cause of death in children less than 1 year of age in developed countries. Cardiac chan-
neloropathies have been found to be responsible of a significant percentage of SIDS cases. The involvement of cardiac channelopathies in cases of sudden cardiac death in babies (SIDS) is supported by data such as Hypertrophic (HC), Dilated (DCM) or Arrhythmogenic Right Ventricular (ARVC) cardiomyopathies as the underlying cause of some cases in the absence of a visible phenotype remains currently poorly known. We have previously re-
ported the presence of known HCM-associated mutations in a big cohort of 288 unrelated SIDS cases using high-throughput genotyping techniques. Some of them have shown to produce defective proteins that disrupt the sarcomeric Ca2+ homeostasis which may ultimately affect the cardiac contractile properties leading to disease phenotypes. Here, we present our results from the study of a SIDS co-
hort composed of 41 unrelated cases underwent massively parallel sequencing of 81 genes, mainly arrhythmogenic, structural, and aortic disease-related genes as-
associated with increased risk of SCD. Computational filtering of the output data was performed in correlation with altered function of the proteins (misense, nonsense, frameshift, duplication or intron variants), allelic frequency within populations and measures of quality and sequence read mapping. As a result, 62 validated vari-
ants were categorized as a function of their pathogenic likelihood, according to current recommendations. A total of 36 variants (56%) were novel and, therefore, was not associated with SIDS (P=0.047). The remaining 26 variants (32%) reported in population studies without any clinical association and 4 variants (6.5%) initially reported as disease-causing but lacking conclusive sup-
porting evidence of causation. Interestingly, we also found 2 missense variants (L514T and V177L) in TTN genes previously associated with HCM and myopathy, respectively. After a review of the literature, public and private databases, we cat-
egorized these variants as “likely pathogenic”, since several primary reports as disease-associated are available for each variant and functional studies support a potential involvement of the proteins in the disease development, although more further studies are necessary to consider them as “pathogenic”. These and previous results are altogether encouraging and the fast development of Next-Generation Sequencing platforms have widened the limits of research in
A-BSPM parameters were significantly associated with shock incidence (npT a1 appropriate ICD shocks occurred and 15 patients died. Two of the eight selected parameters is presented. Using Kaplan-Meier survival curves (KM), chi-square tests (CHI), and calculation of ROC areas. A selection of the best parameters is presented. The prevalence of preexcitation syndrome was low in patients with poor outcomes: 3462 ± 1193, p < 0.0001. Baseline and 2nd day NSE (ng/mL) were not different, but significant differences on 3rd, 4th day after CA were found: NSE on 3rd day: 71.4 ± 70.6 vs. 22.4 ± 4.11, p < 0.0001; and NSE 4th day: 83.3 ± 14.8 vs. 9.1 ± 0.011. No significant differences were found in return of spontaneous circulation (ROCS) interval (22.1 ± 12.2 vs. 26 ± 13 min., p = NS), baseline 100 ± 1.95 vs. 0.58 ± 1.21, 2nd day 1.69 ± 1.94 vs. 1.84 ± 2.72 g/L, p = NS), baseline LVEF (40.2 ± 7.3 vs. 7.6 ± 6.8%, P = NS) in comparison of subgroups with good and poor outcome. ROC curve for good outcome showed AUC of 0.83 (95%CI 0.72-0.94, p < 0.001) and identified optimal cut-off of NT-proBNP > 1195 ng/mL to predict good outcome with a specificity of 81% [95%CI 63-93], sensitivity of 83% [95%CI 64-91], and predictive value of 80% and a negative predictive value of 90%. No significant differences were reported for PS.

Methods: We studied consecutive 197 patients with first anterior acute ST-elevation MI. ECGs of 86 patients could be evaluated before the AMI onset. ECGs of remained patients were evaluated after ST resolution. J-wave was defined as an elevation of the QRS-ST junction (>0.1mV): KM logRank p = 0.032, HR 4.6 (95%CI 1.4-14.9), chi = 0.028, npT a2 (number of positives T-waves χ2 test; CHI p = 0.028). Independent predictors of VF occurrences were J-wave (odds ratio = 0.51, 95%CI 0.28-0.95; p = 0.001) and Killip class ≥ 2 (odds ratio = 9.3, 95%CI: 2.35-40.27; p < 0.01). Additionally, despite similar infarct size and left ventricular function, incidence of VF related death during hospitalization or SCD during follow-up was significantly higher in the J-wave group than in the non J-wave group (n=8 vs. n=3, p = 0.02). Independent predictors of VF related Death or SCD were chronic kidney disease (odds ratio = 11.28, 95%CI 1.07-194; p = 0.04) and J-wave (odds ratio = 7.6, 95%CI 1.9-31; p = 0.05).

Conclusions: In anterior ST-elevation myocardial infarction, the presence of inferior J-wave appears to be a risk marker of not only VF occurrences, but also poor prognosis.
nondiagnostic APs were exceptional after 59 years. Elderly patients were more frequently symptomatic with a higher risk of AF and of poorly-tolerated tachycardia than younger patients. Therefore elderly patients with a preexcitration syndrome require the same management as younger patients.

NON-INVASIVE STUDIES

PS528 | BENCH
Impaired heart rate recovery index in patients with sarcoidosis
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Introduction: Sarcoidosis, an inflammatory granulomatous disease, associated with various cardiac disorders, including threatening ventricular arrhythmias and sudden cardiac death. Heart rate recovery after exercise is a function of vagal reactivation, and its impairment is an independent prognostic indicator for cardiovascular and all-cause mortality. The aim of our study was to evaluate heart rate recovery in patients with sarcoidosis.

Methods: The study population included 56 patients with sarcoidosis (23 men, mean age = 47.3 ± 13.0 years, and mean disease duration = 38.4 ± 9.7 months) and 54 healthy control subjects (20 men, and mean age = 46.5 ± 12.9 years). Basal electrocardiography, echocardiography, and treadmill exercise testing were performed in all patients and control participants. The heart rate recovery index was defined as the reduction in the heart rate at peak exercise to the rate 1st-minute (HRR1), 2nd-minute (HRR2), 3rd-minute (HRR3) and 5th-minute (HRR5) after the cessation of exercise stress testing.

Results: There are significant differences in HRR1 and HRR2 indices between patients with sarcoidosis and control group (24.9 ± 6.4 vs 33.7 ± 10.8; p < 0.001 and 45.4 ± 8.9 vs 53.2 ± 11.9; p = 0.001, respectively). Similarly, HRR3 and HRR5 indices of the recovery period were lower in patients with sarcoidosis, when compared with indices in the control group (52.7 ± 12.4 vs 60.8 ± 13.0; p < 0.001 and 59.8 ± 12.9 vs 68.2 ± 12.6; p < 0.001, respectively) (Figure). Exercise capacity was notably lower (9.2 ± 2.1 vs 11.6 ± 2.8 METs; p < 0.001, respectively) and systolic pulmonary arterial pressure at rest was significantly higher in patients with sarcoidosis compared with control group (29.7 ± 5.5 mm Hg vs 25.6 ± 5.7 mm Hg, p < 0.001, respectively). Furthermore, we demonstrated that HRR indices were related with radiographic stage.

Conclusions: The heart rate recovery index impaired in patients with sarcoidosis as compared with control subjects. When the prognostic significance of the heart rate recovery index is considered, these results may partially explain the increased occurrence of arrhythmias and sudden cardiac death in patients with sarcoidosis. This study calls attention to the importance of heart rate recovery index that may be clinically helpful in the recognition of high-risk patients.

PS529 | BEDSIDE
Electrocardiographic markers of arrhythmogenic risk in left ventricular hypertrophy
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Purpose: Left ventricular hypertrophy (LVH) is considered a risk factor for malignant arrhythmias and sudden cardiac death (SCD). The aim of the study was to assess non-invasive markers of SCD. Markers of disturbed repolarization (positive late potentials and T wave alternans (TWA)) using Holter heart rate turbulence (HRT), and microvolt T-wave alternans (MTWA) were most frequent in patients with LVH and least frequent in athletes. HRV as well as HRT parameters were the most unfavourable in HTN-LVH group, while in athlete’s heart group, despite similar grade of LV hypertrophy, were normal. There were no significant correlation between studied HRV, HRT, LP and TWA parameters and degree LV muscle thickness or type of hypertrophy.

Conclusions: Different aetiology of LVH is associated with various distribution of electrocardiographic markers of SCD. Markers of disturbed repolarization are more frequently observed in HCM group, while HRV and HRT parameters are most unfavourable in HTN-LVH. In athletes with LVH markers of SCD are uncommon which suggests good prognosis in this type of LV hypertrophy.

P5300 | BEDSIDE
The activation of RASS and sympathetic nervous system in patients with vasovagal syncope
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The renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system are important in the maintenance of vertical position. They both are activated with time and the duration of tilt testing may influence the activation. The aim of the study was to assess the activation of RAAS and catecholamines during tilt-induced vasovagal syncope.

The study population consisted of 192 patients (F 140, M 52), aged 49.8 ± 19.3 years, with the vasovagal syncope during diagnostic tilt testing. Plasma renin activity (PRA) and aldosterone were measured in a supine position before test (1), immediately after syncope (2) and 10 minutes after syncope (3). Adrenaline and noradrenalin were measured at (1) and (2). The groups were divided according to the phase of tilt test in which syncope occurred.

Results are shown in the table.
HRV by spectral analysis for each five minutes at baseline (hrv0), syncope period (hrv1), and just before hrv2 (hrv1).

Results: Forty-four patients were diagnosed as VVS by HUTT (mixed type: 20, cardioinhibitory type: 7, vasodepressor type: 17). In patients with VVS, TWA values in taw0 and taw1 were 5.3±7.1, 9.6±13.5 respectively, and the TWA value was significantly higher just before syncope than that at baseline (p<0.038). Average HF values of HRV in hrv0, hrv1, hrv2 were 115±147, 109±154, 502±1018Hz (p=6.3×10−4) respectively, and average LF/HF values were 5.0±3.2, 5.1±3.3, 2.8±1.7 (p=3.6×10−4) respectively.

Conclusions: TWA value was significantly higher just before syncope than that at baseline. By analyzing HRV during HUTT, parasympathetic tone was abruptly augmented in conjunction with suppression of sympathetic tone just before syncope. Therefore the fluctuation of TWA values may associate with ANS. Consequently this study suggested that such abrupt change of ANS might influence on myocardial repolarization.

Results: See Table 1. In addition, prevalence of (+) TT was similar in pts. with different underlying diseases and in both genders. No correlation was found between age and (+) TT.

Conclusions: 1. A high suspicion of vaso-vagal etiology of syncope by adding different criteria of the anamnesis is not related to a higher prevalence of (+) TT. 2. The information provided by the anamnesis and the tilt test is not redundant.

P5304 | BEDSIDE
Estimation of possible syncope-induced brain injury and clotting disturbances during positive head-up tilt test in patients with vasovagal syndrome
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Syncope is an effect of temporal, global hyperperfusion of brain. It is known that even short episodes of circulatory arrest may lead to brain injury. Some release of brain injury markers - neuron-specific enolase (NSE) as well as clotting disturbances was described in relation to tilt-test (HUTT) induced syncope in patients with vasovagal syncope.

Aim of study: Evaluation of injury inducing of vasovagal syncope (VVS) on the brain evaluated by release of NSE, in relation to clotting changes during HUTT in pts. with VVS.

Study population: 60 pts. (38 women) aged 18-74yrs (mean age 35,6), with NSE, referred to HUTT.

Methods: All pts. underwent standard HUTT. All pts. lies at supine position by 30 minutes after antecubital vein cannulation. Blood sample for NSE evaluation was collected before and 1 hour after HUTT. Before HUTT and at the onset of HUTT-provoked syncope blood sample was collected for analysis of clotting parameters: prothrombin time (INR), activated partial thromboplastin time APTT, serum concentrations of fibrinogen (FIB) and d-dimer (d-Dim).

Results: HUTT was positive in 51 pts. (85,0%). Significant increase of NSE level after HUTT in all pts. With HUTT-induced syncope, (3,3 vs. 4,2 ng/ml; p<0,01) was observed. There were no significant increase of NSE in pts. with negative HUTT. Substantial increase of serum levels of FIB (3,1 to 3,3 g/l p<0,006), d-Dim (263,0 vs 379,0 ug/l; p<0,001) with decrease of APTT (30,9 to 25,6 ± p<0,01) and INR (1,1 vs 1,03; p<0,03) were observed in patient fainted during HUTT.

Correlation between syncope induced rise of NSE and d-dimer level before HUTT (K=0,32; p<0,04) and after the test (K=0,35; p<0,04) were found. It suggest that activation of fibrinolysis revealing by rise of d-dimer concentration may protect the brain injury related to the syncope induced by orthostatic stress.

Conclusions: Syncope induced by orthostatic stress during tilt test in pts. With vasovagal syncope is concerned both release of brain injury markers and induction of changes in clotting-fibrilization process.

Endogenous activation of fibrinolysis during HUTT-induced syncope, revealing by rise of d-dimer concentration, may protect against of brain injury related to clinical circumstances in patients with vasovagal syncope.

P5305 | BEDSIDE
Influence of sleep disordered breathing on heart rate turbulence in heart failure patients

Purpose: Sleep-disordered breathing (SDB) is associated with adverse outcomes in patients with heart failure (HF). Heart rate turbulence assessed by Holter ECG has been used in order to predict sudden cardiac death. Recent studies have suggested that heart rate turbulence has a predictive value for adverse prognosis in HF patients. We investigated the relationship between SDB and heart rate turbulence in HF patients.

Methods: In this study, 75 patients with HF and SDB were examined. Patients with atrial fibrillation and receiving implantable pacemaker device therapy were excluded. We simultaneously performed Holter ECG during 24-hr period and polysomnography in night time, and examined apnea hypopnea index (AHI) and heart rate turbulence (turbulence onset and turbulence slope) during 24-hr period.

Results: All patients were divided into two groups based on the presence of severe SDB: Group A (AHI≥30, n=58) and Group B (AHI<30, n=17). Turbulence slope was significantly lower in Group B than in Group A during 24-hr period (night time: 6.9 vs. 3.6; day time: 7.0 vs. 3.7; all day: 6.6 vs. 3.5 ms/RR, P<0.05, respectively). Turbulence onset did not differ between two groups (night time: 0

Table 1: Prevalence of (+) TT for each score

<table>
<thead>
<tr>
<th>(+) TT</th>
<th>% (+) TT</th>
<th>P</th>
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<tr>
<td>Vaso-vagal criteria</td>
<td>21/73</td>
<td>28.8</td>
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<tr>
<td>Cardiogenic criteria</td>
<td>36/113</td>
<td>31.9</td>
</tr>
<tr>
<td>30/105</td>
<td>29.6</td>
<td>0.44</td>
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<td>5/30</td>
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<tr>
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<tr>
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<td>17/78</td>
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<tr>
<td>7/17</td>
<td>41.1</td>
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Figure 1. Turbulence slope in HF with SDB

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OSA mechanisms for increased ventricular arrhythmias and sudden cardiac death in well pronounced QT-prolongation after repetitive OSA-maneuvers may represent fluence ventricular repolarisation and dispersion in repolarisation differently. In was not significantly different, when measured during normal breathing. This QT of QT from 426.5 ± 47.0 ms at baseline to 474.4 ± 59.2 ms (p=0.007), but TpT was not significantly different, when measured during normal breathing. This QT-prolongation was not observed in animals without OSA-maneuvers.

Conclusion: Acute and chronic application of obstructive respiratory events influence ventricular repolarisation and dispersion in repolarisation differently. Increased dispersion in ventricular repolarisation during acute OSA-maneuvers as well pronounced QT-prolongation after repetitive OSA-maneuvers may represent mechanisms for increased ventricular arrhythmias and sudden cardiac death in OSA.

**PS306 | BENCH**

Effects of acute and repetitive obstructive respiratory events on ventricular repolarization in a pig model for obstructive sleep apnea

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**Introduction:** Obstructive sleep apnea (OSA) is associated with sudden cardiac death. Obstructive respiratory events, as occurring in OSA, are associated with negative intrathoracic pressure, which may disturb ventricular repolarization resulting in arrhythmias.

**Methods and results:** A Lewis lead model for OSA indices of ventricular repolarization (QT-intervals) and dispersion of repolarization (Tpeak to Tend (TpTe), TpTe/TQT ratio) were determined during and after repetitive tracheal occlusions with applied negative thoracic pressure (OSA-maneuver) for 3 hours (n=7). 5 animals without OSA-maneuvers served as a control.

**Results:** 2 minutes of acute OSA-maneuver resulted in negative thoracic pressure, pronounced hypoxia and hypercapnia and was associated with a non-significant shortening in RR-interval (769 ± 84 ms to 722 ± 115 ms, p=0.11). QT-intervals were prolonged from 468.8 ± 39.8 ms to 442.9 ± 73.5 ms (p=0.05) whereas TpTe was prolonged (from 48.7 ± 10.6 ms to 59.9 ± 10.8 ms, p<0.01) and the TpTe/TQT ratio was increased from 0.09 ± 0.01 to 0.12 ± 0.02 (p<0.01). Additionally, repetitive obstructive respiratory events over 3 hours caused a prolongation of QT from 426.5 ± 47.0 ms at baseline to 474.4 ± 59.2 ms (p=0.007), but TpTe was not significantly different, when measured during normal breathing. This QT-prolongation was not observed in animals without OSA-maneuvers.

**Conclusion:** Acute and chronic application of obstructive respiratory events influence ventricular repolarisation and dispersion in repolarisation differently. Increased dispersion in ventricular repolarisation during acute OSA-maneuvers as well pronounced QT-prolongation after repetitive OSA-maneuvers may represent mechanisms for increased ventricular arrhythmias and sudden cardiac death in OSA.

**PS307 | BEDSIDE**

Utility of a Lewis lead for distinguishing atrioventricular re-entrant tachycardia from atrioventricular nodal re-entrant tachycardia

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**Purpose:** A Lewis lead configuration can help to detect atrial activity. We investigated the utility of a Lewis lead to distinguish orthodromic atrioventricular re-entrant tachycardias (AVRTs) through accessory pathways from typical atrioventricular nodal re-entrant tachycardias (AVNRTs).

**Methods and results:** Thirty consecutive patients (17 male, 59 ± 14 year-old) with narrow QRS tachycardia documented on the electrocardiogram (ECG) who had an electrophysiology study (EPS) between July 1, 2012 and February 1, 2014 were included in this study. A Lewis lead, which is a bipolar chest lead with the electrode on the right aspect of the sternum at the second intercostal space instead of the right arm and the electrode on the fourth intercostal space instead of the left arm, were recorded during tachycardias. Ten patients were diagnosed with AVRTs and 20 patients with典型AVNRTs on EPS. In 6 of 10 patients with AVRTs, the positive P wave can be seen in lead I with the Lewis lead configuration and in 14 of 20 patients with AVNRTs. The RP interval of AVRTs was significantly longer than those of AVNRTs (86 ± 17 msec vs. 164 ± 22 msec, P < 0.001).

**Conclusions:** A Lewis lead configuration may help to make difficult differential diagnosis among the re-entrant supraventricular tachycardias, owing to its ability to locate P waves.

**S5309 | BEDSIDE**

A comprehensive approach to persistent atrial fibrillation: percutaneous MAZE-like electrical left atrial appendage isolation followed by LAA closure


**Purpose:** The optimal ablation strategy for patients (Pts) with atrial tachyarrhythmias (ATA) despite of permanent PV isolation is controversial. Aside from rator ablation and left atrial substrate modification electrical left atrial appendage (LAA) isolation (I) was discussed. The latter, however, is associated with increased risk of LAA thrombus formation. We therefore aimed to investigate the concept of percutaneous electrical LAAI followed by LAA closure (C).

**Methods:** Pts with ATA non responsive to PVI underwent a MAZE-like ablation procedure with the goal of LAAI. An electroanatomical mapping system and an irrigated 3.5mm tip catheter were used. By creating a septal-anterior line, a roof line and a mitral isthmus line LAAI was achieved, confirmed by a spiral catheter in the LAA (Fig. 1). The patients continued oral anticoagulation therapy (Group A) or underwent LAAC after 6 weeks (Group B). Follow up included ambulatory Holter monitoring and office visits.

**Results:** Between June 2010 and February 2014, complete LAAI was performed in 45 pts (25 Male, 68 ± 10 years, procedure time 134 ± 44 min, fluoros time 16 ± 7 min). In 16/45 (6.6%) pts cardiac tamponade occurred (managed conservatively). 16/45 (35%) patients received a LAAC (Group B) without major procedural complications. During a mean follow up of 336 ± 240 days, 33% of pts experienced a documented AF recurrence after the blanking period. In Group A bleeding (1 pt) and periprocedural bleedings (2 pts) were observed. No adverse events were noted in Group B.

**Conclusion:** Percutaneous MAZE-like procedures resulting in LAAI followed by interventional LAAC may be a favourable comprehensive approach to lower the risk for both AF recurrence and thromboembolism. However, complex ablation increases the risk for cardiac tamponade.

**PS310 | BEDSIDE**

Evaluation of periesophageal nerve injury after pulmonary vein isolation using the 13C-acetate breath test

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**Purpose:** Pulmonary vein isolation (PVI) has become an important option for treating patients with atrial fibrillation (AF). Periesophageal nerve (PEN) injury after PVI causes pyloric spasms and gastric hypomotility. This study aimed to clarify the impact of PVI on gastric motility and assess the prevalence of gastric hypomotility after PVI.

**Methods:** Thirty consecutive patients with AF underwent PVI under luminal esophageal temperature (LET) monitoring. The 13C-acetate breath test was conducted before and after the procedure for all patients (PVI group). Gastric emptying was evaluated using the time to peak concentration of 13CO2 (Tmax). The test was also conducted in another 20 patients who underwent catheter ablation procedures other than PVI (control group).

**Results:** The number of patients with abnormal Tmax (> 60 min) increased from 7 (23%) to 13 (43%) and from 3 (15%) to 5 (25%) after the procedure in the PVI group and control group, respectively. The mean Tmax was longer after PVI than before PVI (64.1 ± 14 min vs. 57.7 ± 15 min, P = 0.006), whereas there was no significant difference before and after the procedure in the control group. However, no significant difference in Tmax was observed between the two groups (P = 0.27).

**Conclusions:** Asymptomatic gastric hypomotility occurred most frequently after PVI. However, the average impact on PVI on gastric motility under monitoring of LET was minimal.
Background: Circumferential pulmonary vein isolation (CPVI) is widely accepted for drug refractory atrial fibrillation (AF) and electrical disconnection of PV is the key concept of CPVI. Insufficient ablation at the first round of CPVI creates residual conduction gaps that require additional ablation, and we assume that the gap is a predictor of early PV recurrence (EPVR) during the procedure. The aim of this study is to evaluate the relationship between the residual PV conduction gap and EPVR.

Methods: We enrolled 110 paroxysmal AF patients underwent CPVI. After the first round of CPVI, additional ablation was applied to the conduction gap on the CPVI line if ipsilateral PV (IPV) was not isolated. EPVR was provoked by both time- and ATP-induction just after CPVI, 30, and 60 min. We classified ipsilateral IPV perimeter into 8 segments and evaluated the relationship between the segments of residual PV conduction gap after the first round of CPVI and EPVR using Chi-square test.

Results: 136/220 (61.8%) of IPV were isolated after the first round of CPVI, and 84/220 IPV (210/1760 segments) were required additional ablation to achieve complete PV isolation. EPVR were observed in 23/220 IPV (27/1760 segments), 40/220 IPV (25/1760 segments) and 4/152 IPV (7/1216 segments) just after CPVI, 30 min and 60 min respectively. Residual conduction gaps predict EPVR just after CPVI, 30 min, and 60 min (HR=4.49 (P<0.001), 6.13 (P<0.001), and 7.9 (P=0.04), respectively).

Conclusion: Residual PV connection gap after the first round of CPVI is a strong predictor of EPVR even after additional ablation.

PS5312 | BEDSIDE
Efficacy of a single hybrid ablation procedure in patients with long standing persistent atrial fibrillation in comparison to a standard endocardial approach: two years results
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Introduction: Unfortunately the success rate of catheter ablation of long standing persistent atrial fibrillation (LS-PVAF) remains poor even after multiple ablation procedures. Combining epicardial and endocardial approach (hybrid ablation) we could show a success rate of 76% one year after ablation. The objective of this study is to compare the efficacy of hybrid ablation with the standard endocardial, 3D-guided ablation in patients (pts) with LS-PVAF.

Methods: For this purpose pts with LS-PVAF, ablated using hybrid approach (group 1) were matched to those after conventional, 3D-guided radiofrequency ablation (group 2). The endpoint of this study was a number of pts free of any atrial arrhythmia -30 seconds at 24 month follow up (FU) after a single procedure in each group. In group 1 epicardial ablation was first performed via an endoscopic subxiphoid access utilizing Numeris® Coagulation Device. It was secondly followed during the same day by endocardial ablation utilizing EnSite NavX Velocity™ system. During this endocardial part voltage mapping was performed, detected gaps closed and additional linear and/or CFAEs ablations applied as needed. In group 2 conventional endocardial procedure was performed using EnSite NavX Velocity™ system. After completion of wide area circumferential ablation a step-up protocol was applied, aiming conversion into SR during ablation. Pts in group 1 were prospectively followed at 1, 2, 3 months with 48 h holter ECG and every 3 months thereafter. Pts free of AF after 3 months underwent implantation of loop event recorder, Reveal™, Medtronic Inc. Pts in group 2 were prospectively followed every 3-4 months with 72 h holter ECG.

Results: In each group 26 pts were included. Clinical and demographic characteristics between these groups did not differ but age (female, age 53±1 vs 59±2 years, p=0.042, LA area 26±1.7 vs 27±1 cm², p=ns in group 1 and 2 respectively). AF was persisting since 50±8.8 months and 19±4.4 months after last cardioversion attempted (group 1) vs 49±10 and 17±3 months (group 2), p=ns. 10 pts (39%) in each group have already undergone repeated AF catheter ablation. All pts were highly symptomatic with EHRA class 4. After a median follow up of 588 (IQR 407-795) days 19 (73%) pts in group 1 and 8 (31%) in group 2 were free of AF/AT without AADs (p<0.01).

Conclusions: A single hybrid ablation of LS-PVAF in pts with severe atrial enlarge ment represents a much more effective treatment modality as compared to a standard endocardial approach. Further evaluation of long-term results is required.

PS5313 | BEDSIDE
Left atrial fibrosis is a predictor for outcome after Cryoballoon ablation in patients with paroxysmal atrial fibrillation - lessons learned from LGE-MRI
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Background: Cryoballoon ablation is an alternative energy source for pulmonary vein isolation (PVI) in patients with paroxysmal atrial fibrillation (PAF).

Methods: and result: Fifteen-patients with PAF (51±8, female, 61±2.1 years old. 61.2±10.6 years old were included in this study. All patients underwent LGE-MRI to quantify the degree of left atrial fibrosis (LAF). Based on the degree of LAF patients were stage into two groups: in patients with early stages of LAF (e.g. ≤ 20% of the LA, Utah Stage 1 & 2, Group A) and in patients with progressed stages of LAF (> 20% of the LA, Utah 3 & 4, Group B). 52 (62.7%) patients were staged in Group A, while 31 patients (37.3%) were stage in Group B (Figure 1, blue columns). A total of 14 patients (16.87%) were found with recurrent AF/BIB 90 days after ablation. Success rate at 3 months after PVI was significant better in patients with early stages of structural remodeling of LA (90.38% vs 70.97%, p=0.022; Fig. 1, red columns). Degree of LAF detected using LGE-MRI was significant higher in patients with recurrence (21.97±8.8% vs. 16.68±7.42%; p=0.021, Fig. 2).

Conclusion: From our preliminary results the degree of left atrial fibrosis detected using LGE-MRI predicts success rates for Cryoballoon-Ablation in patients with paroxysmal atrial fibrillation. As patients with paroxysmal AF can show varying degrees of fibrosis, LGE-MRI for assessment of the degree of LAF might be able to support the choice of the adequate energy source for PVI in these patients.
PS317 | BEDSIDE
Atrial fibrillation termination caused by pulmonary vein isolation prior to complex fractionated atrial electrograms guided ablation
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Background: Whether there is correlation of atrial fibrillation (AF) termination during ablation and good outcome or not is still controversial based on pulmonary vein isolation (PVI) combined with other anatomical and/or electrogram guided ablation. Then we analyzed how often AF termination was caused by pulmonary vein isolation (PVI) prior to complex fractionated atrial electrogram (CFAE) guided ablation, how predictable the AF termination by PVI in the good outcome.

Methods and results: This study included 132 consecutive patients (81 paroxysmal/51 persistent AF, mean age of 60 years old) who underwent AF ablation combined with ipsilateral PVI during AF spontaneously or by induction prior to CFAE ablation. Six patients to be achieved PVI during sinus rhythm, because AF could be maintained only with isoproterenol infusion, were excluded to analyze the AF termination caused by PVI. In the rest of 125 patients, 86 (55 paroxysmal/30 persistent) were their first session, and 39 (19 paroxysmal/20 persistent) had a history of AF ablation solely guided by CFAE. In the 125 patients, PVI during AF caused AF termination 45% in paroxysmal and 20% in persistent; 36% and 13% in the patients of their first session, and 68% and 30% in the patients had a history of CFAE ablation, respectively. AF was not inducible in 4 paroxysmal patients of their first session and 2 persistent patients had a history of CFAE ablation. AF was terminated 92% of paroxysmal and 70% persistent AF combined with CFAE ablation. There were no difference in the total RF duration between the AF-termination group (96 min) and non AF-termination group (96 min). AF termination was caused by the ablation of the electrograms of the ablation catheter showed CFAE in 67%. AF termination was caused by mean of 46% of RF points achieved the PVI in the RF site of PVI. PVI was confirmed with a circular catheter and completed electrically in the end of the session. The recurrence rate in the patients with or without AF termination by PVI were 56% (59% of PAF, 50% persistent) and 47% (41% of PAF, 56% with persistent) with mean of 21 months follow up.

Conclusion: AF termination by PVI is not a predictor of AF recurrence in PVI combined with CFAE ablation. PVI during AF is not favorable to assume their overall health condition to be “much better”, 6 patients “slightly better” after PVI than before, and 2 patients reported “no change”.

PS316 | BEDSIDE
Single-center experience with a novel multipolar ablation device for pulmonary vein isolation
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Background: We report on the initial experience with a novel single device circular irrigated radiofrequency (RF) ablation catheter.

Methods: 19 patients (60±14 years) with paroxysmal (8) and persistent (11) AF underwent pulmonary vein isolation (PVI) by using a novel decapolar mapping and ablation catheter between June and December 2013. Ablation was guided by electroanatomical mapping and RF energy was delivered in the antral region of pulmonary veins (PV) with any or all of the 10 irrigated catheter electrodes. Patient baseline and procedural characteristics were documented and a follow-up (FU) was performed by questionnaire or telephone interview.

Results: Overall, 66/74 targeted PV (89%; 1 patient with unsuccessfully cardioverted, PVI could not be proved) could be isolated within a mean procedure time of 150±34 minutes and a mean RF delivery time of 969±323 seconds per patient. Total fluoroscopy time was 15.5±3.9 minutes with a dose of 2.465±1.869 mGy.cm². No procedure-related complications were observed. During FU (1-7 months) 2 patients (11%) (1 paroxysmal, 1 persistent) were in SR without antiarrhythmic drugs (AADs), 11 patients (58%) (4 paroxysmal, 7 persistent) in SR with AADs and 6 patients (32%) (3 paroxysmal, 3 persistent) had a relapse of AF. In a questionnaire (11) or a telephone interview (5) 8 patients reported their clinical status to be “much better”, 6 patients “slightly better” after PVI than before, and 2 patients reported “no change”.

Conclusion: PVI using the novel irrigated RF multipolar ablation device requiring only 1 transseptal puncture appears to be acutely effective. No clinical complications were identified. The short term efficacy seems to be comparable to established ablation tools and strategies, but long term efficacy and FU trials are needed.
OUTCOME IN ATRIAL FIBRILLATION ABLATION

P5320 | SPOTLIGHT
The impact of atrial fibrillation termination mode during catheter ablation procedure on maintenance of sinus rhythm
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Background: Catheter ablation is a common and effective procedure to address atrial fibrillation (AF) refractory to antiarrhythmic drugs. AF can be terminated directly into sinus rhythm (SR); evolving into regular atrial tachycardia (AT) and subsequently into SR after direct current (DC) cardioversion if AF persists. Scarcely data are available on the relationship between clinical outcomes and termination mode after one catheter ablation. We evaluated for the first time the association between 1-year ablation efficacy and termination mode after repeated catheter ablation procedures.

Methods and results: This prospective study involved 400 consecutive patients (62.7±7.2y) who underwent catheter ablation for drug-refractory persistent AF (4.6±2.4 months) using a stepwise ablation approach.

AF was terminated by radiofrequency application directly into SR in 135 patients; patients who failed SR experienced reversion to AT (29.4%) which were treated with additional ablation for extra-PV foci or left atrial posterior wall (LAPW) for LPV isolation. In patients with paroxysmal AF, 81% (13/16) of EEPVI group with nine ablation sites including EST had reached 39 degrees three months follow-up.

Results: A total of 224 PVs were analyzed. Eleven of the 224 PVs (5%) were basally isolated. In 82 PVs (36.5%), PVVP could not be recorded during ablation (2 PVs showing current (DC) cardioversion PV) where included in this group. Forty-nine PVs (22%) were in AF and were excluded from analysis. Therefore, AS was analyzed in 82 PVs (36.5%). One vein could not be isolated; of the remainder 81 PVs the AS was unchanged in all before isolation: the pattern of isolation was sudden in 30 (13%), after a 2:1 block period in 12 (5%) and after a progressively delay in 39 (17%).

Conclusions: During a cryoablation procedure, the absence of changes in the PV AS after a conduction delay suggests that this energy produces a very homogeneous lesion.

P5321 | BEDSIDE
Efficacy and safety of left anterior ridge and carina first ablation to prevent esophageal complications in patients with atrial fibrillation
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Purpose: Severe esophageal complications such as gastric hypo-motility or left atrial appendage stasis after catheter ablation (CA) for patients with atrial fibrillation (AF) have been reported. Esophageal temperature (EST) monitoring may be a useful tool to know the temperature inside the esophagus during left atrial posterior wall (LAPW) ablation. However, its efficacy for preventing gastric hypo-motility which must be caused by vagal nerve injury outside the esophagus is not well known. The AT into SR in this study was to evaluate the efficacy and safety of left anterior ridge and carina first ablation to minimize the left atrial posterior wall ablation near the esophagus for pulmonary vein isolation.

Methods: Consecutive 86 patients with AF (61±10 years, 64 males, 58 paroxysmal AF) underwent LAPW isolation for left atrial esophageal fistula after catheter ablation (CA) for patients with atrial fibrillation (AF) have been reported. EST was monitored by a temperaturesensitive thermistor (thermocouple) probe insulated in a plastic catheter surrounded by a balloon inflated with air. EST was measured in three orthogonal axes (X=anterior to posterior diameter, Y=right to left atrial body without appendage (LAVbody) and LA appendage (LAAV). LA diameter was divided into two volumes: LA body without appendage (LAVbody) and LA appendage (LAAV). The LA diameter was measured in three orthogonal axes (X=antero-posterior diameter, Y=right to left diameter, Z=top to bottom diameter). Measurements were duplicate by two experienced researchers in blind manner.

Results: LA was measured by the method of discs (0.625 mm thick) and 3D reconstruction. LA volume was measured by the method of discs (0.625 mm thick) and 3D reconstruction. Total LA volume (LAVtotal) was divided into two volumes: LA body without appendage (LAVbody) and LA appendage (LAAV). LA diameter was measured in three orthogonal axes (X=antero-posterior diameter, Y=right to left diameter, Z=top to bottom diameter). Measurements were duplicate by two experienced researchers in blind manner.

Conclusions: Negative remodeling of LA was observed after successful ablation of persistent or chronic atrial fibrillation using cardiac CT.

P5322 | BEDSIDE
Reduction of cardiac tamponades in AF ablation using balloon technologies

Purpose: The major cause of death during catheter ablation of atrial fibrillation (AF) is related to cardiac tamponade (CT). The risk of CT may be linked to different procedural steps such as transseptal puncture (TP), catheter manipulation during left atrial (LA) and pulmonary vein (PV) mapping and ablation.
P5326 | BEDSIDE
Pulmonary vein isolation with a new multi-polar irrigated radiofrequency ablation catheter: feasibility, efficacy and safety
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Purpose: Simultaneous multipolar ablation catheters for pulmonary vein isolation (PVI) have been proposed in order to simplify the atrial fibrillation (AF) ablation procedure. A new multipolar circular open-irrigated radiofrequency ablation catheter (nMARQTM) combining both mapping and multi-ablation capability through open-irrigation design has recently been developed. Our study aims to assess the feasibility, the acute success and the safety of this new technology with a particular interest in the incidence of periprocedural silent cerebral lesions (SCL) in patients undergoing AF ablation.

Methods: 29 patients (age 55±14 years) with paroxysmal AF underwent PVI using the nMARQTM system. PVI was confirmed by circular multipolar mapping catheter (Lasso). A cerebral magnetic resonance imaging (MRI) was performed before and after the procedure.

Results: The ablation procedure with the nMARQTM was feasible in all the patients without the use of a steerable sheath. PVI was achieved in 98% (117/119) of pulmonary veins identified and in 96% (28/29) of patients treated. Mean procedural time was 128±50 min, while mean fluoroscopy time was 1.7±2.8 min. Mean total RF time was 15.3 min. Out of 29 procedures, no procedural complications, including SCL, occurred.

Conclusions: In our experience, PVI with nMARQTM catheter was feasible with good acute success and safety profile. No procedural complications, including new SCL detected by post-ablation brain MRI, were reported.

P5327 | BEDSIDE
Assessment of left atrial volume in patients with atrial fibrillation: a correspondence between echocardiography and 3D mapping
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Background: Left atrial (LA) enlargement is a predictor of worse outcome after catheter ablation (CA) for atrial fibrillation (AF). We investigated the correspondence between two LA volume (LAV) indices assessed by echocardiography (ECHO) and LAV obtained by 3D electroanatomical mapping (CARTO) in patients undergoing CA for AF.

Methods: We performed analysis in 816 pts (59±10.9 years; 66% males; 49% paroxysmal AF) from three ablation centres. ECHO LAV indices assessed by ellipsoid model (LAVE) and by biplane area-length method (LAVA) were compared with CARTO-derived LAV (LAV3D) by Pearson’s correlation and modified Bland-Altman method. LAV3D validated by CT image registration in a subset of patients was considered a gold standard.

Results: Mean LAVE was 69±24 ml, LAVA was 88±30 ml and LAV3D was 131±46 ml. Correlation between LAVE or LAVA and LAV3D was modest (r=0.70 and r=0.80, respectively), and significant less tight for LAVA (p<0.001, LAVE and LAVA underestimated LAV3D with absolute bias (95% CI) of 64 ml (–2 – 130) and 57 ml (–17 – 131), and relative bias of 54% (24 – 83) and 63% (24 – 102; p<0.0001 for their mutual difference). Fig. 1.

Conclusion: ECHO indices systematically underestimated CARTO-derived LA volume by ~ 40% so that the magnitude of absolute bias was greater for enlarged LA. LAVE compared to LAVA had lower accuracy but higher precision to quantify the true LAV.
PS328 | BEDSIDE
Evolution and management of acute and delayed reopening after the lariat endo epicardial closure

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Introduction: Thromboembolic events represent one of the most serious complications of atrial fibrillation. Left atrial appendage (LAA) clot is the dominant cause of stroke in AF patients. Therefore endocardial and epicardial LAA closure devices have been developed. We sought to evaluate the follow up and the management of incomplete acute closure and delayed reopening of the LAA after lariat endo epicardial ligation.

Methods: This was a multicenter study of consecutive patients undergoing LAA ligation for stroke prevention in atrial fibrillation. At implant successful ligation was defined as Lariat deployed with ≤5mm residual leak by trans-esophageal echocardiogram (TEE).

Results: A total of 74 Lariat cases, TEE complete follow up was available in 63 pts. Out of these 11 pts the device could not be deployed because of non favorable anatomy. Out of procedural deaths or strokes, and the rate of major bleeding was 9.3%. In one left atrial appendage leak after the lariat procedure. Most of these leaks can be managed by the current devices.

Conclusion: Our registry showed that 27% of patients have various degree of incomplete acute closure and delayed reopening of the LAA.

PS331 | BEDSIDE
Arrhythmia risk stratification patients with dilated cardiomyopathy for primary prophylactic ICD therapy

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Arrhythmia risk stratification with regard to prophylactic implantable cardioverter-debrillator (ICD) therapy is a completely unsolved issue.

Purpose: This study was designed to determine a potential noninvasive arrhythmia risk predictors in patients (pts) with dilated cardiomyopathy (DCM).

Methods: The study enrolled 234 pts with idiopathic DCM and ischemic DCM. Arrhythmia risk stratification was performed prospectively during 39±7 months of follow-up, including analysis of left ventricular ejection fraction (LV EF) and size on echocardiography, QTc dispersion, heart rate turbulence (HRT) and microvolt T-wave alternans (mTWA). Also we analyzed age, gender, NYHA, 6-MWT, BNP level and data of 24-h Holter ECG (nsVT, PT, ectopy). Arrhythmic events were defined as sustained VT, VF, sudden death, resuscitation or ICD discharges.

Results: By multivariate regression analysis, with multipliers of determination R=0,70; F=30,8; positive mTWA (p<0,000), LV end-diastolic diameter (p=0,015) and QTc dispersion (p=0,027) were detected as independent risk predictors in pts with sinus rhythm only. Unfortunately, HRT (TS) value has been beta 0,35 (p=0,049). Thus, for risk estimation of fatal arrhythmic events (in pts with sinus rhythm) classification formula is presenting:

$$AR = (1 - 0,01 x mTWA - 0,009 x LV endDD + 0,002 x QTd)$$

In pts with atrial fibrillation (AF) multivariate regression analysis also identified QTc dispersion (p=0,004), gender (p=0,018) and LV ejection fraction (p=0,000) as significant risk predictors with multipliers of determination R=0,93; F=12,9. So, for pts with AF formula separating is looks:

$$AR = (1 - 0,033 x LV EF + 0,36 x gender (1 male, 0 female) + 0,005 x QTd)$$

Conclusion: Formula’s estimate may be helpful for arrhythmia risk stratification in patients with atrial fibrillation. However, a longer follow-up is needed to verify our results. In DCM patients the early implantation of ICD is recommended, especially in pts with more than one risk factor.

PS332 | SPOTLIGHT
Lay as first responders in the treatment of ventricular fibrillation: doubled survival rate in Piacenza “Progetto Vita” (PV) from 1999 to 2013

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The system of early defibrillation called “Progetto Vita” (PV) was organized within a traditional Emergency Medical System (ACLS-ambulance) and ambulance of volunteers (BLS-ambulance). Lay volunteers were trained to use only the automated external defibrillator (AED) (PV-AED) without performing Cardio pulmonary resuscitation (CPR). The main aims of this study were:

Objective: To evaluate survival rate from out-of-hospital cardiac arrest and ventricular fibrillation (VF) in this early defibrillation program in patient treated by ACLS or BLS ambulance and by lay volunteers.

Methods: A retrospective observational design has been used to investigate the survival rate on out-of-hospital sudden cardiac arrest (SCA) therapy organized in the Italian city of Piacenza, in which police and lay volunteers are trained to use automated external defibrillators (AEDs).

Data were collected with the use of a database according to the Ulstein-style for all cases of out of hospital cardiac arrest from June 1999 to December 2013. Data collections include also the cardiac rhythm recorded by AED or monitor ECG and were divided into two groups, according to the type of first responder: ACLS-ambulance or BLS-ambulance in group 1, PV-AED in group 2.

STATISTICAL ANALYSIS

The sample will be described by means of the usual descriptive statistics: mean and standard deviation for continuous variables and proportions for categorical ones. To compare the survival rate from VF and SCA pts student’s t-test for continuous variables, chi-square for categorical variables, or the correspondent non parametric tests will be used when appropriate.

Results: Among dispatched sudden cardiac arrest, (VF) was recorded as primary rhythm in 516/3832 pts (13,47%) with a total survival rate from VF of 134/516 (25,97%). In group 1 survival rate (on motor vehicle) was 22,15% vs 50,72% (p<0,001) in group 2. From SCA, in group 1 survival rate from SCA was 3,21% vs 39,13% (p<0,0001) in group 2.

Conclusions: PV-AED only trained to defibrillate saved more pts in VF cardiac arrest than ACLS-ambulance or BLS-ambulance. The extensive use of AED by lay volunteers saved up to 50,72% of VF cases that was almost doubled compared to ACLS-ambulance and BLS-ambulance. BLS training does not influence survival when AED is applied after early call.
P5333 | BEDSIDE
Chronic obstructive pulmonary disease is a risk factor for ventricular arrhythmias independent of left ventricular systolic function
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Background: Chronic obstructive pulmonary disease (COPD) is associated with increased cardiovascular morbidity and mortality, yet the exact pathophysiological links remain unclear. Whether the presence and severity of COPD is associated with ventricular tachycardia (VT) independent of the left ventricular ejection fraction (LVEF) remains unknown.

Methods: We identified consecutive adult patients who underwent pulmonary function testing, 24-hour Holter monitoring, and trans-thoracic echocardiography between 2000 and 2009. Demographic data as well as relevant co-morbidities were gathered from the electronic medical record. Severity of COPD was classified according to the GOLD classification, VT diagnosed as >3 consecutive ventricular beats at a rate >100/minute.

Results: From 6350 patients who were included (age 66±15 years, 48% woman, 92% Caucasian, LVEF 59±12%) COPD was diagnosed in 2799 (44%). COPD was shown to predict successful ablation sites but has not been studied in a randomized trial. We report an initial cohort of pts from an ongoing randomized trial.

Conclusions: COPD is associated with increased risk of VT, proportional to severity and independent of the LVEF. This provides insight into the markedly increased cardiovascular morbidity and mortality of COPD patients, and further studies should explore which anti-arrhythmic strategies would best apply to the COPD patients.

P5334 | BEDSIDE
Impact of automated template matching during PVC ablation: results from a randomized controlled trial
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Introduction: Radiofrequency ablation (RFA) is an established treatment of symptomatic PVC. Commonly, subjective pace mapping (PM) and activation mapping (AM) in the presence of spontaneous ectopy are utilized. The automated template matching tool (ATM) of a commercially available EP recording system was shown to predict successful ablation sites but has not been studied in a randomized trial. We report an initial cohort of pts from an ongoing randomized trial.

Methods: Patients were randomized 2:1 to either ATM or conventional mapping. Mapping in the control group (CG) was guided by subjective PM and AM if spontaneous PVC were present. In the intervention group (ATM group) an ATM was utilized for an observer assessment the paced morphology. A 3D geometry was obtained in a pts and an electro-anatomical map was acquired if sufficient PVC were present. Follow up (FU) was performed at 3 months post ablation and consisted of 24 hr Holter ECG and assessment of symptoms. Endpoints were acute ablation success, defined as cessation of PVC at the end of the procedure, and recurrence of PVC at FU.

Results: Fifty-seven pts (Age 54±16, LVEF 56±12%) with a PVC burden of 20±13% in pre ablation Holter and 20±17 PVC/min at the start of the procedure were included. Thirty-six were randomized to ATM and 21 to CG. Ablation sites were: ROTV n=29 (52%), LVOT n=19 (34%), Great Cardiac Vein n=4 (7%) and Aortic Sinus n=4. There was no significant difference in baseline parameters or ablation site. Complications were: VF during RFA n=3, pericardial tamponade n=1 and AV-fistula n=1.

Acute ablation success was 44/57 (77%, CG 15/21 and 29/36 ATM group; p=n.s). There were significantly less RF applications in the ATM group (8±5 vs 13±11; p=0.016). At FU, PVC burden was lower (0.9±2% vs 3.6±6% p=0.047) in the ATM group. Also, symptom based recurrence rate was lower in the ATM group (8/36, 22% vs 8/21, 38%) but did not reach significance.

Conclusions: ATM guidance has a significant impact on catheter ablation for PVC. The number of RF applications was reduced. Furthermore, PVC burden at FU was significantly lower in the ATM group, emphasizing its value in RFA of PVC. Moderate success rates may be related to patient selection in a high volume center with a significant number of PVC not originating from the RVOT.

P5335 | BEDSIDE
Decennial analysis of safety in epicardial- and endocardial- vt ablation

Background: Endocardial- and epicardial- VT Ablations are increasingly performed, but there are still limited information about its safety and complications.

Methods and results: Between 2002 and 2012 complications in 1032 endo- and epicardial- VT Ablations were analysed. In 765 patients (pts; 479 male; 56±15years) 872 endocardial- and in 133 pts (11 male; 52±15 years) 160 epicardial- VT Ablations were performed. Out of 1032 procedures (proc.) in 769 proc. (75%) a retrograde transaortic and in 344 proc. (33%) an antegrade transseptal approach was performed.

A left atrial appendage perforation was observed in 2/344 proc.(0,6%) via the transseptal sheath, whereas in 1/769 proc. (0,1%) a perforation of the left ventricle (LV) was seen during retrograde transaortic mapping of the LV. A perforation of the right ventricular apex (RVA) during placement of the RV Catheter was pre-sent in 3/1032 proc. (0,3%). Due to epicardial puncture in one patient (0,9%) a perforation of the right coronary artery (RCA) was seen. In two pts (1,3%) a perforation of the liver and in another patient (0,6%) a perforation of the colon was observed. In these three patients the epicardial sheath was inserted via the liver or colon to the epicardial space. Furthermore in another patient (0,6%) a perforation of the aorta ascended occurred.

Cardiac tamponades/Pericardial effusion were seen in 13/160 proc. (8,1%) during epicardial- and in 10/872 proc. (1,1%) during endocardial-VT Ablation. A none fatal pulmonary embolism was observed after epicardial VT Ablation. A TIA/Stroke could be observed in 2/872 (0,2%) after endocardial and in 2/160 (1,3%) after epicardial VT Ablation.

Conclusions: The risk of potential severe complications in endocardial- VT ablation is moderate, whereas in epicardial- VT Ablation a higher incidence was observed.

P5336 | BENCH
Continuous light-induced myocardial alterations and decrease of ventricular fibriillation threshold in hypertensive rats are attenuated by Omacor intake
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Background and purpose: Continuous light suppresses melanin production that might be deleterious for the heart since melanin in addition to regulation of circadian rhythms exhibits antihypertensive, free radicals scavenging and antiarrhythmic effects. The latter was recently shown in our study. Deficiency of melanin as well as omega-3 FA was observed in pts suffering from CHD and hypertension or in hypertensive rats. This can contribute to disease progression and pro-arrhythmia. The purpose of this study was to examine the cardioprotective effects of omega-3 FA intake in rats exposed to continuous light.

Design and methods: Male spontaneously hypertensive (SHR) and age-matched normotensive rats were housed under standard 12 light/12 dark cycle or exposed to 24 hour continuous light/day for 6 weeks. Half of them received Omacor (omega-3 ethyl ester, 250/150 mg diet). Left ventricular tissue was used to determine transcription of electrical cell-cell coupling proteins connexin 43 (Cx43), pro-inflammatory NFκB and iNOS using real-time PCR. Western blotting was used for protein expression of Cx43 and PKC. Inducible ventricular fibrillation (VF) was examined using isolated Langendorff-perfused heart.

Key results: Continuous light caused mild elevation of BP in normotensive and enhanced it in SHR as well as decreased threshold to induce VF in both groups comparing to rats under normal light cycle. Myocardial Cx43 mRNA level was not altered, but Cx43 protein and its functional phosphorylated forms (which affect electrical coupling) were decreased in SHR due to continuous light and partially restored by Omacor. Treatment with Omacor also attenuated of continuous light-induced increase of myocardial INOS and NFκB that are known to down-regulate Cx43. In parallel, the intake of Omacor increased threshold to induce VF.

Conclusions: Findings indicate that continuous light itself affects Cx43 channels-mediated cardiac cell-to-cell communication and enhances propensity of hyper- tensive rats to malignant arrhythmias. These adverse effects can be partially, eliminated by treatment with Omacor.

This work was supported by VEGA 2/0046/12, SK-CZ-0027-11 and SKG grants.
P5327 | BEDSIDE
Shape and size of RVOT Isochronal map as a tool to distinguish RVOT/LVOT tachycardia
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In patients with early transition zone (R−S V3) there is a lack of reliable criteria in surface electrocardiographic features for differentiation between right ventricle outflow tract (RVOT) and left ventricle outflow tract (LVOT) premature ventricular contractions (PVCs). This may lead to unnecessary extensive and ineffective energy applications in RVOT in patients (pts) with arrhythmia originating from LVOT. Aim of our study was to determine if the data derived from the isochronal mapping such as area and shape of earliest isochron, could improve localization of site of origin (SOO) of outflow tract (OT) PVCs, particularly with V3 transition zone.

Methods: A series of 17 consecutive patients with symptomatic drug refractory PVCs and/or non-sustained or sustained VT originating from the RVOT/LVOT and an apparently normal heart with early transition zone (R−S V3), who underwent successful ablation of OT ventricular arrhythmia was included in the study. Electrophysiological study (EPS) was performed in all patients after written informed consent was obtained. A 6F quadripolar catheter was introduced from the left femoral vein and placed at the right ventricular apex for pacing. Mapping and pacing in the RV were performed using a 7F 4-mm tip ablation catheter (E2 Steer Thermocoool NAV Bi-Directional, Biosense, Webster). Because the total number of mapped points does not properly reflect the mapping accuracy, the minimum density of points required to include the electroanatomic map of a given chamber was defined as a fill threshold of 10. Electroanatomic 3D mapping data of the right ventricle outflow tract (10-ms isochronal shape and diameters) were obtained in 9 pts with localization in the LVOT and in 8 pts in the RVOT. The typical 10-ms earliest isochron in RVOT tachycardia was usually round and small (3-6 mm in diameter) comparing to the elliptic form with a shorter longitudinal and longer perpendicular diameter in the case of LVOT site of origin.

Conclusions: In conclusion, in patients with PVCs originating from RVOT, longer perpendicular diameter in the case of LVOT site of origin.

P5328 | BEDSIDE
Right atrial volume and function in adult congenital heart disease

Methods: A series of 17 consecutive patients with symptomatic drug refractory PVCs and/or non-sustained or sustained VT originating from the RVOT/LVOT and an apparently normal heart with early transition zone (R−S V3), who underwent successful ablation of OT ventricular arrhythmia was included in the study. Electrophysiological study (EPS) was performed in all patients after written informed consent was obtained. A 6F quadripolar catheter was introduced from the left femoral vein and placed at the right ventricular apex for pacing. Mapping and pacing in the RV were performed using a 7F 4-mm tip ablation catheter (E2 Steer Thermocoool NAV Bi-Directional, Biosense, Webster). Because the total number of mapped points does not properly reflect the mapping accuracy, the minimum density of points required to include the electroanatomic map of a given chamber was defined as a fill threshold of 10. Electroanatomic 3D mapping data of the right ventricle outflow tract (10-ms isochronal shape and diameters) were obtained in 9 pts with localization in the LVOT and in 8 pts in the RVOT. The typical 10-ms earliest isochron in RVOT tachycardia was usually round and small (3-6 mm in diameter) comparing to the elliptic form with a shorter longitudinal and longer perpendicular diameter in the case of LVOT site of origin.

Conclusions: In conclusion, in patients with PVCs originating from RVOT, longer perpendicular diameter in the case of LVOT site of origin.
Conclusions: These observations demonstrated that spleen-derived IL-10 plays a role in modulating cardiac remodeling, via its anti-inflammatory effects. Further investigations are required to elucidate the mechanisms by which IL-10 plays this role.

Methods: Six-week old male SD rats were divided into Sham-operation group, AAC+Sham group, AAC+SPX group and AAC+SPX (AAC+SPX) group at post-operatively 2, 4 and 28 weeks. The spleen-derived IL-10 levels were measured in the serum of each group.

Results: The spleen-derived IL-10 levels were significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01). In addition, the survival rate was higher in the AAC+SPX group compared to the AAC+Sham group (p<0.001). The left atrium weight was also significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01). The infiltration of M1 macrophages in the left atrium was also significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01). The expression of IL-10 in the left atrium was also significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01).

Conclusions: These observations demonstrated that spleen-derived IL-10 plays a role in modulating cardiac remodeling, via its anti-inflammatory effects. Further investigations are required to elucidate the mechanisms by which IL-10 plays this role.

PS342 | BENCH Splenectomy exacerbates pressure overload-induced atrial inflammation and fibrosis in rats
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Purpose: Spleen reserves monocytes, which can modify the inflammatory response to injury. Our aim was to investigate the hypothesis that splenectomy (SPX) would promote pressure overload-induced atrial inflammation and fibrosis (AF).

Methods: Six-week old male SD rats were divided into Sham-operation (Sham+Sham) group, AAC+Sham group, AAC+SPX group with SPX (AAC+SPX) group. At post-operatively 2, 4 and 28 weeks, 6 rats were examined in each group.

Results: The spleen-derived IL-10 levels were significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01). In addition, the survival rate was lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01). The left atrium weight was also significantly higher in the AAC+SPX group compared to the AAC+Sham group (p<0.01). The infiltration of M1 macrophages in the left atrium was also significantly higher in the AAC+SPX group compared to the AAC+Sham group (p<0.01). The expression of IL-10 in the left atrium was also significantly lower in the AAC+SPX group compared to the AAC+Sham group (p<0.01).

Conclusions: These observations demonstrated that spleen-derived IL-10 plays a role in modulating cardiac remodeling, via its anti-inflammatory effects. Further investigations are required to elucidate the mechanisms by which IL-10 plays this role.

PS343 | BENCH Endonuclease G-like-1 (EXOG), a mitochondrial endo/exonuclease has a role in mitochondrial function and ROS mediated cardiomyocyte hypertrophy
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Purpose: The heart is one of the most energy consuming organs. This energy is used to maintain proper contractile function and is produced mainly in the mitochondria by oxidative phosphorylation (OXPHOS). The production of reactive oxygen species (ROS) is an unavoidable byproduct of OXPHOS. Increased ROS production has detrimental effects on the cells, inducing DNA damage and apoptosis. Endonuclease G-like-1 (EXOG) and Endonuclease G are mitochondrial endo/exonucleases with poorly investigated functions in the heart. Whereas EXOG has been implicated in mitochondrial DNA repair, Endonuclease G appears to play a role in apoptosis, but a recent study in cardiomyocytes showed its importance in mitochondrial function and cardiac hypertrophy. Whether EXOG has additional functions as well, is not clear, but it is interesting to note that EXOG is present in a human genomic locus linked to cardiovascular disease. The goal of this study was to elucidate the role of EXOG in mitochondrial function in cardiomyocytes.

Methods: EXOG knockdown mediated knock-down of EXOG was performed in neonatal rat cardiomyocytes. The Seahorse XF24 Extracellular Flux Analyzer was used to measure mitochondrial bioenergetic functions, including OCR (oxygen consumption rate), mtDNA amount, mtDNA damage and reactive oxygen species (ROS) production. Oxidative phosphorylation (OXPHOS) was also measured.

Results: Knockdown of EXOG did not induce mtDNA damage, but increased mitochondrial OCR (n=6, P<0.01), and GA TK to identify single nucleotide polymorphisms and insertion/deletions. In each individual we identified over 38,000 SNPs and 3,400 Indels, which were classified as pathogenic or potentially pathogenic.

Conclusions: These observations demonstrated that spleen-derived IL-10 plays a role in modulating cardiac remodeling, via its anti-inflammatory effects. Further investigations are required to elucidate the mechanisms by which IL-10 plays this role.

PS343 | BENCH Isolation and in vitro characterization of skeletal muscle myoblasts from chronic heart failure patients
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Background: Peripheral muscle wasting is a common finding in CHF. Recent advances in clinical research have confirmed the negative impact of muscle wasting on patient survival. Although innovative research in molecular biology is improving our understanding of how muscle mass is maintained, effective treatment for muscle wasting in CHF has yet to be developed. Consequently, primary skeletal muscle biopsies are an attractive tool for investigating skeletal muscle atrophy.

Purpose: To develop a protocol for obtaining pure populations of human chronic heart failure (CHF) myoblasts that can be used under standardized conditions. These cells are highly enriched in skeletal muscle biopsies and have been expanded in a controlled environment. Myogenic phenotype and their ability to differentiate into myotubes in vitro was verified by immunostaining and flow cytometry. Cellular viability (Annexine-V) and apoptosis (7-AAD) were assessed using flow cytometry.

Results: Primary muscle cells cultured on single plates revealed a large cell population (>10 mm) consisting of 90% desmin-positive myoblasts. Immunohistochemistry results showed that desmin and α-actinin proteins were expressed in the cytoplasm of CHF myoblasts. Differentiation of human CHF myoblasts was analyzed until day 6 and myogenesis was characterized by expression pattern of the paired box (Pax) transcription factor Pax7 and by the myogenic regulatory factors (MRFs) myogenic determination factor 1 (MyoD1), Myogenin and MRF4, indicating their skeletal muscle cell identity. Pax7 (72.7% ± 11.8%), MyoD1 (82.9% ± 6.7%) and MRF4 (72.1% ± 14.1%) were stable throughout the process of myogenesis. CHF myoblast differentiation is marked by the onset of Myogenin expression (13.0% ± 3.60%) on day 2, whereas levels of MRF4 (72.19% ± 14.11%) remained stable.

Conclusions: Satellite cell-derived myoblasts from CHF patients demonstrated a robust proliferation and an excellent differentiation. Skeletal muscle myoblast cell cultures offer the potential for the in vitro study of mechanisms that underlie muscle wasting in CHF patients.

PS345 | BENCH Whole exome sequencing of a family with 3 sibling affected by bicuspid aortic valve disease
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Introduction: Bicuspid aortic valve (BAV) is the most common cardiac malformation affecting 1–2% people worldwide. Despite its high prevalence, the pathogenesis of BAV is largely undetermined, although gene mutations leading to alterations in cell migration and signal transduction, in conjunction with non-genetic factors such as blood flow during valvulogenesis, may contribute to its formation.

Methods: We applied next generation whole exome sequencing (NGS) to identify single nucleotide polymorphisms and insertion/deletions. Overall, the bioinformatical tools Burrows-Wheeler Aligner, SOAPsnp, Samtools, Varscan, BAUV presentation in the three daughters and their two unaffected parents. The next generation whole exome sequencing (NGS) approach was used to identify new genetic variants.

Results: In each individual we identified over 38,000 SNPs and 3,400 Indels, of which >1,000 did not have any impact. Forty one SNPs were detected in at least two of the affected siblings but neither parent, and only 3 of those were detected in all three BAV patients: HFM1 (ATP dependent DNA helicase, TSPAN2 (tetraspanin family member) and TTF2 (transcription termination factor 2) (data not shown). Of these, only one was detected in all three BAV patients: HFM1 (ATP dependent DNA helicase, TSPAN2 (tetraspanin family member) and TTF2 (transcription termination factor 2) (data not shown). Of these, only one was detected in all three BAV patients: HFM1 (ATP dependent DNA helicase, TSPAN2 (tetraspanin family member) and TTF2 (transcription termination factor 2) (data not shown).

Conclusions: Whole exome sequencing of a family with 3 sibling affected by bicuspid aortic valve disease
aim was to determine the effects of improved function may be achieved at the cost of limited contractile reserve. Our 5 months after the gene transfer with starting doses of 2.5 n=6) or saline (saline group, n=6). Dobutamine stress test was performed 2 little is known how this treatment influence the response to Sarcoplasmic reticulum Ca2+ ATPase (SERCA2a) gene transfer im-

Methods: We implemented NGS based screening after targeted PCR enrichment have failed due to overlapping clinical features and the identification of mutations

Results: SERCA2a gene transfer improved LV ejection fraction (EF) from be-

Conclusion: SERCA2a gene transfer in chronic heart failure showed similar rel-

Purpose: Sarco/endothelial nitric oxide synthase gene polymorphisms and coronary artery disease: Are Asians more vulnerable than other races? H. Rai1, F. Parveen1, S. Kumar1, A. Kapoor1, N. Sinha2, 1Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India; 2Sahara Hospital Lucknow, Lucknow, India

Methods: We performed multiple genome-wide approach using exon array and RNA Sequenc- ing studies with CAD as end point, published up to December 2013, testing

Results: Among Fourteen studies from Asian (5,496 subjects) and 26 from NAE (16,521 subjects) group were included for G894-T polymorphism. All the genetic models among Asian ethnicity showed significant association (OR=1.5, 1.9 and 1.4 re-

Conclusions: The present study, which is the most comprehensive meta-

Conclusions: Mtus1 splice variant inhibits cardiac hypertrophy and exacerbates heart failure S. Ito1, M. Asakura1, K. Min1, M. Imazu1, K. Shindo1, H. Asanuma2, M. Kitakaze1, 1National Cerebral and Cardiovascular Center, Clinical Research and Development, Suita, Japan; 2Kyoto Prefectural University of Medicine, Kyoto, Japan

The molecular mechanisms of heart failure have not been completely elucidated. We performed multiple genome-wide approach using exon array and RNA Se-

Methods: We implemented NGS based screening after targeted PCR enrichment of mutations across genes which are either associated with H-T AD-associated genes (FBXL1, TGFB1R2, SMAD3, TGFB2, ACTA2 and COL3A1) in the diagnostic workflow. Between November 2012 and December 2013 141 samples from unrelated probands presenting ei-

Results: The median age of the cohort was 41.7 years (IQR 29.3 – 52.7y). We found a causal mutation in 22 patients (16%)

Conclusion: Mtus1 splice variant translates in cardiac-specific and affects the expression of apoptotic and antiapop-

Conclusions: This work demonstrated that heart failure due to mtus1A overexpression is associated with

Methods: We performed transcriptomic analysis of neonatal rat cardiomyocytes transgenic for mtus1A, followed by gene expression using deep sequencing. In order to identify the best transgenic model, we considered the expression level and the area of the left ventricle which was significantly reduced in the mtus1A group as compared to the wild type.

Results: Our method could identify a novel mutation responsible for heart failure. It was found at the 5'-splice site of the exon and gene expression profiles of murine hypertrophic and failing hearts in-

Conclusions: This study identified a novel mtus1A variant involved in human heart failure. In addition, we showed that this variant could be a potential therapeutic target for heart failure.
Identification of suitable reference genes for gene expression studies in normal and pathological human heart tissues

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Purpose: Quantitative real-time RTPCR (RT-qPCR) has become the method of choice in gene expression analysis, but requires an accurate normalization based on the use of reference genes showing invariant expression across various pathological conditions. By contrast, few data exist on appropriate reference genes for human heart. Our aim was to determine a set of suitable reference genes in human atrial and ventricular tissues, from right and left cavities in control and various diseases.

Methods: Expression of 16 reference genes (ACTB, POLR2A, YWHAZ, PGK1, PPIA, GAPDH, IPOB, HMB5, GUSB, 18S, B2M, RPLPO, TP, TBP, UBC) was assessed in tissue from right and left ventricle from healthy and heart failure (HF) patients; tissue from right atrium from patients in sinus rhythm (SR) with or without atrial dilatation, patients with paroxysmal atrial fibrillation (AF), with chronic AF or HF; and tissue from left atrium from patients in SR and in AF. RT-qPCR was performed in Taqman® Human Endogenous Control Arrays on a 7900HT system. Expression variability of these genes was evaluated by geNorm and NormFinder algorithms, BestKeeper software tool and comparative Delta-Ct method.

Results: Preliminary consensus analysis of the variability scores obtained for each reference gene expression shows that the most stable genes are: GUSB, IPOB, POLR2A, YWHAZ when comparing either right and left ventricle or atrium based on heart and HF patients; POLR2A, IPOB, PPIA, HPRT1 and GAPDH when comparing either right and left atrium or atri from all pathological groups. 18S, TBP, ACTB, TFRC and B2M genes were identified as the least stable reference genes, confirming that they are not worth of selection for normalization in human heart samples.

Conclusions: The overall most stable reference genes across different heart cavities and health settings were POLR2A, IPOB, GAPDH, PPIA, YWHAZ and GUSB. HPRT1 and HPRT1 could be also a good option for some specific experiments. This study could provide useful guidelines for reference gene selection in qRT-PCR studies in human heart.

Identification of suitable reference genes for gene expression studies in normal and pathological human heart tissues

P5352 | BENCH

Sudden death due to left dominant arrhythmo-cardiomyopathy with digenic heterozygosity: the challenge of risk stratification in familial carriers of single nucleotide variations

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Background: Mutations in genes encoding for desmosomal proteins are the most common cause of arrhythmogenic cardiomyopathy (AC). Compound/digenic heterozygosity has been identified as one of the most important determinants of malignant arrhythmic outcome. The impact of two single nucleotide variations (SNV) in the AC phenotype expression in a small family was assessed.

Methods: A 40- years old competitive athlete with a history of idiopathic right ventricular outflow tract tachycardia (normal 12 lead ECG and 2D echo) and successful catheter ablation, died suddenly during a cycling competition. Autopsy identified a concealed left dominant AC. Conventional genetic screening did not reveal a channelopathy-related AC genes [desmoplakin, desmoglein-2 (DSG2), desmocollin-2 (DSC2), junctional plakoglobin and plakophilin-2, catenin-a, desmin, phospholamban] and parallel exome sequencing was carried out. SNV segregation and disease penetrance was further assessed in the family members.

Results: By exome and conventional sequencing two SNVs in different desmosomal genes were identified in the proband: one in exon 14 of DSG2, c.2137 G>A (rs79241126, E713K), previously reported in AC cases as an “uncertain” variant with minor allele frequency (MAF) equals to 0.037; and the other SNV in exon 16 of DSC2, c.2603 C>T (rs141873745, S968F), considered a variant “likely to be pathogenic” since can alter the functional properties of the protein, has no available reported MAF and in silico analysis predicted a malignant outcome (Polyphen-2: malignant, SIFT: probably deleterious).

Conclusions: The results support the concept that some rare variants in desmosomal genes could determine a severe phenotype with septal and LV late-enhancement at cardiac magnetic resonance, in the absence of ventricular arrhythmias and 2D echo abnormalities.

Conclusions: The data herein reported confirm that digenic heterozygosity predicts a more severe phenotype and arrhythmic outcome in AC. However, the risk conferred by SNV in family members needs to be evaluated further by follow-up studies.

Cardiac Electrophysiology: When Things Go Wrong

P5353 | BEDSIDE

Genetic screening of sudden cardiac death victims with structural and unspecific abnormalities of the heart

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Purpose: Sudden cardiac death (SCD) is responsible for a large proportion of deaths in young individuals. In a forensic investigation, many of the cases show structural abnormalities, although often unspecific and therefore not diagnostic. A major proportion of these cases are suspected to be caused by inherited cardiac diseases. It is generally expected that implementation of genetic investigations in forensic medicine may increase the diagnostic rate. The purpose of the study was to explore the yield of genetic testing using next-generation sequencing (NGS) in forensic pathology, by investigating the frequency of pathogenic mutations in a cohort of deceased individuals with structural abnormalities of the heart.

Methods and results: Genetic investigation was performed in unrelated and deceased individuals under the age of 50 with structural abnormalities of the heart. Individuals with a post-mortem diagnosis of hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy or unspecific findings of the heart were included. With Haloplex Target Enrichment System (Agilent), all coding regions of 100 genes associated with inherited cardiomyopathies and channelopathies, were sequenced on the Illumina MiSeq platform. Preliminary results show that 40% of the deceased are identified with a probably pathogenic mutation, likely to be the cause of death.

Conclusions: By investigating a wide range of cardiac associated genes with NGS, it was possible to detect probably pathogenic mutations disposing to a cardiac disease, in suspected SCD victims with structural abnormalities at autopsy. Genetic investigation with NGS can be used as a diagnostic tool in forensic setting.

P5354 | BENCH

Systematic screening of rare coding variants in genes involved in cardiac arrhythmias

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The development of new strategies based on next-generation sequencing enables the large-scale screening of genes involved in rare diseases. We have developed a custom design based on the Haloplex™ technology to sequence the coding regions of 163 candidate genes, including all genes previously linked to cardiac arrhythmias. In total, 570 individuals were included in this study. To validate our design, we first analysed 42 patients with inherited cardiac arrhythmias. Among the 69 genetic variants previously identified in these patients, 68 were detected automatically after Haloplex library preparation and Illumina sequencing. The undetected variant is a substitution located in a low-coverage region. Subsequently, 361 additional patients were analysed (178 patients with Brugada syndrome; 89 patients with early repolarization syndrome; 94 cases of progressive cardiac conduction defects). We also analysed 167 controls, over 65 years of age and showing no signs of cardiac rhythm or conduction abnormalities. The mean coverage was 57X and we found 5 rare functional variants per patient on average. Then, burden tests were performed to detect genes significantly associated to cardiac arrhythmias. This approach also identified potential new disease genes, and replication in an independent cohort is in progress.

Our study will lead to a catalogue of mutations in genes linked to hereditary cases of sudden cardiac death. The systematic screening of our cohorts will also guide our future molecular investigations for these diseases and contribute towards improving the prevention of sudden cardiac death.

Systematic screening of rare coding variants in genes involved in cardiac arrhythmias

P5355 | BENCH

Class I antiarrhythmic drugs target cardiac two-pore-domain K+ (K2P) background channels

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Purpose: Class I antiarrhythmic drugs are commonly used for rhythm control in atrial fibrillation (AF). In addition, class I drugs are administered to suppress ventricular tachyarrhythmias in selected cases. The multichannel blocking profile

Cardiac biology / Cardiac electrophysiology: when things go wrong

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of class I compounds includes reduction of cardiac potassium currents in addition to their primary mechanism of action, sodium channel inhibition. Blockade of two-pore-domain potassium (K2P) channels in the heart causes action potential prolongation and may provide antiarrhythmic action in AF. This study was designed to elucidate inhibitory effects of class I antiarrhythmic drugs on K2P channels.

Methods: Whole-cell patch clamp and two-electrode voltage clamp electrophysiology was used to study K2P channel pharmacology in Chinese hamster ovary cells and Xenopus oocytes.

Results: Human K2P2.1 (TREK-1) and hK2P3.1 (TASK-1) channels were systematically tested for their sensitivity to clinically relevant class I (amilnide), IB (mexiletine), and class IC (propafenone) antiarrhythmic compounds. Mexiletine and propafenone inhibited K2P2.1 (IC50 = 182 μM;7 μM) and K2P3.1 channels (IC50 = 69.1 μM; 7.5 μM) in neuronal cells. Amilnide did not significantly affect K+ current amplitudes. K2P channels were blocked in open and closed states, resulting in resting membrane potential depolarization. Open rectification properties of the channels were not affected by class I drugs.

Conclusions: Class I antiarrhythmic drugs target cardiac K2P K+ channels. Blockade of K2P2.1 and K2P3.1 potassium currents is linked to antiarrhythmic therapy and provides mechanistic evidence to establish cardiac K2P channels as antiarrhythmic drug targets.

P5356 | BENCH
Different catecholamines induce different patterns of takotsubo-like cardiac dysfunction in an apparently afterload dependent manner

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Aims: Takotsubo cardiomyopathy (TCM) is characterized by regional cardiac dysfunction that cannot be explained by an occlusive coronary lesion. Catecholamines are implicated in the pathogenesis but the mechanisms involved are unknown. Because the endogenous and the most commonly used exogenous catecholamines have well defined adrenoceptor subtype affinities, inferences can be made about the importance of each adrenoceptor subtype based on the ability of different catecholamines to induce TCM. We studied which of five well-known catecholamines, with different receptor subtype affinities, could induce TCM-like cardiac dysfunction in the rat.

Methods: 255 rats received intraperitoneally isoprenaline (1/12-adrenoceptor agonist), epinephrine (1/23-adrenoceptor agonist), norepinephrine (1/2-adrenoceptor agonist), dopamine (1/20-adrenoceptor agonist) or phenylephrine (α-adrenoceptor agonist). Each catecholamine was given in five doses. We measured blood pressure through a catheter inserted in the right carotid artery and studied cardiac morphology and function by echocardiography.

Results: All catecholamines induced TCM-like cardiac dysfunction. Isoprenaline induced hypotension and predominantly apical dysfunction whereas the other catecholamines (with well defined adrenoceptor subtype affinities) induced restenosis of the aorta after administration of the respective catecholamine. When we continuously infused hydralazine (h) to rats that received epinephrine or norepinephrine to maintain systolic blood pressure >120 mmHg after isoprenaline administration prevented apical TCM-like dysfunction.

Conclusions: Catecholamine-induced TCM-like cardiac dysfunction appears afterload dependent rather than dependent on a specific adrenoceptor subtype.

P5357 | BEDSIDE
Exercise training improves arterial baroreflex control of muscle sympathetic nerve activity in patients with chronic heart failure


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Purpose: Previous studies have demonstrated that arterial baroreflex control of muscle sympathetic nerve activity (ABR-MSNA) is impaired in heart failure (HF). We tested the hypothesis that exercise training would improve the oscillatory pattern of muscle sympathetic nerve activity (LF-MSNA/HF-MSNA), and the gain and latency of the ABR-MSNA in patients with chronic HF.

Methods: Twenty-six consecutive, randomized HF patients, functional class II-III NYHA, EF <40%, peak VO2<20ml/kg/min were divided into two groups: Trained (T, n=13, 57±2 years) and untrained (UT, n=13, 49±4 years). Muscle sympathetic nerve activity (MSNA) was directly recorded by microneurography and blood pressure was measured on a beat-to-beat basis during 10 min period. Time series of MSNA and systolic arterial pressure were analyzed by autoregressive spectral analysis method. Gain and time delay of the ABR-MSNA was obtained by bivariate autoregressive analysis method. Exercise training was performed on a cycle ergometer at moderate intensity, three 40-min session/week for 16 weeks.

Results: Baseline MSNA, LF-MSNA/HF-MSNA, gain and latency of the ABR-MSNA were similar between T and UT groups. T patients showed decreased resting MSNA (Δ=15±5 vs 0.1±0.3 bursts/100 heart beats, P=0.02) and increased LF-MSNA/HF-MSNA (Δ=0.3±0.1 vs. -0.3±0.2, P=0.04) compared to UT patients. In contrast to T patients, UT patients showed a reduction in the gain of ABR-MSNA (Δ=0.1±0.4 vs. -1.7±0.6, P=0.03) and an increase in the latency of the ABR-MSNA (Δ=0.4±0.6 vs. 3.3±0.9 s, P=0.02).

Conclusions: Exercise training decreases resting MSNA and improves the oscillatory pattern of MSNA in patients with chronic HF. In addition, exercise training reverses the deterioration in the ABR-MSNA.

P5358 | BENCH
Vagal mechanisms controlling exercise capacity

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Purpose: Remote ischaemic preconditioning known to protect the heart against ischaemia/reperfusion injury increases parasympathetic (vagal) tone and enhances athletic performance. Vagal preganglionic neurons of the dorsal motor nucleus of the vagus nerve (DVMN) mediate remote preconditioning cardioprotection. Since athletes are known to have heightened vagal tone (as measured by heart rate variability and resting heart rate) we used an experimental (animal) model to test the hypothesis that acute withdrawal of vagal tone impairs exercise capacity.

Methods: In male Sprague-Dawley rats (380-420g), a lumbar visceral branch was used to transduce DVMN neurons to express an inhibitory Gi-protein-coupled Drosophila allatostatin receptor (AlstR) (n=8) or green fluorescent protein (GFP) as a control (n=8). Application of a natural ligand of AlstR - an insect peptide allatostatin (5-17) produces selective and rapid silencing of targeted neurones. A separate pharmacological study investigated the role of muscarinic and neuronal nicotinic oxides-mediated training desensitization using systemic treatment with atropine methyl nitrate (2mg/kg, i.p., n=5) or selective neuronal NO synthase inhibitor 7-nitroindazole (7-NI) (30mg/kg, i.p., n=8).

Forced exercise experiments were conducted on a single rodent lane treadmill with a shock grid set at the minimum threshold of 0.1 mA. Rats were preselected for this compliance after 3 days of a shock grid protocol and randomly allocated. The recruitment protocol involved speeds of 20-30 cm/s over 5 minutes after 15 minutes of acclimatisation. Speeds were then raised in increments of 5 cm/s in 5 minute intervals until the hind limbs made grid contact four times within a two minute period. The calculated work done (Joules, J) was used as an index of exercise capacity.

Results: Baseline exercise capacity was similar in rats expressing AlstR and GFP in the DVMN (47±4.6 vs 58±8.1 J, P=0.304). Acute inhibition of the DVMN vagal preganglionic neurons following allatostatin application resulted in a dramatic reduction in exercise capacity (8±1.2 vs 62±1.8 J, P<0.0001). In rats given atropine methyl nitrate and vehicle no significant difference in exercise capacity was noted (112±8.20 vs 111±7.24 J, P=0.8652), N rats however, produced a significant reduction compared to vehicle (32±6.6 vs 19.2 J, P=0.0002) as did 4 hours of methyl atropine (63±1.23 J vs 58±1.7 J, P=0.0019).

Conclusion: Results of these experiments suggest that parasympathetic tone generated by the DVMN neurons controls exercise performance via an NO-mediated mechanism.

P5359 | BENCH
Intravenous vagal nerve stimulation (VNS) in acute myocardial infarction (AMI) markedly reduces the infarction size and improves cardiac function in the chronic phase

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Purpose: Despite the widespread practice of coronary reperfusion therapy, AMI remains one of the major causes leading to heart failure in the long term. Although
VNS has been shown to exert powerful anti-infarct effects, the technical difficulty associated with VNS precludes its application under emergent settings of AMI. In this study, we developed a novel technique of intravenous VNS and evaluated how the VNS affects the infarct size and cardiac function 4 weeks after AMI with reperfusion.

Methods: In 11 mongrel dogs, we ligated a left anterior descending coronary artery for 3 hours, then reperfused. For the intravenous VNS, we performed the field electrical stimulation between a pacing catheter in the superior vena cava and an electrode pad attached to the back. We delivered VNS from the beginning of ischemia to 1 hour after reperfusion. We titrated the strength of VNS to lower heart rate by 20–30%. We divided animals into 3 groups, sham operation/no stimulation (Sham, N=4), ischemia-reperfusion (I/R, N=4), and I/R-VNS (I/R-VNS, N=4). 4 weeks after ischemia, we evaluated hemodynamics and left ventricular function in terms of end-systolic elastance (Ees). We also histologically estimated the infarct size.

Results: During operation, mean heart rate were significantly lower in I/R-VNS than in I/R (107±12 vs. 134±16 bpm, p<0.05), while blood pressure didn't differ among 3 groups. I/R-VNS strikingly decreased the infarct size more than 80% (p<0.05, Fig. 1) and improved Ees (p<0.05, Fig. 2). I/R-VNS markedly decreased left ventricular end-diastolic pressure (5.0±3.6 vs. 23.8±2.5 mmHg, p<0.05) and serum NT-pro BNP (843±256 vs. 3667±1637 pmol/ml, p<0.05).

Conclusion: Intravenous VNS in AMI markedly reduces the infarct size and improves cardiac function in the chronic phase.

P5360 | BENCH
Funny current mediated pacemaker activity in the sinoatrial node of sodium-calium exchanger knockout mice
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Purpose: The sodium-calciium exchanger (NCX) is the major Ca extruder of myocytes. In the sinoatrial node (SAN) both NCX and funny current (If) participate in the depolarization that initiates pacemaker activity. To clarify the relative contribution of NCX to SAN pacing, we created an atrial-specific NCX knockout (KO) mouse. This mouse does not express any NCX in the atrial region, including the SAN. Phenotypically, NCX KO mice lack P-waves on their electrocardiograms and have quiescent isolated SAN cells. Recording the CA dynamics in a novel prepa-ration that includes the SAN and atria, we investigated wether atrial remodelling may have obscured residual pacemaker activity in NCX KO SAN tissue.

Methods and results: Using high speed 2D confocal microscopy we found that the KO SAN exhibited bursts of organized Ca transients alternating with pauses, characterized by abundant intracellular Ca waves. Although, the overall rate of Ca transients in NCX KO SAN (2±2Hz; n=25) was reduced by the numerous pauses, the frequency of Ca transients during the bursts was rapid. Their average frequency (~4Hz; n=24) was not significantly different from WT (~5Hz; n=24). When considering only the rate during the burst, we found that 6 out of 10 KO SANs responded significantly to β-adrenergic stimulation (isoproterenol 10μM; 52±16% rate increase). This response was smaller but still comparable to the increase in WT SANs (70±6%; n=6). The pacemaker activity of both genotypes responded to the f forskamer (IVA, 9μM). At higher doses of IVA (27μM) WT SANs decreased their rate by 43±4%, while KO SAN Ca transients were effectively eliminated.

Conclusions: These results indicate that If generates the burst pacemaker activity found in the NCX KO SAN, and allows the partial β-adrenergic responsiveness of the KO.
**Conclusions:** Appropriate amount of CTCF is necessary for the fetal gene expression program in cardiac hypertrophy. CTCF has the possibility to link functional signaling pathways from the cell surface.

**Results:** Isolated neonatal rat ventricular cardiomyocytes (NRVCM) under stimulation with different G-protein-coupled receptor agonists. The impairment of GRK2-mediated Akt/PKB phosphorylation suggested the PI3K/Akt pathway as the critical signaling cascade of the observed hypertrophic response. This could be confirmed by increased Akt/PKB phosphorylation in both PE and ANG II stimulation with resulting hypertrophy. These findings were reproducible by adenosine GRK2 overexpression. The increase in cell size as well as the observed upregulation of fetal gene response could be abolished by siRNA mediated GRK2 knockdown.

**Conclusion:** Our data show a novel role of GRK2 promoting cardiac hypertrophy by GRK2-PI3K-mediated Akt phosphorylation and inactivation of GSK3β resulting in enhanced fetal activity. Thus, GRK2 knockdown could be a promising therapeutic approach targeting cardiac hypertrophy.

**Conclusions:** The HF induced by pressure-overload to the heart affect the global gene expression of the lung including up-regulation of genes coding secretory proteins involved in cardiovascular diseases and cardiac functions. The reactive pulmonary expression of secretory proteins may play a role in the cardiopulmonary interaction and contribute to the pathophysiology of the HF.

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**Purpose:** The increase in protein activity and upregulation of G-protein coupled receptor kinase 2 (GRK2) is a hallmark of cardiac stress and heart failure. Inhibition of GRK2 has shown to improve cardiac function and survival and moreover diminishes cardiac remodeling in various animal models of cardiac disease suggesting potential involvement in cardiac hypertrophy. We have previously shown that conditional GRK2-KO mice present attenuated hypertrophic response with maintained ventricular geometry and heart-to-body weight ratio following aortic constriction while wildtype mice present hypertrophy and dilatation. Hence the aim of the present study was to further enlighten the molecular effects of GRK2 on cardiomyocyte hypertrophy.

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Progressive cardiac hypertrophy and heart failure

mice (-31% vs. -25%), accompanied by a stronger degree of cardiac hypertrophy (heart weight–tibia length ratio 9.3 vs. 13.1; p < 0.05). In isolated working hearts, a decrease in cardiac power (-28%) was accompanied by a decrease in palmitate oxidation (-33%), glucose oxidation (-39%), and oxygen consumption (-17%), whereas rates of glycolysis were increased (+40%; all p < 0.05). Respiration rates (-36%), ATP synthesis (-55%) and the ATP/O ratio (-33%) were decreased in cardiac mitochondria from SIRT3−/− mice. HPLC measurements revealed a decrease of the myocardial ATP/AMP ratio (-21%) and of myocardial energy charge (-8%). Using LC-MS/MS, we identified increased acetylation of 85 reversible acetylation of various energy metabolic enzymes.

Conclusions: SIRT3 is required to maintain mitochondrial and contractile function, and may regulate myocardial mitochondrial energetics by reversible acetylation of various energy metabolic enzymes.

P5368 | BENCH
Oestradiol improves mitochondrial function and prevents cardiac diastolic dysfunction in a mouse model of human hypertrophic cardiomyopathy mutation

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Purpose: Clinical findings show that female sex and/or the sex hormone estrogen (17β-oestradiol, E2) may contribute to the sexual dimorphism in hypertrophic cardiomyopathy (HCM). However, the underlying mechanism is not completely known. Taking into account the sexual dimorphism in cardiac metabolism and function, the aim of the project was to explore the effect of ovariectomy (OVX) and 17β-oestradiol (E2) replacement on myocardial and mitochondrial functions in C57BL/6J (C57) genetic mice, generated by cardiac-restricted expression of human HCM mutation.

Methods: The C57TQ92 mice were ovariectomized at twenty weeks of age and were treated with placebo (OVX group) or E2 (OVX+E2 group) for twelve weeks before sacrifice. Wild-type and C57TQ92 female mice with sham operation were used as control groups. Echocardiographic recording and histopathological studies were performed. At the mitochondrial level, respiratory control and ATP levels were determined. Some key components related to mitochondrial energy metabolism such as the mitochondrial proton-potential dependent adenine nucleotide translocator (ANT), a co-activator 1α (PGC-1α) and their downstream molecules were also performed using western blot and RT-PCR analysis. The levels of oxidative damage markers and antioxidant defence were determined.

Results: C57TQ92 mice had impaired diastolic compared with wild-type mice. In response to ovariectomy, cardiac diastolic function further decreased. Myocardial energy metabolism such as ATP levels and mitochondrial respiratory ratio also decreased significantly in OVX group. Consistent with this, PGC-1α and PPAR-α also decreased significantly. E2 supplementation partially restored the mitochondrial function as well as reduced oxidative damage, thus improved diastolic function.

Conclusions: Our study showed that administration of 17β-oestradiol improved myocardial diastolic function, prevented myocardial energy disorder as well as reduced myocardial oxidative stress in R92Q mice. The significance of the findings is further enhanced in view of E2 on phenotype modification role in HCM.

P5369 | BENCH
PGC-1α pathway regulates cardiac metabolic changes in porcine model of ST segment myocardial infarction


Purpose: In the context of myocardial infarction (MI) the availability of metabolites is clearly restricted, therefore a fuel metabolic shifts takes place. Previous studies have indicated that peroxisome proliferator activator receptor co-activator alpha (PGC-1α) pathway is a crucial regulator of cardiac metabolism in response to cardiac stress. Here we address the role of PGC-1α in regulating metabolic changes of the heart.

Methods: We studied a group of 12 common swine in which anterior MI was induced by means of angioplasty balloon inflation. A series of 6 swine were sacrificed at 48h post-infarction (acute infarction group) and another series of 6 swine were sacrificed at 3 weeks (chronic infarction group). Metabolites such as: glucose, pyruvate, ketone bodies, and lipids were analyzed in serum (mmol/L) at baseline, 75 min after balloon inflation, 2 h, 48 h and 3 weeks after reperfusion by means of enzymatic analysis. Results were compared to baseline levels. Genes related to PGC-1α such as: PGC-1α, ERR-α, PPAR-α, and HIF-1α were analysed (fold changes) in infarcted, adjacent and remote areas of porcine hearts 48h or 3 weeks post-infarction by molecular biology. Results were compared to 5 control swine without infarction.

Results: In all groups, after 2h of infarction, a striking increase of lactate (3.2±0.6 vs. 0.8±0.3) and non-esterified fatty acids (0.6±0.2 vs. 1.8±0.3) was observed in serum compared to baseline (p<0.001 in both cases). Conversely, a significant decrease of glucose (5.2±0.3 vs. 3.8±0.2) and β-Hydroxybutyrate (1.8±0.5 vs. 0.6±0.2) occurred at the same time (p<0.001 in both cases). All values reverted progressively to baseline after 3 weeks. In comparison with controls, molecular biology analysis of acute infarcted hearts revealed a significant decrease of expression in mRNA and protein levels of transcription factors related to lipid and mitochondrial metabolism: PGC-1α (0.3±1.0 vs. 1.2±0.2 fold), ERR-α (0.8±0.3 vs. 1.6±0.2 fold) and PPAR-α (0.9±0.3 vs. 1.7±0.2 fold) (p<0.01 in all cases). Values didn’t change significantly after 3 weeks. However genes related to glucose metabolism were significantly increased in acute infarcts compared to controls: GLUT-1 (3.8±0.4 vs. 1.1±0.3 fold), HIF-1α (4.2±1.3 vs. 1.1±0.2 fold) (p<0.01 in both cases). These values recovered control levels after 3 weeks.

Conclusion: A metabolic deregulation mediated by PGC-1α decreased expression takes place in the context of acute MI. This is mediated by a decrease of fatty acid oxidation and an increase of glucose utilization and it reverts after 3 weeks.

P5370 | BENCH
SIRT3 deficiency exacerbates LPS-induced cardiac dysfunction

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Myocardial dysfunction is a well described complication of endotoxemia and sepsis, which may be related to simultaneous development of myocardial mitochondrial dysfunction. The mitochondrial NAD+ dependent deacetylase Sirtuin 3 (SIRT3) improves mitochondrial function and decreases mitochondrial ROS production. Since sepsis results in cardiac NAD+ depletion, we hypothesized that impairment in SIRT3 activity due to NAD+ depletion may contribute to the development of myocardial mitochondrial and contractile dysfunction under septic conditions. SIRT3−/− or wildtype mice were investigated 6 hours following injection of E. coli lipopolysaccharide (10 mg/kg) or saline. In isolated working hearts, wild type animals treated with LPS showed a decrease in aortic developed pressure (systolic: 0.5±0.4 vs. 1.7±0.5 mmHg; p<0.05), cardiac power (25.1±1 vs. 31.8±1 mW/g; p<0.05), palmitate oxidation (494±28 vs. 335±15 nmol/min/g; p<0.05) and cardiac efficiency (4.0±0.3 vs. 6.0±0.4%; p<0.05) without changes in myocardial O2 consumption (MVO2). Additional deficiency of SIRT3 resulted in further decrement of contractile parameters, accompanied by a marked decrease in cardiac efficiency (-51%, p<0.001) and an increase in MVO2 (22%, p<0.05) when animals were treated with LPS. This decrease in cardiac efficiency was accompanied by unchanged mitochondrial ADP-stimulated O2 consumption in isolated mitochondria, whereas ATP synthesis was reduced, suggesting mitochondrial uncoupling. Thus, acute endotoxemia impairs cardiac contractility, and additional SIRT3 deficiency further impairs cardiac dysfunction and impairs cardiac efficiency, possibly due to increased mitochondrial uncoupling. Impaired SIRT3 activity due to preexisting myocardial NAD+ depletion, as may occur in many cardiac pathologies, may predispense the heart for exacerbation of cardiac dysfunction under septic conditions.

P5371 | BENCH
Different characteristics of diabetic cardiomyopathy in rat models of type-1 and type-2 diabetes mellitus

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Purpose: Diabetic cardiomyopathy, a cardiac manifestation of diabetes mellitus (DM), is characterised by specific structural, molecular and functional alterations of the myocardium. Upon this concept we investigated whether type-1 or type-2 diabetes lead to different alterations in cardiac function or histological and molecular changes.

Methods: Our experiments were carried out in a rat model of type-1 (streptozotocin induced) and type-2 DM (Zucker Diabetic Fatty rats). Left ventricular (LV) function was characterised using a pressure-volume (P-V) conductance catheter system. Load independent indices of LV contractility (preload recruitable stroke work (PRSW)) and indices of LV relaxation (time constant of LV pressure decay (Tau)) and stiffness (LV end-diastolic pressure (LVEDP)) were calculated, respectively. In addition to our functional measurements TUNEL assay was performed to evaluate degree of apoptosis. Myocardial gene expression analysis was performed by qRT-PCR, expression of proteins was investigated by western blot and immunohistochemistry.

Results: In comparison to the control, type-1 DM resulted in decreased LV systolic performance: decreased systolic pressure, maximal dp/dt and PRSW (45.39±15.3 vs. 76.44±4.05 mmHg, p<0.05). Type-2 DM was associated with increased LV stiffness (LVEDP: 9.4±0.5 vs. 7.7±0.4 mmHg) while systolic indices were altered to only a lower extent. We observed cardiac hypertrophy and degeneration with histomorphological examination. More pronounced nitro-oxidative stress resulted in increased DNA-damage. Overexpression of c-fos and c-jun and downregulation of eNOS were observed in type-1 diabetic rats. On the other hand TGF-β1 and ANF mRNA-levels were significantly higher in type-2 diabetic model.

Conclusions: Diabetic cardiac alterations are characterised by decreased systolic function in type-1 and increased stiffness in type-2 diabetes. Acute endotoxemia and diabetic cardiomyopathy different processes can be identified in the two models. (Supported by the grant OTRA PD100245)

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P5372 | BENCH
The GLP-1 metabolite (9-37) improves myocardial function in the TAC model by reducing myocardial hypertrophy and improving glucose uptake


Introduction: Diastolic dysfunction and myocardial hypertrophy are early signs of hypertensive cardiomyopathy. GLP-1 (7-37) is an incretin hormone which is released in response to nutritional stimuli from the gut and increases glucose metabolism by increasing glucose dependent insulin secretion from the β-cell. GLP-1 (7-37) is rapidly cleaved to its inactive metabolite GLP-1 (9-37) which is unable to bind to the GLP-1 receptor and does not cause insulin secretion. Nevertheless both peptides have been found to hold cardioprotective actions.

Methods and results: To investigate the effects of GLP-1 on hypertensive cardiomyopathy we injected 6 week old C57BL/6J mice with an adeno associated viral vector system overexpressing GLP-1 (7-37), GLP-1 (9-37) or Lac Z (control) (n=15/group). Cardiac hypertrophy was induced by transversal aortic constriction (TAC). Overexpression of GLP-1 (7-37) led to the expected improvement of metabolic parameters (p<0.01) while GLP-1 (9-37) had no effect. Despite, both peptides similarly reduced myocardial hypertrophy (p<0.01; n=5-10/group) and reduced myocardial collagen content (gemiin stain and PGR all p<0.05; n=6-8/group) and apoptosis (caspase-3 p<0.05). Interestingly however, only GLP-1 (9-37) showed a significant improvement of diastolic myocardial function (dp/dt-min) while reducing LVEDP (all p<0.05; n=13/group after 4 weeks under dobutamin-stress by milar catheter). This was accompanied by a significant reduction of myocardial F18-FDG-glucose uptake (p<0.01; n=11/group in the PET) in GLP-1 (9-37) expressing mice. Nonetheless, no significant differences in the expression of the glucose transporters GLUT1 (p=0.01) and GLUT4 (p=0.01). In addition, GLP-1 (9-37) expressing mice were found to hold increased ACC phosphorylation (p=0.05) pointing to activation of AMPK as a possible mechanism.

Conclusions: The GLP-1 metabolite (9-37) improves hypertrophic cardiomyopathy in the TAC model by reducing myocardial glucose uptake, ventricular hypertrophy and apoptosis.

P5374 | BEDSIDE
Left ventricular rotational mechanics in cirrhotic patients: a speckle-tracking echocardiographic study

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Purpose: Cirrhotic cardiomyopathy is a complex and not fully defined entity which has been connected to impaired myocardial contractile reserve to stress and altered diastolic relaxation. Aim of this study enroled patients with cirrhotic cardiopathies of different etiologies and stages, to assess left ventricular (LV) systolic performance at rest through both “classic” echocardiographic indices and novel deformation-rotational dynamics parameters, trying to identify the pathophysiology of contractile dysfunction in cirrhosis.

Methods: Seventy seven male cirrhotic patients (mean age 54.4±9.7 years) and 20 healthy control subjects were prospectively enrolled. All subjects underwent standard echocardiography and subsequent offline analysis to evaluate LV ejection fraction (EF), strain, strain rate and strain rate indices and finally LV rotation using speckle-tracking echocardiography. The untwisting delay is now recognized as a distinctive trait for Hypertrophic Cardiomyopathy (HCM) thanks to 2D and 3D speckle tracking echocardiography (2DSTE and 3DSTE). However, it has never been related to the temporal evolution of Left Ventricular (LV) shape during heart cycle. This is possible thanks to the concept of homologous times in order to evaluate shapes of LV at comparable electro-physiological events. We test here the hypothesis that the untwisting-rate is significantly correlated with the shape of trajectories in time of the LV.

Methods: Here we compared healthy subjects (n=50) with patients affected by HCM (n=11). We used 3DSTE (Toshiba, Artida) allowing the manual digitization of homologous landmarks and the identification of homologous electrophysiological time frames. We analysed the shape of LV trajectory during heart revolution. We chose 9 homologous electrophysiological times, including R wave peak, end of T wave, end-systolic volume, mitral valve opening and Q wave peak, and we predicted LV shape at those times. A modified Geometric Morphomorphs tool was used in improvement of detect differences and trajectories shape attributes.

Results: We found that healthy subjects have a faster untwisting (Fig. 1) during diastole for global untwisting-rate and in particular for 3 out 4 apical segments in comparison to HCM patients (p<0.05). The global untwisting rate was significantly related to the shape modifications of LV trajectory in time (p<0.05).

Figure 1. Untwisting rate trajectories.

Conclusions: As the untwisting is an important parameter for the evaluation of LV function, its significant correlation with the shape of LV motion trajectory in time could allow considering the trajectory analysis, in the near future, as a new potential pre-clinical diagnostic metric in HCM patients evaluation.

P5376 | SPOTLIGHT
Does timing matter for strain measurements?

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Current speckle tracking based strain measurements are highly automated. It remains often unclear, however, where a particular analysis software defines the zero-baseline and the systolic strain measurement position. This study was set-up to investigate, to which extent timing definitions influence strain measurements.

Methods: 50 subjects (10 healthy volunteers, 10 patients with ischemic heart disease and 10 patients with typical LBBB) underwent a complete echocardiographic exam. 2D strain images from the apical 4 chamber view were analyzed by a single reader. End-diastole (ED) and end-systole (ES) were defined as peak R and aortic valve closure (derived from CW Doppler), respectively. Using this reference, global (GLS) and segmental (SS) longitudinal end-systolic strain was measured. Measurements were repeated with changing the definition of either ED or ES by ± 4 frames. Resulting strain changes were expressed as absolute percentage of the reference value. The mean frame rate was 61/sec.

Results: Changing the definition of ED and ES resulted in significantly different GLS and SS values in all subjects. GLS was less affected than SS. Measurements in normals were least sensitive and those in dysynchronous hearts most...
sensitive to changes in the definition of ED and ES. See figure (grey shaded areas indicate significant differences).

Conclusions: The exact temporal definition of end-systole and diastole has a major impact on accurate strain measurements. Particularly segmental strain in dysynchronous hearts can vary up to 20% per frame. Manufacturers are asked to improve their respective software algorithms and users must take this into account when using speckle tracking strain clinically.

P5377 | BEDSIDE
Feasibility of a new hybrid imaging system featuring fusion of multislice coronary tomography and 3-D speckle-tracking echocardiography
E. Casas Rojo1, C. Fernandez-Gotlin1, W. Gorissen2, R. Mogelvang3, C. Hassager4, A. Fuchs3, K.F. Kolded3, S. Fernandez Santos3, T. Segura De La Cal1, J. Zamorano Gomez1, University Hospital Ramon y Cajal, Department of Cardiology, Madrid, Spain; 4Toshiba Medical Systems, Zoetermeer, Netherlands;

Background: Multislice coronary tomography (MCT) and 3D strain speckle-tracking (3DS) are two of the greatest advances in cardiology imaging in the recent years. Their main limitation is the lack of integration of the information they give separately, as MCT provides only anatomical data, and 3DS contributes exclusively functional information. We suggest that a new system featuring at the same time coronary anatomy and myocardial mechanics would overcome that limitation.

Objective: We tested a hybrid imaging software prototype capable of managing at the same time data from both MCT and 3DS, and displaying them as a single series of hybrid images. The aim was to test the feasibility of the system both with rest and stress 3DS echocardiography.

Results: 15 patients (11 male, 4 female) aged 56.1±9.9 with chest pain history and confirmed or suspected significant stenoses in MCT were included and underwent 3DS echocardiography at rest. 5 of them also underwent stress echocardiography by clinical indication. Abnormal regional contractility at rest was identified on 10 patients, and 3D-strain defects matched with the location of coronary stenoses in all cases. Fig.1 shows hybrid image in a patient with significant stenosis in LAD artery and low regional strain at the apex of left ventricle in the rest study. Stress 3DST showed ischemia in one patient, with perfect matching of one of the diseased vessels, and it discarded ischemia in four patients with uncertain lesions on CT.

Conclusion: Hybrid imaging from MCT plus 3D myocardial mechanics is feasible from ordinary data obtained with both techniques separately and processed with a new software, either with resting or stress echocardiography. Clinical studies will test the usefulness of this approach.

P5379 | BEDSIDE
Echocardiographic assessment of wall shear stress: association with the development of adverse remodeling after myocardial infarction

Introduction: Adverse remodeling after myocardial infarction includes the potential development of ventricular aneurysms. Wall shear stress (WSS) may have a determining role in this process. The goal of this study is to analyze, through advanced echocardiographic calculations, the association between the intensity of WSS and the presence of ventricular aneurysms.

Methods: Patients with intraventricular aneurysm underwent echocardiographic examination with Vector Flow Mapping (VFM), an advanced echo-modality capable of calculating flow-generated WSS from flow velocity variation next to the wall. WSS in the aneurysmatic area was analyzed and the size and shape (depth and width) of the aneurysm were measured.

Results: 11 patients (10 males, aged 70.4±8.4, LVEF 43.8±10.5) were studied. Intensity of peak WSS throughout the cardiac cycle was graded on a 0–6 scale. A cut-off point of 4 was established to differentiate patients with intense (7, 63.6%) from those with moderate or mild (4, 36.3%) degrees of WSS. Patients with WSS ≥4 presented significantly deeper aneurysms (13.2±4.2 mm vs. 7.9±2.1 mm, p<0.01) and a tendency to larger aneurysms (15.2±5.9 mm vs. 12.1±5.9 mm, p<0.05) compared with patients with WSS <4. Additionally, none of the patients with WSS ≥4 presented thrombus inside the aneurysm (0/7, 0%), while 3 out of 4 (75%) presenting WSS <4 showed a thrombus inside the aneurysm.

Conclusions: The development of larger and deeper ventricular aneurysms in patients with ischemic cardiomyopathy seems to be associated with the presence of high levels of wall shear stress on the infarcted region. Additionally, patients with lower shear stress on the aneurysm are at higher risk of developing thrombi inside the aneurysmatic area.

High-intensity wall shear stress

Table 2: Evolution of RV parameters

<table>
<thead>
<tr>
<th></th>
<th>RV FAC</th>
<th>Global RVs Free wall RV long S</th>
<th>Septal RV long S</th>
<th>T Ei index</th>
</tr>
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<tbody>
<tr>
<td>Controls</td>
<td>23.3±4.0</td>
<td>49.7±7.9</td>
<td>52.6±4.7</td>
<td>3.8±1.4</td>
</tr>
<tr>
<td>Basal</td>
<td>12.1±2.6</td>
<td>44.1±9.6</td>
<td>18.1±3.4</td>
<td>19.9±4.5</td>
</tr>
<tr>
<td>3 months</td>
<td>14.9±3.8</td>
<td>45.0±7.8</td>
<td>19.0±4.3</td>
<td>19.7±4.5</td>
</tr>
<tr>
<td>6 months</td>
<td>16.1±3.7</td>
<td>43.7±9.3</td>
<td>20.2±4.2</td>
<td>24.4±5.8</td>
</tr>
<tr>
<td>1 year</td>
<td>16.1±4.2</td>
<td>45.0±11.2</td>
<td>21.3±4.6</td>
<td>25.4±7.1</td>
</tr>
<tr>
<td>2 years</td>
<td>18.8±4.1</td>
<td>44.4±9.3</td>
<td>22.3±3.8</td>
<td>28.4±6.3</td>
</tr>
</tbody>
</table>

*p<0.01, #p<0.05.

Figure 1

*Figure 1*
P5380 | BEDSIDE
How could quantitative longitudinal peak systolic strain help in the detection of left ventricular wall motion abnormalities in our daily echocardiographic practice?

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Purpose: Transthoracic echocardiography (TTE) is the most commonly used tool for the detection of left ventricular wall motion (LVMW) abnormalities. Experienced cardiologists use visual evaluation, which is responsible for a high interobserver variability. Automatic Function Imaging (AFI) provides segmental Longitudinal Peak Systolic Strain (LPSS) values and is more reproducible. However, AFI has not yet entered into routine. Hence, the role of segmental LPSS values in the prediction of LVMW in our in-hospital daily practice has not been fully evaluated.

Methods: We investigated how on-line segmental LPSS values could predict segmental LVMW. Echocardiograms were performed by a single sonographer in his daily clinical practice. LVMW was evaluated on-line and LPSS values calculated according to a 19-segments model, on apical 3-, 4- and 2-chamber views. The analysis involved 507 consecutive and unselected TTE between Aug-2012 and Nov-2013. N=11514 segments were recorded. After excluding the apexes, 10647 segments entered the analyses. N=10590 segments were successfully tracked (99.5%). Segments were classified as normal (1), hypokinetic (2), akinetic (3), dyskinetic (4) and paradoxal (5, for the septum) and a segmental LPSS value was associated to each segment.

Results: Segmental LPSS values were normal for basal (95% median) and normal apical apical segments were (mean: %95% Conf. Interv): -16.4%; [-16.6-16.2%]; -18.1%; [-18.3-17.9%] and [-21.1%; [-23.3-20.8%] respectively, the difference being significant between the three. Segmental LPSS values for hypokinetic basal/hypokinetic median and hypokinetic apical segments were: -7.7%; [-9.2-6.3%]; -10.1%; [-11.3-9.0%] and -8.9%; [-10.2-7.5%] respectively. These three hypokinetic values being significantly different from the three normal values, but not significantly different from the other abnormal segments’ LPSS values (akinetic, dyskinetic, and paradoxal).

Conclusion: On 10590 segments successfully tracked, LPSS values could differentiate normal from abnormal segments (eye LVMW abnormalities), but could not differentiated the different levels of abnormality. These results remain important in our daily echographic practice.

P5381 | BEDSIDE
Peroperative improvement in left ventricular longitudinal motion after transcatheater aortic valve implantation predicts better outcome

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Purpose: Global early diastolic peak strain rate (SRe) represents the mean early diastolic performance of all left ventricular (LV) segments and has been experimentally demonstrated to depend on LV relaxation. Speckle-tracking Automated Function Imaging (AFI) is a relatively simple method to measure echocardiographic longitudinal strain. We explored its potential to measure SRe in a large patient population.

Methods: We examined 427 consecutive patients with (339) and without (88) heart diseases (ranges, age: 14-93 y, HR: 40-130 bpm, systolic arterial pressure: 90-180 mmHg, ejection fraction, LVEF: 15-78%), using GE Vivid 79 systems. AFI-derived peak maximum early diastolic SRe (SRe' peak) and time to peak SRe (SRe' time) were obtained in the 3 apical views from the first diastolic frame the strain curves and averaged.

Results: Peak SRe and SRe' were normally distributed and respectively 1.86±1.83 s' (95% CI 1.68, 2.03) and 153±42 ms (95% CI 144, 162) in normals and 0.98±0.6 and 187±76 in patients (both, p<0.001). They were both decreased in dilated cardiomyopathy (n=33; 0.53±0.28, 245±86; p<0.001), CAD with normal preload (n=30; 0.71±0.51, 201±72; p<0.001), and aortic stenosis (n=23; 0.9±0.38, p<0.001; 163±38, p=ns); there was a trend towards an increase in SRe in athletes (n=12; 2.34±0.86). At multiple regression analysis, adjusted for LV preload, mitral regurgitation, filling pressures, stroke volume and left atrial volume, SRe was positively determined by tissue Doppler peak systolic mitral annulus velocity, and negatively by age, LV wall motion score index, mass index, heart rate and mitral E wave deceleration time (r=-0.74, p<0.001), whereas SRe' peak was positively determined by LV wall motion score index, mitral E wave deceleration time, and systolic pulmonary pressure, and negatively by heart rate (r=0.6, p<0.001). When LV isovolumic relaxation time was set as the dependent variable, it was determined negatively by tissue Doppler peak early relaxation.
diastolic mitral annulus velocity, heart rate, and LV filling pressures, and positively by SRe derived from TDI (r = 0.69, p < 0.0001). Notably, SRe derived from TDI was greatly reduced in all grades of LV diastolic dysfunction (DD): no DD, 1.67±0.8 (95% CI 1.56-1.78); grade I DD, 0.79±0.44 (95% CI 0.72-0.86); grade II DD, 0.7±0.58 (95% CI 0.33-1.07); grade III DD, 0.67±0.23 (95% CI 0.55-0.78); all p < 0.001.

Conclusions: AFI-derived SRe and SRetp are both related to LV relaxation and its determinants. Unlike tissue Doppler velocities of the mitral annulus, they reflect global LV relaxation, and appear clinically promising, although presently not measurable “online”.

P5384 | BEDSIDE
Can global longitudinal strain predict left ventricular ejection fraction in echographic daily practice?

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Purpose: Transthoracic echocardiography (TTE) is the most commonly used tool for the evaluation of left ventricular ejection fraction (LVEF). Its reproducibility remains a matter of controversy. Speckle tracking allows the assessment of left ventricular (LV) systolic function, by the measurement of Global Longitudinal Strain (GLS). It is more reproducible. However, GLS has not yet entered into routine. Hence, its role in the prediction of LVEF has not been fully evaluated.

Methods: On 507 consecutive unselected TTE (excluded N=53), we investigated how online 2-dimensional GLS could predict LVEF (biplane Simpson method). Simple linear regression was used to assess the relationship between LVEF and GLS. The tests were repeated for each class of echogenicity (good, moderate, poor). ROC analyses was used to identify the threshold of GLS that predicts LVEF < 40%.

Results: The most frequent indication for TTE was stroke (N=235). Median LVEF (Inter Quartile Range, IQR) was 59% (50-70) and median GLS (IQR) was -19% [-21-16]. A correlation was found between LVEF and GLS in the whole series (N=507), with r=0.53 (p<0.0001), and LVEF = -1.45GLS+38.04 GLS. For poor echogenicity (N=76), r=0.53 (p<0.0001) and LVEF = -1.48GLS+41.65, where GLS explained 26.6% of LVEF variation, and for one unit decrease in GLS, we would expect a 1.46 unit increase in LVEF. When echogenicity was moderate (N=187) or good (N=244), the correlation was better. The area under ROC curve was 0.97 and GLS ≥ -14% allowed to detect LVEF <40% with a sensitivity of 95% and a specificity of 86%.

ROC analyses: prediction of LVEF <40%.

Conclusion: GLS is easy to obtain and accurately detects LVEF <40% in unselected patients. It may especially be helpful when echogenicity is poor.

P5385 | BENCH
Predictors of mortality and/or transplantation in patients submitted to echo guided CRT optimization


Introduction: Cardiac resynchronization (CRT) is a therapy for patients (pts) with low ejection fraction (EF) (<35%), electrical dyssynchrony and heart failure. 25-30% do not respond clinically and 35-65% do not obtain left ventricular (LV) reverse remodeling.

Objective: To analyze retrospectively pts submitted to echo guided CRT optimization (OP) after implantation (IMP) and review the results and predictors of mortality or heart transplantation (HTX).

Methods: Clinical data (age, gender, rhythm, time delay from IMP to OP and follow up after OP) and echocardiographic data (LV end diastolic and end systolic diameters and volumes, LVEDD, LVESD, LVEDV, LVESV), EF, left atrial dimension, dyssynchrony parameters (Pitfalls, interventricular mechanical delay, lateral or septal delay) and all segments and basal maximal delays and standard deviations with multiple TSI) and other parameters (E/e’, E/A, pulmonary artery systolic pressure, (PASP)) were analyzed. The revision of mortality was complete. OP was based on iterative method with analysis of Doppler LV inflow and outflow while AV and/or VV delays were changed. Pts were divided into 2 groups according to the absence (GI) or presence of major adverse events (death or HTX) (GII).

Results: 63 pts (42 male, mean age 63±11 years, EF pre IMP 24.6±5.5%, pre OP 29.0±9.6%, performed 11.3±19 months thereafter. 52 were in sinus rhythm, 53 had previous LBBB, 14 had previous mitral regurgitation > IIIV. 35 were treated for cardiomyopathy, 25 ischemic. AV was modified in 45 pts, VV in 40 (both in 22). OP was repeated once in 10 pts and twice in 2 pts, 15 pts (23.8%) belonged to GII. Global mortality was 21% and 2 pts were submitted to HTX. LVESD pre IMP was greater in GII (p<0.05). e’ velocities were lower and E/e’ max delay, posterior delay, all segments and basal standard deviation were higher pre OP in GII (p<0.05). At 6 months of FUP there was also a difference between the 2 groups in what concerns: EDD, ESD, PASP, E/Vp, E/e’ (all p<0.05). No parameter derived OP was related to outcome.

Conclusion: Pts submitted to VV and/or AV OP after CRT have a bad prognosis: MACE in 24% after 31 months of follow up. More dilated ventricles preimplantation and pre OP were related to worse outcome and the presence of residual significant dyssynchrony and worse LV function (EF and E/e’) before OP were relevant for prognosis. After OP the greatest predictors of outcome were enlarged ventricles, and residual significant diastolic dysfunction. The immediate changes obtained during OP were not significantly related to prognosis.

NEW INSIGHT IN DOBUTAMINE STRESS ECHO

P5387 | BEDSIDE
The novel index of contractile function: shape of dynamics’s curve of cardiac output during dobutamine stress echocardiography

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Purpose: The purpose of study was to examine of myocardial contractile reserve (MCR) by novel index of contractile function.

Methods: 66 patients with heart disease and with (n=51) or without (n=15) heart failure were studied during dobutamine stress echocardiography with characterization of MCR by Doppler imaging. Measured rest echo parameters, brain natriuretic peptide (BNP) and Minnesota Living with Heart Failure Questionnaire (MLHFC) scores were assessed in all the patients. During the stress test with the help of continuous wave Doppler the blood flow in the ascending aorta was registered. Value of cardiac output (CO) during the stress test was calculated every 10-20 bpm increase. All patients were separated into two groups. Group A (n=33) were patients with decreased MCR and byphasic dynamics of CO (figure, curve A). Group B (n=33) were patients with normal MCR defined as an increment of CO up to submaximal HR and monophasic dynamics of CO (curve B).

Results: The two groups statistically significant (p<0.05) differed for the end-diastolic volume (174.3±94.2 mL in group A vs 110.2±41.5 mL in group B), end-systolic volume (110.6±87.6 mL in group A vs 53.1±34.7 mL in group B), ejection fraction (EF) (44.9±18.7% in group A vs 54.3±13.7% in group B), BNP level (109.5±78.9 pg/mL in group A vs 34.5±39.3 pg/mL in group B) at rest; the CO at load-peak (6.93±2.32 L/min in group A vs 8.02±3.33 L/min in group B) and MLHFC scores (19.6±23.9 in group A vs 4.8±11.3 in group B).

Conclusions: MCR is a measure of the ability of the myocardium to increase its contractility with stress. The normal response is an increase CO up to submaximal HR and monophasic dynamics of CO.

P5388 | BEDSIDE
The medium term prognostic value of dobutamine stress echocardiography in patients with high risk scores of coronary artery disease according to NICE clinical guideline 95

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Coronary artery disease (CAD) is an important differential diagnosis of chest pain. The 2010 NICE Clinical Guideline 95 (CG95) recommends investigating the coronary artery disease by coronary angiography (CA) as first line investigation. However, a significant proportion of these patients will instead receive dobutamine stress echocardiography (DSE), which is recommended for moderate risk patients. A negative DSE in high risk patients will be considered as negative for significant CAD, but the prognosis of these patients, who are usually discharged from cardiologist follow up, is unclear. This study aims to assess the prognosis of high CAD
risk patients following a negative DSE in the first two years following implementation of NICE CG95. In this retrospective study, we identified high CAD risk patients who were referred for DSE from the rapid access chest pain clinic (RACP). We clarified the reasons why patients were not referred for CA. Patients with negative DSE were followed up via the hospital’s electronic record system, which contains all clinical information including inpatient and outpatient attendances, clinical letters, test results, and date of death.

504 patients were referred for DSE from the RACP between September 2010 and August 2012. 164 patients possessed high risk for CAD. 52 were referred based on patient choice, 54 based on clinical assessment, and 7 had contraindications to CA. 117 high risk patients had a negative DSE; these cases were followed up for a median of 21 months. 4 (3.4%) high risk cases had persistent cardiac symptoms requiring additional hospital review and investigations following a negative DSE, of which 1 case (0.8%) had significant CAD identified on angiography requiring percutaneous coronary intervention. The remaining 113 (96.6%) were free from significant clinical complaints requiring hospital attendance.

In the first 2 years following the implementation of NICE CG95, we identified a significant number of high CAD risk patients who were offered DSE. The reasons for selecting DSE over conventional angiography were due to the clinician’s judgement of appropriateness and patient choice in equal parts. The medium term outcome of those who have had a negative DSE is favourable, with only a few (<5%) requiring additional cardiac investigation and 1 case (<1%) of significant coronary disease. Thus, a negative DSE is a reliable objective indicator of good prognosis in patients with high risk of CAD in a chest pain clinic.

**P5389 | BEDSIDE**

**Relative wall thickness is associated with subendocardial dysfunction during dobutamine stress echocardiography**

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**Purpose:** ST segment depression (STD+) on stress ECG and a hypertensive response to stress (HR+) are known markers of adverse prognosis. To address whether STD+ and HR+ may be related to subendocardial ischaemia in individuals without inducible regional wall motion abnormalities during stress (RWMA), we investigated the significance and myocardial consequences of these abnormal findings (STD+ or HR+) using echocardiographic strain as a marker of myocardial tissue deformation.

**Methods:** In this cross-sectional study of 100 low cardiovascular risk pts (age 61±13 yrs; 59% male) without RWMA during DSE, we studied 25 consecutive STD+ pts (<1mm horizontal ST-depression on ECG) and 25 consecutive HR+ pts (SBP 180mmHg at peak), compared with 50 randomly selected controls without STD+ or HR+. Using velocity vector imaging (VVI), longitudinal endocardial and epicardial peak strain global index (PSi) in 12 basal and mid-cavity myocardial segments were averaged from 3 apical views at rest and peak stress. LV mass, volumes and EF were calculated according to AHA guidelines.

**Results:** Demographics, LV volumes and EF, mass and relative wall thickness (RWT) were similar between groups. Although STD+ and HR+ groups had higher resting SBP than controls, there were no differences in resting endocardial or epicardial PS between the 3 groups. At peak stress, epicardial PS was similar in all groups, but endocardial PS in STD+ (<14±3%) and HR+ groups (13±1±4%) was lower than controls (17±5, p<0.01). In a multivariable model (R2=0.25, p<0.01), ST depression (B=0.31, p<0.01) and RWMT (B=0.27, p<0.01) were predictors of endocardial PSi but not LV mass were correlated with endocardial PSi.

**Conclusions:** Pts with stress-induced STD+ or HR+ have impaired subendocardial function, which is associated with increased RWT rather than LV mass.

**P5390 | BEDSIDE**

Stress echocardiography and long-term prognosis in patients after successful primary percutaneous intervention and incomplete revascularization of non-culprit lesions

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**Background:** Stress echocardiography is important noninvasive tool for the detection of myocardial ischemia. Nevertheless its role in risk stratification after primary percutaneous intervention (pPCI) has been incompletely documented. Aim of this study was to assess prognostic value of stress echocardiography after successful pPCI for acute myocardial infarction (AMI). Also, we sought to evaluate prognostic value of (HRR) in stable coronary artery disease.

**Methods:** Our study comprised of 104 patients successfully treated with pPCI. All patients performed stress echocardiography according Bruce protocol in order to assess residual ischemia in coronary artery other than treated vessel. Stress echocardiography was considered positive for ischemia in the case of new or worsening of preexisting wall motion abnormalities. Duke treadmill score, wall motion score index (WMSI) at rest as well as HRR in the first minute after exercise was calculated in all patients. Lesion severity on culprit coronary arteries was assessed by quantitative coronary angiography. All the patients were followed for the occurrence of hard cardiac events: cardiac death, myocardial infarction and coronary artery bypass graft (CABG) intervention.

**Results:** Out of 104 patients 14 patients had positive stress echo test and they were scheduled for elective PCI, remaining 90 patients were included in the study (59 male, 31 female). The average age was 56.9 ± 13.4. During the follow up period (mean 44±13 months) hard cardiac events occurred in 9 patients with negative stress echocardiography (3 deaths, 3 myocardial infarcts, 3 CABG). There was statistically significant difference between patients with and without hard cardiac events regarding Duke score (p=0.019) and HRR (p=0.026). As a result of this, the ASE has defined the appropriate use criteria for echocardiograms exist?

**Conclusions:** Negative stress echo test after successfully pPCI in patients with incomplete revascularization had excellent negative prognostic value for the occurrence of the hard cardiac events. Whereas HRR as well as Duke treadmill score can further stratify risk in these patients.

**P5391 | BEDSIDE**

Does a method to increase appropriately indicated exercise echocardiograms exist?

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**Background:** The burden of diagnostic tests requested without an appropriate indication is remarkable because it means an unnecessary use of limited resources. As a result of this, the ASE has defined the appropriate use criteria for echocardiography in 2011. Our aim was to increase the number of exercise echocardiograms (EE) with a appropriate indication using a simple intervention. Methods: We collected all the EE request forms that arrived at our institution during the intervention period: 50 appropriate (89,3%), 3 inappropriate (5,4%), 1 uncertain (2,0%) and 2 unclassifiable (1,1%). 56 request forms belonged to the post-intervention group: 33 appropriate (94,6%), 0 inappropriate (0,0%), 1 uncertain (1,8%) and 2 unclassifiable (3,6%). The appropriate EE percentage was significantly higher after intervention than before it: Risk Difference 14% (Confidence Interval of 95%: 24% to 3%) and Odds Ratio 2,7 (p<0.029). We did not find significant differences between groups in age (61,2 vs 63,7 years), sex (57% vs 70% male), left bundle branch block (8% vs 9%) or left ventricle ejection fraction (59% vs 57%). The most common indication settings were those related to symptoms (59% vs 57%). The most common indication settings were those related to symp- totic ischemic heart disease and did not change with intervention: “evaluation of ischemic equivalent nonsute” (24% vs 29%, p<0.01) and “postrevascularulation “ (18% vs 21%, p<0.07).

**Conclusions:** The percentage of EE that are requested following an appropriate indication in our hospital is acceptable (75,6%). A simple intervention (lecture and email reminder) significantly improved this percentage without affecting the prescription profile.
Paralympics respond differently to exercise load with respect to the presence of spinal cord injury. A stress echo study

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Objective: Athletes with spinal cord injuries (SCI) have different exercise physiology from other Paralympics: preload cannot be adequately increased, which limits exercise capacity. We evaluated the response of left ventricular (LV) and right ventricular (RV) function to exercise with respect to the type of injury.

Methods: We studied 13 SCI and 34 non-SCI athletes, age 30.7±9.5 years, 17% female, body mass index (BMI) 25.7±7.2 years, in elite sport 7.2±6. We performed an echocardiographic exam at rest and after physical stress. Workload with stepper was 612±2.1365.3 gsm. For wheel-chair athletes we used dumbbell (3.8 kg) reps.

Results: SCI-athletes were older and had smaller BMI, LV end-diastolic diameter and LV mass index and decreased baseline LV twist values; RV dimensions and other LV and RV functional parameters didn’t differ between groups.

Heart rate (HR) increased significantly during exercise in non-SCI-athletes but with borderline significance in SCI-ones – table 1. Maximal HR was higher in non-SCI compared to SCI-athletes (p=0.003). After exercise SCI-athletes had improvement in LV deformation indices and LV diastolic function, while LV twist didn’t increase significantly. RV function improved only during isovolumic contraction, while functional parameters during exercise did not respond to exercise. In contrast, non-SCI-athletes showed improvement of RV systolic indices after exercise (exception was RVGLS). LV systolic response to exercise paralleled that of SCI-athletes, but diastolic function wasn’t affected.

Exercise response in SCI/non SCI athlete

<table>
<thead>
<tr>
<th>Parameter</th>
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<th>SCI athletes</th>
<th>p</th>
<th>Non-SCI athletes</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>59.6 ± 9.75</td>
<td>97.4 ± 1.95</td>
<td>0.05</td>
<td>68.14 ± 1.37</td>
<td>20.00</td>
</tr>
<tr>
<td>LV deformation GLS (%)</td>
<td>−20.1 ± 2.5</td>
<td>−23.4 ± 3.4</td>
<td>0.03</td>
<td>−19.6 ± 2.2</td>
<td>23.1 ± 2.8</td>
</tr>
<tr>
<td>GLSR (s⁻¹)</td>
<td>−1.12 ± 0.16</td>
<td>−1.47 ± 0.33</td>
<td>0.03</td>
<td>−1.13 ± 0.17</td>
<td>−1.61 ± 0.42</td>
</tr>
<tr>
<td>LV E/e’</td>
<td>7.4 ± 1.7</td>
<td>6.4 ± 1.5</td>
<td>0.013</td>
<td>6.1 ± 1.2</td>
<td>6.5 ± 1.2</td>
</tr>
<tr>
<td>LV twist (°)</td>
<td>6.3 ± 0.44</td>
<td>10.6 ± 0.56</td>
<td>0.04</td>
<td>4.4 ± 0.43</td>
<td>16.5 ± 0.9</td>
</tr>
<tr>
<td>RV s’ (cm/s)</td>
<td>11.1 ± 1.5</td>
<td>14.9 ± 3.2</td>
<td>0.04</td>
<td>13.2 ± 2.4</td>
<td>18.3 ± 1.5</td>
</tr>
<tr>
<td>RV V IVA (cm²)</td>
<td>2.9 ± 1.1</td>
<td>5.6 ± 2.8</td>
<td>0.001</td>
<td>3.4 ± 1.1</td>
<td>6.2 ± 2.4</td>
</tr>
<tr>
<td>RV deformation GLS (%)</td>
<td>−29.9 ± 6.4</td>
<td>−33.2 ± 6.2</td>
<td>0.03</td>
<td>−27.6 ± 6.9</td>
<td>−28.3 ± 13.2</td>
</tr>
<tr>
<td>GLSR (s⁻¹)</td>
<td>−2.4 ± 0.54</td>
<td>−3.0 ± 0.72</td>
<td>0.05</td>
<td>−2.18 ± 0.75</td>
<td>−3.19 ± 1.12</td>
</tr>
</tbody>
</table>

Conclusion: Paralympics with SCI show impaired RV response to exercise compared to non-SCI-athletes, probably related to decreased sympathetic drive (HR response and preload changes). Whether this has a protective or damaging effect on RV, remains to be elucidated.

Enhancing patient selection for coronary angiography through the use of carotid ultrasound plaque quantification combined with stress testing as a screening tool

A.M. Johi, M.F. Hetu, C.S. Simpson, P.E. Ewart, M.F. Matangi on behalf of the CardioVascular Imaging Network at Queen's University, Kingston, Canada.

Purpose: To determine if addition of carotid wall thickness to stress testing enhanced sensitivity for prediction of significant CAD and improved selection for angiography.

Methods: Carotid ultrasound was performed on 320 consecutive patients undergoing same-day angiography. 209 patients had recently received at least one imaging based stress test and were selected for analysis. Mean far distal carotid intima-media thickness (CIMT) and maximal plaque height were measured and compared to angiographic scores for prediction of significant CAD. Significant CAD was defined as presence of at least one major epicardial coronary vessel with ≥50% luminal narrowing. Literature threshold values for increased CIMT (>0.8 mm) and plaque definition (>1.5 mm) were used for stratifying patients as low or high risk CAD. Stress test and ultrasound results, alone or combined, were analyzed for accuracy in stratifying patient risk of CAD.

Results: Adding maximum plaque height, measured by carotid ultrasound, to stress testing increased the negative predictive value (NPV) from 28% to 71%, and the sensitivity from 78% to 99%. Stress test/carotid ultrasound combination testing would have re-stratified 34/36 patients from low risk to high risk as confirmed by angiography.

<table>
<thead>
<tr>
<th>Test (N=209)</th>
<th>Sensibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress test</td>
<td>TN 14</td>
</tr>
<tr>
<td>CIMT ≥0.8 mm</td>
<td>FP 35</td>
</tr>
<tr>
<td>Plaque height ≥1.5 mm</td>
<td>TN 34</td>
</tr>
<tr>
<td>Stress test + CIMT ≥0.8 mm</td>
<td>FP 35</td>
</tr>
<tr>
<td>Stress test + plaque ≥1.5 mm</td>
<td>TN 34</td>
</tr>
</tbody>
</table>

Conclusion: In patients undergoing stress testing, CIMT and carotid plaque improved identification of significant stenosis. Carotid plaque quantification significantly improved the NPV of stress testing suggesting this is a practical tool to rule out significant CAD and enhance selection of patients for angiography.
P5396 | BEDSIDE
Combined analysis of myocardial function, viability and perfusion in patients with chronic total occlusion in relation to angiographic collateral flow
L.A. Malek, M. Spiewak, M. Klopotowski, M. Marczak, A. Witkowski. National Institute of Cardiology, Warsaw, Poland
Purpose: Indications for revascularization in chronic total occlusion (CTO) of the coronary artery depend on the interplay between myocardial function, viability and inducible ischemia. Technical feasibility of the procedure often relies on the angiographic collateral flow to the occluded artery. The aim of the study was to comprehensively assess these two aspects of qualification for the revascularization procedure.
Methods: The study included 54 patients (mean age 63 years, 85% males) with CTO referred for cardiovascular magnetic resonance to assess indications for revascularization. All patients underwent stress perfusion cardiovascular magnetic resonance imaging with means of dipyrindamide. The presence of well-developed collateral flow was defined as a collateral connection grade=2 and Rentrop score=3.
Results: In the whole group, wall motion score index (WMSI) of the segments supplied by the CTO correlated with infarct size (rho=0.531, p=0.001) and the size of reversible perfusion deficit in that area (rho=0.284, p=0.04). The presence of well-developed collaterals (n=24, 44%) was less likely related to systolic dysfunction of the segments supplied by the occluded artery (mean WMSI 1.34±0.44 vs. 1.64±0.67, p=0.04) in comparison to lack of well-developed collaterals. Patients with well-developed collaterals had a lower frequency of previous myocardial infarction of the CTO zone (33% vs. 67%, p=0.03), but had similar frequency of transmural infarctions (21% vs. 23%±0.83). They less frequently presented perfusion deficits of the CTO area during hyperemia (42% vs. 70%, p=0.03) and the size of deficits was smaller (median 0.06% [interquartile range 0-1.8%] vs. 7.17% [IQR: 1.53%] of the left ventricular mass, p=0.04).
Conclusions: Systolic dysfunction of the segments supplied by the occluded artery is related to both reversible (due to ischemia) and irreversible injury (previous infarction). Left ventricular segments supplied by CTO with well-developed collaterals are less prone to inducible ischemia; have smaller size of ischemia and inducible ischemia. Technical feasibility of the procedure often relies on the angiographic collateral flow to the occluded artery. The aim of the study was to comprehensively assess these two aspects of qualification for the revascularization procedure.
MULTIMODALITY IMAGING IN VALVULAR HEART DISEASE AND AORTA
P5398 | BEDSIDE
Role of Doppler echocardiography and tissue Doppler imaging in patients with chronic rheumatic mitral stenosis and normal sinus rhythm
A.E.H. Amin, A.A.F. Farrag, W.A.A. Ammar, W.A.E. Elarousy. Cairo University Hospitals, Department of Cardiovascular Medicine, Cairo, Egypt
Purpose: Rheumatic mitral stenosis (MS) predisposes to left atrial (LA) thrombus formation and subsequent embolization. A strong body of evidence recommends anticoagulant therapy in the setting of atrial fibrillation (AF). However, there is no consensus on when to start anticoagulation in MS and normal sinus rhythm (NSR). Tissue Doppler imaging (TDI) is an echocardiographic modality that demonstrates tissue velocities. LA wall fibrosis and hypertrophy secondary to rheumatic MS can be reflected on LA as well as appendage (LAA) wall velocities derived from PW-DTI. We examined TDI derived velocities as predictor of thromboembolic events in MS and NSR.
Methods: Our study included 79 patients with 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 rheumatic MS. Patients with well-developed collaterals had a lower frequency of previous myocardial infarction of the CTO zone (33% vs. 67%, p=0.03), but had similar frequency of transmural infarctions (21% vs. 23%±0.83). They less frequently presented perfusion deficits of the CTO area during hyperemia (42% vs. 70%, p=0.03) and the size of deficits was smaller (median 0.06% [interquartile range 0-1.8%] vs. 7.17% [IQR: 1.53%] of the left ventricular mass, p=0.04).
Conclusions: Systolic dysfunction of the segments supplied by the occluded artery is related to both reversible (due to ischemia) and irreversible injury (previous infarction). Left ventricular segments supplied by CTO with well-developed collaterals are less prone to inducible ischemia; have smaller size of ischemia and inducible ischemia. Technical feasibility of the procedure often relies on the angiographic collateral flow to the occluded artery. The aim of the study was to comprehensively assess these two aspects of qualification for the revascularization procedure.

P5399 | BEDSIDE
Transesophageal echocardiography in tavi without balloon pre-dilation: experience of a single center
F. Islas, C. Almeria, C. Olmos, A. De Agustín, P. Marces-Alberca, J.L. Rodrigo, J.J. Gómez, C. Macaya, L. Perez De Isla, E. Garcia. Hospital Clin San Carlos, Cardiovascular Institute, Madrid, Spain
Purpose: Transcatheter aortic valve implantation (TAVI) is an alternative therapy in high-risk patients with severe aortic stenosis. Balloon pre-dilation is still a common procedure for valve preparation, however, TAVI without pre-dilation has been described as a feasible and safe procedure. The aim of this study is to show the usefulness of transesophageal echocardiography (TEE) during the patient selection and TAVI procedure guidance to aim a high success rate with minimal complications.
Methods: 63 patients with severe aortic stenosis did not considered candidates to balloon pre-dilation. Treatment were selected for TEE evaluation prior to TAVI. After 2D and 3D TEE evaluation and measurement of aortic annulus and root, mobility of valve cusps, orifice characteristics and valve area, degree of calcification of the valve and aortic regurgitation, patients were considered, according to our criteria for TAVI without balloon pre-dilation.
Results: Mean age was 82±5 years. Mean aortic valve area was 0.61±0.16cm² and mean aortic annulus diameter was 2.2±0.125cm. Edwards Sapien pros thesis were implanted in 62% (n=39), some degree of paravalvular leakage was seen in 62% of patients (n=38) and only 22% (n=14) required post-dilation due to regurgitation grade >3. Only 1.6% (n=1) of patients had severe paravalvular regurgitation that required a second intervention. Permanent pacemaker was needed in 6% of patients (n=4). No clinical embolisms were observed during the procedure and the follow-up.
Criteria for TAVI without pre-dilation

<table>
<thead>
<tr>
<th>Valve area</th>
<th>Valve annulus</th>
<th>Absence of calcium nodules*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable for TAVI</td>
<td>0.4cm²</td>
<td>ECCentric or Tor orifice</td>
</tr>
<tr>
<td>Non-Favorable for TAVI</td>
<td>≤ 1.6 cm²</td>
<td>eccentric from the leaflets</td>
</tr>
</tbody>
</table>

Conclusion: The proper assessment of aortic annulus diameter, distribution of calcium, mobility of the leaflets and characteristics of the residual orifice with TEE allows to select patients with the ideal conditions for TAVI without balloon pre-dilation. Using these criteria the success rate with minimal complications.

P5400 | BEDSIDE
Mitril valve and left ventricular reverse remodeling after surgical repair of submitial left ventricular aneurysms assessed with multi-slice computed tomography
N. Solowjowa, A. Penkalla, M. Dandel, M. Pasic, Y. Weng, R. Hetzer, C.H. Knosalla. German Heart Center Berlin, Berlin, Germany
Purpose: Surgical repair of submitial aneurysms may present a technical challenge especially if the mitral valve (MV) apparatus is involved. We present the center surgical experience with the potential of multi-slice computed tomography (MSCT) in assessment of changes of MV and LV geometry and aneurysm morphology.
Methods: Between 05/06 and 12/13, 24 patients (n=20±4, ages 38-78, mean 62.3±3 years; mean NYHA class 2.91) with submitial LV aneurysm were operated. Echocardiography and MSCT were performed before and a short time after surgery. LV and aneurysm end-diastolic/end-systolic, stroke volume and aneurysm defect area (ADA) were measured and indexed to body surface area (LV-EDVI/LV-ESVI, A-EDVI/A-ESVI, SVI, SVI respectively). LV ejection fraction (LVEF) and cardiac index (CI) were calculated on the basis of MSCT data. MV geometry was characterized by intercommisural and anteroposterior MV annulus diameter (IC and APD respectively), MV annulus area (MVA), coaptation distance (CD), tenting area (TA), MV closure angle (MCVA), interpapillary muscle distance (IMD), distance between MV annulus and posterior papillary muscle head (AnAPMD).
Results: Thirty-five and 5-year survival was 91.3% and 82.6%, respectively. 58.5% of patients were operated urgently, 26% needed concomitant MV surgery, but repair were performed in 47.5%, linear repair in 52.5%. There was a statistically significant increase in LVEF and decrease in LV volumes in the overall population after surgical ventricular repair. Preoperative measured MVA, CD and TA were significantly higher in patients who needed MV repair/replacement (MVA 10.7±1.9 vs. 8.8±1.5, p=0.038; CD 12.7±2.9 vs. 10.1±1.6, p=0.026; TA 3.1±1.6 vs. 1.8±0.4, p=0.020). Postoperative reduction of mitral regurgitation from grade 0.84 to 0.25 in the remaining 17 patients without concomitant mitral
valve surgery corresponded with improvement of RV geometry with significant reduction in ICD, APD, MWA, TA, CD, MVCA and IMD. We found no clinical or CT-morphological variables of statistical significance that were predictive for decision between linear and patch repair.

**Conclusions:** Surgical reconstruction of submural LV aneurysms can be performed with good early and mid-term results. MSCT with possibility to analyze the coherence of ventricular remodeling and geometrical changes in mitral valve apparatus represents an excellent diagnostic tool for pre-operative planning of this complex surgery.

### P5401 | BEDSIDE

**Profitability of coronary computed tomography as evaluation before valve surgery**

S. Prado Diaz1, D. Iglesias Del Valle2, E. Retoyo Salicio3, E. Cuesta3, J.A. Blazquez4, J.M. Mesa5, S.C. Valbuena Lopez3, M. Moreno Yanguela6, J.L. Lopez-Sendon1, G. Guzman Martinez1,1 University Hospital La Paz, Dept. of Cardiology, Madrid, 3 University Hospital Infanta Sofia, Dept. of Cardiology, Madrid, 4 University Hospital La Paz, Dept. of Radiology, Madrid, 5 University Hospital La Paz, Dept. of Cardiovascular Surgery, Madrid, Spain

**Purpose:** The ESC recommends evaluating coronary angiography with IC indi-
cation in most patients who are going to valve surgery. Nowadays coronary com-
tputed tomography angiography (CTA) is the chosen technique in patients without
history of coronary artery disease nor suspected myocardial ischaemia. We anal-
ysed the profitability of non-invasive versus invasive coronary angiography (ICA)
during a year in a tertiary hospital.

**Methods:** We analysed all patients with coronary CTA performed between Jan-
uary and December 2011 to evaluate coronary artery disease prior to valve
surgery. Multislice CT with 64 detectors was used. When calcium score showed
high Agatston score coronary CTA was not performed and patients were remitted
to ICA. If CTA results were not conclusive, or significant lesions were present, they
were remitted to cardiac catheterization. Procedure costs were: calcium score
32.26€, coronary CTA 199€ and night at hospital 741.66€. For ICA, one day of
hospitalization is needed if no complications appeared. We evaluated profitability
of coronary CTA as first choice versus ICA.

**Results:** 104 patients, whose mean age was 67.2±12.8, were submitted to per-
calcium score, and 20 (19.2%) of them were submitted to ICA. 80.8%
and larger RV end-systolic volume (93.2

### P5402 | BEDSIDE

**Geometrical remodeling of the tricuspid valve in functional tricuspid regurgitation assessed with multi-detector row computed tomography**

P.J. van Rosendaal, E.M. Joyce, S. Katsanos, P.J.M.R. Debonnaire, V. Kamperidis, F. Van Der Kley, A.J.H.A. Scholte, J.J. Bax, N. Aymone Marzan, V. Delgado. Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

**Purpose:** Multi-detector computed tomography (MDCT) may help to understand the
underlying mechanisms of functional tricuspid regurgitation (TR). Present
evaluation aimed to assess the geometrical changes of the tricuspid valve in pa-
ients with functional TR using MDCT and to correlate these changes with the TR
grade.

**Methods:** In 114 patients (47 men, age 81±8 years), including 33 (28.9%) pa-
tients with TR≥3+, the tricuspid valve and right ventricle were geometrically anal-
yzed with 320-slice MDCT. The antero-posterior and septal-lateral diameters, per-
imeter and area of the annulus, degree of tethering of the anterior, septal and
posterior tricuspid valve leaflets and right ventricular (RV) volumes and ejection
fraction were assessed and subsequently correlated with TR grade in multimodality
analysis. The utility of CMR or ICD leads was excluded.

**Results:** Patients with TR≥3+ had larger tricuspid annulus area (1539.7±260.2
mm² vs. 1228.4±243.5 mm², p<0.001), larger septal and anterior leaflet angles
and larger RV end-systolic volume (93.2±28.9 ml vs. 64.2±23.6 ml, p<0.001)
as compared with patients with TR<3+. The antero-posterior tricuspid annulus
diameter was independently correlated with TR≥3+, after adjusting for pulmonary
hypertension and RV end-systolic volume (Table).

<table>
<thead>
<tr>
<th>Multivariate</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pulmonary artery pressure (mmHg)</td>
<td>1.06 (1.01–1.12)</td>
<td>0.030</td>
</tr>
<tr>
<td>Right ventricular end-systolic volume (ml)</td>
<td>1.03 (1.01–0.06)</td>
<td>0.015</td>
</tr>
<tr>
<td>Tethering anterior tricuspid leaflet (°)</td>
<td>0.94 (0.79–1.13)</td>
<td>0.522</td>
</tr>
<tr>
<td>Tethering septal tricuspid leaflet (°)</td>
<td>1.18 (0.98–1.41)</td>
<td>0.079</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>0.95 (0.91–1.00)</td>
<td>0.052</td>
</tr>
<tr>
<td>Moderate-severe mitral regurgitation (%)</td>
<td>3.40 (0.88–13.10)</td>
<td>0.075</td>
</tr>
</tbody>
</table>

**Conclusions:** In patients with TR≥3+, MDCT demonstrated larger tricuspid an-
nulus and RV dimensions and the antero-posterior annulus diameter was inde-
pendently correlated with the grade of functional TR.

### P5403 | BEDSIDE

**Evaluation of valvuloarterial impedance in aortic valve stenosis by cardiac magnetic resonance**

G. Soulati1, E. Bollache1, F. Pontneau1, L. Perdrix1, C. Defrance1, V. Zghalina1, P. Achouh1, C. Latremouille1, N. Kachenoura2, E. Mousseaux1, European Hospital Georges Pompidou, Paris, France; 4 National Institute of Health and Medical Research (INSERM home), U678, Paris, France

**Purpose:** In aortic valve stenosis (AVS), valvuloarterial impedance (ZVA), as left
ventricle afterload estimation, has been proposed in echocardiography (TEE) to
predict adverse outcome better than conventional parameters such as aortic valve
area (AVA). However its calculation method differs from standard temporal arterial
characteristic impedance (Zc) assessment. The aim of our study was to apply and
to validate the Zc concept of measurements to estimate ZVA by using cardiac
magnetic resonance (CMR) and carotid tonometry central blood pressure data.

**Methods:** The study included 40 patients (76±13 years, 21 males) who under-
went CMR with cardiac magnetic resonance and echocardiography. The same day.
We have evaluated ZVA methods by comparing their links with diastolic dysfunction
estimated by E/Ea ratio at TTE.

**Results:** ZVA were higher in symptomatic when compared to asympto-
tomatic patients using both TTE and CMR methods. In univariate analysis, only
ZVA when calculated with CMR was correlated with E/Ea (R2=0.25, p<0.001).AVA
was also significantly correlated with E/Ea (R2=0.11, p=0.04).

**Conclusions:** By using CMR in association with central aortic blood pressure,
the calculation of ZVA is feasible and can improve left ventricle afterload assessment
in AVS. ZVA in magnetic resonance was better correlated with diastolic dysfunc-
tion than ZVA estimated by TTE. This new way to estimate ZVA may be clinical
useful in evaluation of patient with AVS, especially in asymptomatic patients.

### P5404 | BEDSIDE

**Multi-center investigations for prevalence of abdominal aortic aneurysm in elderly Japanese patients with hypertension using pocket-sized echocardiography - AAA Japan Study -**

H. Oe1, S. Fukuda2, H. Watanabe3, K. Iwakura3, M. Daimon3, J. Yoshikawa3, H. Ito4 on behalf of AAA Japan Study. 1Okayama University Hospital, Okayama, Japan; 2Osaka Ekiakai Hospital, Department of Medicine, Osaka, Japan; 3Tokyo Bay Urayasu/Ichikawa Medical Center; Heart Center, Urayasu, Japan; 4Sakurabashi-Watanabe Hospital, Division of Cardiology, Osaka, Japan; The University of Tokyo Hospital, Department of Clinical Laboratory, Tokyo, Japan; 5Sakurabashi-Watanabe Hospital, Division of Cardiology, Osaka, Japan; The University of Tokyo Hospital, Department of Clinical Laboratory, Tokyo, Japan; 6Nishinomiya Watanabe Cardiovascular Center, Nishinomiya, Japan; 7Okayama University, Department of Cardiovascular Medicine, Okayama, Japan

**Background:** The importance of screening programs for abdominal aortic
aneurysm (AAA) is now well recognized, although the ability of physical exam-
injection, as an initial screening tool to diagnose cardiovascular disease, has been
delayed over the last 20 years. The purpose of this study was to determine the
prevalence of AAA in elderly Japanese patients with hypertension and to clarify
the diagnostic accuracy of physical examination in the current era, using minia-
turized pocket-sized echocardiographic imaging device (pocket-echo).

Methods: This study consisted of 1,731 patients with hypertension aged over
60 years (942 males, mean age 75.8±6 years) from 20 collaborating institutions.
Abdominal palpation was examined on physical examination. The pocket-echo
was used for the diagnosis of AAA (defined as greater than 30 mm or more than
1.5 times the diameter of the proximal aorta).

Results: The abdominal aorta was well-visualized in 1,692 (98%) patients. AAA
was discovered in 69 (4.1%) patients. Advanced age and male gender were in-
dependent risk factors associated with AAA. The incidence of AAA was highest
in males aged over 65 years and was lowest in female between 60 and 69 ages
(0.6%). Thirty-three AAA were missed on abdominal palpation (sensitivity of 52%).
Sensitivity of abdominal palpation increased to 75% in AAA greater than 40 mm.

Conclusions: AAA Japan study was the large multicenter cohort investigation
using pocket-echo, to determine prevalence of AAA in Japanese patients with
hypertension aged over 60. The results of the present study strongly indicated
the importance of AAA screening program in high-risk Japanese population as
well as the ability of physical examination to detect large AAA, not for small AAA.

PS5045 | BEDSIDE
Association of abnormal aortic wall properties and arterial wave reflections
with impaired coronary flow reserve in coronary artery disease patients after
successful revascularization
I. Ikonomidou1, V. Tritakis1, G. Pavlidis2, S. Tzortzis2, P. Trivizou2, N. Kadoglou2,
J. Papadakis1, J. Paraskevaidis2, A. Anastasiou-Nana2, J. Lekakis1, I. University
of Athens, Athens, Greece; 2University of Athens Medical School, Attikon
Hospital, 2nd Department of Cardiology, Athens, Greece

Impaired coronary flow reserve (CFR) has a prognostic value in CAD patients. Aortic
wall properties and wave reflections determine coronary perfusion. LV function
and have an independent prognostic value. We investi-
gated the association of aortic stiffness an abnormal wave reflection with resting
coronary flow and coronary flow reserve (CFR) in CAD patients after revascu-
larization.

Methods: We assessed in 55 patients with CAD and who underwent PCI in LAD
or CABG within 6 months. We measured pulse wave velocity using both the Com-
plior (carotid to femoral-PWVc) and Arteriograph apparatus (PWVa-oscillometric
method). Between 2005 and 2007, 542 patients (ps) were referred
for evaluation with transesophageal echocardiography (TEE). Age: 65±0.8±13.32
years. Male gender: 306 patients (ps) (56.5%). The following variables were in-
cluded: reason for ordering the study (embolic source 37.5%, endocarditis 22.5%,
previous to cardiovascular 10.9%, mitral valve disease 10.1%, other reasons
19.4%), risk factors (diabetes, smoking habits, hypertension, dyslipidemia) and
presence of atrial fibrillation. Common carotid intima-media thickness (IMT)
was manually measured or the presence of carotid plaques was registered. According
aortic findings the patients were divided into two groups: a-with un complicated
aortic plaques <4 mm: ps= 413 and b-with complex aortic atheromatosis (CAA):
aortic plaques ≥ 4 mm, with ulcers, thrombi or aortic dehis: ps = 129.

Follow-up: 1596 days (mean: 759 days). A total of 474 ps (87.45%) were contacted; the fol-
lowing events were considered: transient ischemic attack or stroke, AMI, angiina,
revascularization and/or cause of mortality during that period. Multivariate analy-
sis was used to identify independent predictors. A p value <0.01 was considered
statistically significant.

Results: Global mortality during follow-up was 13.3% (n=63). Cardiovascular
mortality was 6.3% (13/365) in the group of patients with simple or uncomplicated
plaques or with absence of plaques and 17.4% (19/109) in the group with CAA
(p<0.01). There were 132 combined cerebrovascular and/or coronary events; 89
in the group without CAA (89/365, 24.4%) and 43 in the group with CAA (43/109;
39.4%) (p<0.01). These differences were significant at multivariate analysis (OR
3.79, 95% CI 1.72-8.30=p<0.0009 and OR 1.89, 95% CI 1.15-3.09=p<0.01
respectively).

Cardiovascular mortality was 2.7% (7/255) in pts without carotid plaques
and 11.4% (25/219) in pts with carotid plaques. These differences had a weak
statistic significant at multivariate analysis (OR 2.83, 95% CI 1.14-7.01=p<0.025).

There were no significant differences in IMT between patients with and without

Conclusions: In this population, CAA was an independent predictor of cardiovas-
cular mortality and combined vascular events and the presence of carotid plaques
was an independent predictor of cardiovascular mortality. IMT was not an inde-
pendent predictor of cardiovascular mortality or combined vascular events.

PS5046 | BEDSIDE
4D echocardiography combined with spatiotemporal image correlation in the
prenatal diagnosis of total anomalous pulmonary venous connection
Y. Zhang, H. Ye, L. Sun, X. Liu, J. Han, X. Gu, Z. Li. Beijing AnZhen Hospital
affiliated to Capital Medical University, Department of Ultrasound, Beijing, China,
People’s Republic of China

Objective: Prenatal diagnosis of total anomalous pulmonary venous connection

INNOVATION IN IMAGING

PS5049 | BECH
Echocardiography combined with spatiotemporal image correlation in the
prenatal diagnosis of total anomalous pulmonary venous connection
Y. Zhang, H. Ye, L. Sun, X. Liu, J. Han, X. Gu, Z. H. Li. Beijing AnZhen Hospital
affiliated to Capital Medical University, Department of Ultrasound, Beijing, China,
People’s Republic of China

Objective: Prenatal diagnosis of total anomalous pulmonary venous connection

INNOVATION IN IMAGING

INNOVATION IN IMAGING

INNOVATION IN IMAGING
PS410 | BENCH
Acoustically active catheter prototype: selective detection of its tip by Doppler ultrasonography
M. Belotlavek1, E. M. Mcmahon1, M. Katayama1, J. C. Westerdale1, I. Z. Nenadic2, M. Fatemi2,3

Purpose: To develop an ultrasound-based catheter navigation system that does not rely solely on catheter tip identification by artifact-prone B-mode (grayscale) echocardiographic scans; instead, the catheter tip is unambiguously detected by a novel use of Doppler ultrasound.

Methods: A 2-mm piezoelectric crystal was affixed at the tip of a catheter prototype and connected to a waveform generator. We hypothesized that crystal vibrations of appropriate frequency and amplitude will interact with an incoming Doppler ultrasound signal and produce a new signal interpreted as a unique Doppler shift. If this hypothesis was correct, then a color spot would be generated and mark the location of the catheter tip in color flow Doppler (CFD) images. We used an elastic mechanical model of a beating left ventricle (LV) with stroke type and connected to a waveform generator. We hypothesized that crystal vibrations of appropriate frequency and amplitude will interact with an incoming Doppler ultrasound signal and produce a new signal interpreted as a unique Doppler shift. If this hypothesis was correct, then a color spot would be generated and mark the location of the catheter tip in color flow Doppler (CFD) images. By adjusting the CFD scale, colors depicting intraventricular flow are minimized and the catheter tip becomes clearly color-marked (Fig. 1C).

Results: We found that driving the crystal by a sinus signal of 1-3 kHz frequency at 10-20 Volts produces interactions interpreted by a clinical echo machine as a novel use of Doppler ultrasound.

Conclusions: We have developed an initial prototype of an acoustically active catheter whose tip can be uniquely color-marked within CFD images. Animal studies are required to preclinically test this novel use of Doppler imaging for catheter tip detection and navigation inside a life heart.

PS411 | BEDSIDE
Role of 18F-FDG PET/CT in the diagnosis of infective endocarditis in patients with implanted cardiac devices: a prospective study
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Purpose: The diagnosis of IE is currently based on the modified DUKE criteria, where the only validated imaging technique is echocardiography and remains challenging. The aim of the study was to assess the diagnostic role of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) in patients with implanted cardiac devices and suspected IE.

Methods: We prospectively analysed 27 patients evaluated for suspected device-related IE between January 2011 and June 2013. The probability of IE was defined at presentation according to the modified DUKE criteria and PET/CT was performed as soon as possible. Patients underwent medical or surgical treatment based on the overall clinical evaluation. During follow up, we considered: lead cultures in patients who underwent extraction, direct inspection and lead cultures in those who underwent surgery and a clinical/instrumental re-evaluation after at least 6 months in patients who received antimicrobial treatment or had an alternative diagnosis and were not treated for IE. After the follow up period, diagnosis was reviewed by the multidisciplinary team, using the modified DUKE criteria and considering the new findings.

Results: Among the 10 patients with positive PET/CT, 7 received a final diagnosis of “definite IE”, one of “possible IE” and two of “reject IE”. Among the 17 patients with a negative PET/CT, 4 were false negatives and received a final diagnosis of “definite IE”. These patients underwent PET/CT after having started antibiotic therapy or had a technically suboptimal exam.

Conclusions: In patients with cardiac devices, PET/CT increases the diagnostic accuracy of the modified Duke criteria, particularly in the subset of patients with “possible IE” in whom it may help the clinician to manage a challenging situation.
diography, increasing the number of adequate echocardiographic studies and determining a large number of releases from the outpatient clinic. This ultrasonic approach has a significant impact on the decision making of the patient, allowing an accurate and rapid diagnosis and a better stratification of patients.

P5413 | BEDSIDE

Right heart in young people by three-dimensional (3D) and Speckle Tracking echocardiography: atrial and ventricular volumes and deformation properties study

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Background: RV (right ventricle) plays an important role in determining cardiac symptoms in several diseases and RA (right atrium) is a quantitative marker of RV dysfunction severity. Real-time 3D echocardiography (3DE) enables accurate ventricular and atrial volume measurement. Speckle Tracking is a sensitive tool to quantitatively assess regional deformation properties.

Purpose: To obtain normal reference ranges for RA volumes, RA EF, by 3D (both software Auto LVQ GE Healthcare and TomTec 4D), RV volumes, RV EF, by 3DE (TomTec) and RA and RV deformation properties by Speckle Tracking and intra-observer variability.

Methods: 70 subjects, 38 males and 32 females, aged 25±7 yrs, without any-cardiovascular disease, were included. By E9GE we measured RA (maximum and minimum) both by biplane method and by 3D and 4D methods, and RV volumes (in apical 4-chamber, short-axis, and coronal views) by tracing endocardial borders at ventricular end-systole and end-diastole. Volumes were indexed for body surface. By Speckle tracking we measured 2D longitudinal systolic RA and RV (Strain (S) and Strain rate (SR) in apical 4-chambers view, at level of RA and RV free wall (basal, medium and apical segments).

Results: We have reported, in young people, references range of RA and RV volumes: 2DRA maximum 32.35±8.2 ml, indexed 18.27±4.14 ml/m2, minimum 15.46±4.12 ml, indexed 8.7±1.91 ml/m2; 4DRA maximum 43.09±11.21 ml, indexed 24.25±5.25 ml/m2; minimum 22.32±6.14 ml; indexed 12.54±2.86 ml/m2; 3D TomTec 41.68±12.22 ml, indexed 23.35±5.69 ml/m2; minimum 23.73±7.9 ml, indexed 13.08±3.7 ml; 3D RV end-diastolic:33.11±ml/m2; end-systolic volume:16.6±dl/ml; and RA and RV ejection fraction: 2D RAEF ±7.5%; 4D RA EF 47.8±7.2%; 3D RA EF 44.6±7.3%; 4D RVEF 67.8±8%. We found a gradient between different segments for RA S (basal –80%, medium 52±9.66%, apical 26.54±3.56%); RA SR (basal 5±0.71S-1; medium 3.33±0.61S-1; apical 2.1±0.26S-1); RV S (apical -25.49±4.8%; medium -29.69±4.78%; basal -30.58±4.8%); RV SR (apical -1.4±0.25± S-1; medium -1.76±0.37 S-1; basal -2.1±0.4 S-1). For RA volumes we found significant differences only between 2DE and 3D methods (p<0.0001) and not between the two 3D methods (p>0.6). Intra and interobserver variability coefficients were 7% and 4% for 3D volumes and 8% and 4% for SR measurements, respectively.

Conclusions: The present study provides normal reference values for RA and RV volumes and EF by 3DE and normal longitudinal RA and RV deformation values in young people. 3DE overcomes the limitations of 2DE to assess the complete anatomy of the RV and 2DE underestimation of RA volumes.

P5414 | BEDSIDE

Gender difference of cardiovascular morphological characteristics of patients with ellipsoid-shaped aortic annulus evaluated by three-dimensional transthoracic echocardiography

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Background: Three-dimensional (3D) transthoracic echocardiography (TTE) has developed and provided a detailed shape of aortic annulus, and then we previously reported that an angle between interventricular septum and ascending aorta (IVS-Ao angle) was independently associated with a morphological change of aortic annulus in patients without cardiovascular disease. The purpose of our present study is to investigate the gender difference of parameters associated with the morphological change of aortic annulus.

Methods: Two-dimensional and 3D TTE were performed in 108 patients without cardiovascular disease (age: 56±18 years, 53 males). Using the cutting image obtained by 3DTEE, we measured the minimum and maximum diameters of aortic annulus, the diameter of Valsalva sinus (Val) and the IVS-Ao angle, and then the eccentricity index of aortic annulus (EI: 1 – minimum diameter/maximum/diameter) was calculated and the Val was indexed by the body surface area. Between male and female patients, we compared the relationships between EI and age, body mass index (BMI) or echocardiographic indexes.

Results: IVS-Ao angle, age and Val index were correlated with EI in both male and female patients (Table). On multivariate regression analysis by these parameters, in male patients, IVS-Ao angle and Val index were independently associated with EI (p=0.05; r=0.29; p=0.01, respectively). On the other hand, in female patients, only IVS-Ao angle had independent association with EI (p<0.05; r=0.51).

Conclusions: Our findings suggest that acute angle between the interventricular septum and the ascending aorta is a morphological change of an ellipsoid-shaped aortic annulus regardless of the gender. In addition, in male patients, dilatation of Valsalva sinus may also leads to ellipsoid-shaped aortic annulus.

P5415 | BENCH

Using volume rendered CT images in teaching anatomy to medical students


Purpose: There is still a big debate on the pros and cons of theoretical and practical teaching methods. Evolution of the multi-detector computed tomography technology has allowed for high resolution imaging and 3D reconstruction of the heart. The objective of this study was to assess if the anatomy of the heart could be taught to first year medical students using volume rendered CT images. Furthermore, we sought to investigate the effectiveness of this practical teaching method compared to theoretical oral lecture and practical dissection practice.

Methods and materials: 73 first year medical students who achieved at least 80% on their first midterm exam took part in the study. Students were randomized into three groups: theoretical lecture (TL, n=22), practical dissection (PD, n=27) and practical radiology (PR, n=24) group. All groups took part in a 2 hour course focusing on the macroscopic features of the heart. The effectiveness of the teaching techniques was tested by a written exam five days after the classes. The exam consisted of 25 theoretical questions and a practical part where 25 features had to be identified on anatomical specimens. Since motivation and other psychological aspects contribute to the effectiveness of a teaching method, a 5 point opinion questionnaire was filled out by the students before and after the exam. Kruskal-Walls ANOVA test was used to compare the three groups.

Results: The PD and the PR group scored significantly higher on the practical questions and on all opinion questionnaire scores compared to the TL group (median score: 9; 6, 5.5, respectively, p<0.05). No significant differences were seen
in the theoretical question scores between the three groups. (median score: 17, 18, 16, respectively, p=0.22).

Conclusions: The results show that practical teaching methods seem to be more effective in teaching anatomy compared to theoretical teaching methods, and suggest that modern radiological approaches can be of additive value in teaching anatomy.

P5417 | BEDSIDE
Neural network model for prediction and prognosis of myocardial infarction in patients with previous revascularization; 15-year experience

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The purpose of this study was to assess the usefulness and accuracy of artificial neural network in the prediction and prognosis of acute myocardial infarction (AMI) in patients with coronary previous artery bypass grafting (CABG).

Materials and results: From January 1999 to January 2014, the baseline characteristics and clinical data were recorded in 4360 consecutive patients. The data set contains 13 predictor variables per patient. It was first randomly split into training (2180 cases) and test sets (2180 cases). Artificial neural network performance in outcome prognosis of AMI was not efficient in the test data set, containing patient data not used for training the network. The program compared actual with predict outcome for each patient, generating a file of comparative results. At the end, results from this file were analyzed and compared, on the basis of receiver operating characteristics (ROC) areas. Logistic regression analysis, as one of standard prediction model, was not efficient for prediction and prognosis of acute myocardial infarction in patients with prior CABG. The results show that a traditional statistical model is not able to perform class separation in multidimensional space and that a nonlinear approach is justifiable. In analyzing the performance of neural network in outcome prognosis of AMI, it is clear that neural network method was better for almost all statistic parameters for all analyzed predictor variables.

Conclusions: In this clinical situation, artificial intelligence appears to be superior to traditional method for prediction and prognosis of AMI in patients with previous CABG.

P5418 | SPOTLIGHT
Learning cardiovascular pathophysiology by creating your own virtual patient with CircAdapt simulator

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Purpose: To develop a user-friendly interactive simulation environment that can be used by medical students and clinical fellows with the aim to improve their understanding of cardiovascular hemodynamics and related physiology and pathophysiology.

Methods and results: The CircAdapt simulator model of the human heart and circulation forms the core of the CircAdapt Simulator freeware. Valves, large blood vessels, atrial and ventricular cavities, myocardial tissue and peripheral resistances are represented by modules each incorporating established physiological and physical principles. These modules form a network, representing the entire cardiovascular system. It enables real-time simulation of dynamic pressure, volume and blood flow velocity tracings in the heart, blood vessels, valves and shunts, if present. The CircAdapt Simulator is designed as an interactive user-friendly shell around the CircAdapt model. Without much foreknowledge, a novice user can intuitively simulate complex pathophysiologic situations by manipulating for instance diameter and leakage of heart valves (figure), contractility and stiffness of cardiac walls, stiffness of arteries, and by the creation of shunts. A wide selection of haemodynamic signals can be displayed as required to show resulting effects. Presently, the CircAdapt Simulator is successfully integrated into the first, second and third year of our institution's medical school.

Conclusions: The CircAdapt Simulator is an innovative freeware tool for teaching cardiovascular physiology and pathophysiology over a wide range of disciplines. It is an excellent tool for education of medical students and for analyzing more complex clinical cases by trainees in different disciplines such as cardiology, neonatology, pulmonology and critical care medicine.

EARLY AND LONG-TERM OUTCOME OF PCI

P5420 | BEDSIDE
Long-term clinical outcome after coronary revascularization in hemodialysis patients

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Background: Although coronary revascularization, regardless of surgical or percutaneous procedures, has been widely performed in hemodialysis (HD) patients, the long-term outcomes remain unknown in such population who are at the highest cardiovascular risk. We investigated clinical outcome after various coronary revascularization in HD patients.

Methods: The CircAdapt Simulator is an innovative freeware tool for teaching cardiovascular pathophysiology.

Results: Learning cardiovascular pathophysiology by creating your own virtual patient with CircAdapt simulator.

Conclusions: The CircAdapt Simulator is an innovative freeware tool for teaching cardiovascular physiology and pathophysiology over a wide range of disciplines. It is an excellent tool for education of medical students and for analyzing more complex clinical cases by trainees in different disciplines such as cardiology, neonatology, pulmonology and critical care medicine.
At follow-up echocardiography, L VEF showed a significant improvement (L VEF: left ventricular function).

Conclusions:

- 71.9% men). During 22,159 patient-years of follow-up 1080 patients died. 30-
- Cardiac deaths after PCI occur mainly in the first month and re-
- non-cardiac causes are responsible for the majority of deaths after 5 years.

**P5424 | BEDSIDE**

Long-term prognostic impact of in-hospital cerebrovascular accidents and stent thrombosis in patients undergoing percutaneous coronary intervention

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**Introduction:** In-hospital cerebrovascular accidents (CVA) and stent thrombosis (ST) are rare but serious adverse events after percutaneous coronary intervention (PCI). CVA and ST are associated with a poor outcome but their relative contribution to long-term mortality has not sufficiently been investigated.

**Methods:** The study included 18,334 consecutive patients who underwent PCI. The CVA and definite ST were diagnosed according to the accepted criteria. Patients were divided into 3 groups: the group with CVA, the group with ST and the group with none of these events. The primary outcome was all-cause mortality. The length of follow-up was 3 years.

**Results:** In-hospital CVA was observed in 90 patients (0.49%) and ST in 59 pa-

**Conclusion:** Treatment with second generation DES, multivessel dis-

**P5425 | BEDSIDE**

Survival after percutaneous coronary intervention (PCI): comparison of patients with or without left anterior descending stenosis in elective PCI for left main disease and triple vessel disease

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**Background:** Patients with significant left anterior descending artery disease, particularly when the proximal segment is involved (termed pLAD), are consid-

**Objective:** We aimed to find out if the long term mortality of patients with pLAD among or short with three vessel lesions (TVD) and/or left main stenosis (LMS) was higher than that without pLAD.

**Methods:** Patients undergoing elective PCI with drug eluting stents (DES) for LMS or TVD were included in this cohort study. Important exclusion criteria were previous coronary artery bypass surgery, high-risk acute coronary syndrome in-

**Conclusion:** The in-hospital occurrence of CVA or ST after PCI is rare but asso-

**Figure 1**

Mortality at 3 years in the three groups.

**Conclusion:** The in-hospital occurrence of CVA or ST after PCI is rare but asso-

**Figure 1**

Mortality in NSTEMI.
used the Kaplan-Meier method to estimate the mortality and calculated adjusted hazard ratios by Cox models.

**Results:** We identified 1,262 patients who met the entry criteria, thereof 24% female. Mean age was 67.7±10.3 years. Median follow-up (interquartile range) was 1120 (985 – 1391) days. Mean SYNTAX score was 21.3±8.6. pLAD was present in 364 patients (28.8%). SYNTAX score in group with pLAD was higher (20±8.4 vs. 24.7±8.2, p<0.001) than that without pLAD. There was no significant difference of one-year, two-year and three-year mortality between both groups (3±0.9% vs. 2.9±0.6%, 5±0.1±2% vs. 5±0.7, 8±0.1% vs. 8±0.1%, p=0.67, 0.64; 0.69). In the cohort with pLAD, one-, two- and three-year mortality between the group with and without pLAD showed also no significant difference (2.1±0.8% vs. 2.7±0.6%, 4.5±1.2% vs. 5±0.8, 7±1.6% vs. 7.2±0.9%, p=0.26; 0.38; 0.62).

Compared to the group without pLAD, the hazard ratio (95%-confidence interval) for mortality in the pLAD group was 1.08 (0.76–1.54, p=0.67). Even after adjustment for SYNTAX score and logistic EuroScore, pLAD was not predictive for mortality (adjusted hazard ratio 1.34 (0.94–1.94), p=0.11). In contrast, SYNTAX score and logistic EuroScore were highly predictive, with hazard ratios (per unit) of 1.05 (1.03–1.07) for SYNTAX score and 1.08 (1.06–1.09) for logistic EuroScore (p<0.001 for both variables).

**Conclusion:** Complexity of coronary artery disease determined with SYNTAX score and clinical risk profile determined with logistic EuroScore are strong predictors of one-year and three-year mortality after elective PCI with DES. In contrast, pLAD as single criterion showed no significant prognostic relevance.

**P5426 | BEDSIDE**

**Are PCI with long stent lengths safe in the DES era?**


**Background:** Long stent lengths have been shown to be predictive of cardiovascular (CV) events and stent thrombosis after percutaneous coronary intervention (PCI), whether it remains true in the DES era remains unclear. In contrast, pLAD as single criterion showed no significant prognostic relevance.

**Purpose:** To compare one-year outcomes after PCI according to total length of stent in the DES era.

**Methods:** Consecutive patients referred to our Cath-Lab for PCI were included within 3 months. Clinical and angiographic data were prospectively entered into the nationwide web-based "Middle-Care" database, one year follow up was obtained by medical report and phone call. Cardiovascular outcomes (death, Target Vessel Revascularization (TVR), MACCE) and stent thrombosis (ARC definition rates) were compared, according to total stent length, in patients with 1) BMS and 2) DES.

**Results:** 4335 PCI were performed in 4216 patients. Mean age was 65±12 years, 28% had diabetes, 91% had radial PCI, 32% had ACS. DES was used in 51%, BMS 44% and DES-BMS in 5%. Total stent length was 28±19 mm.

One-year mortality was 3.1%. Out of 89% eligible for follow-up, 93% were reached.

Conclusions: Long drug-eluting stent lengths aren't associated with an excess of stent thrombosis, new revascularization and CV events at one year compared to smaller ones, unlike BMS.

**P5427 | BEDSIDE**

**Long term outcomes of percutaneous coronary interventions or bypass grafting surgery for left main coronary artery disease in octogenarians: a DELTA registry sub-study**

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**Purpose:** Percutaneous coronary intervention (PCI) with drug-eluting stents (DES) is accepted as a feasible and safe alternative to surgery for the treatment of unprotected left main coronary artery (ULMCA) disease, but the long term clinical outcome in elderly patients is still unclear. Aim of our study was to compare the clinical outcomes of octogenarians with ULMCA disease treated either with PCI with DES or coronary artery bypass grafting (CABG).

**Results:** The primary study endpoint was the composite of death, cerebrovascular accident and myocardial infarction at follow-up. Consecutive patients with ULMCA stenosis treated with PCI or CABG and age >80 years were selected and analyzed in a large, all comers, multinational registry.

**Results:** 304 patients were included: 218 were treated with PCI and 86 with CABG. During the hospital stay and at a median follow-up of 1,088 days the incidence of the primary endpoint was similar in the two groups (27.6% vs 31.1%, log-rank test: p=0.98). The incidence of target vessel revascularization in follow-up was higher in PCI patients (10.1% vs 3.9%, log-rank test: p=0.05). At multivariable analysis, the only independent predictor of the composite primary end-point was left ventricular ejection fraction (HR 0.95, CI 0.91-0.98, p=0.001).

After adjustment with propensity score, the revascularization strategy was not significantly correlated to the incidence of the primary endpoint (HR 0.98, CI 0.95-0.97-1.91, p=0.95).

**Conclusions:** In octogenarians no difference was observed in the occurrence of the primary composite endpoint after PCI or CABG for the treatment of ULMCA disease. However, the rate of TLR was higher in the PCI group.

**P5428 | BEDSIDE**

Pre-treatment with high-dose atorvastatin in patients undergoing percutaneous coronary intervention: long-term follow-up of the ARMYDA (Atorvastatin Reduction for MYocardial Damage during Angioplasty) group designed a series of randomized studies to investigate the effectiveness of statin pre-treatment in patients undergoing percutaneous coronary intervention (PCI). In the ARMYDA and ARMYDA-ACS studies, a reduced incidence of peri-procedural myocardial damage has been demonstrated in patients with both stable and unstable syndromes receiving high-dose statins. In the ARMYDA-RECAPTURE trial, an acute atorvastatin reload, in patients already on statin therapy, showed a significant improvement in clinical outcome. However, nowadays, no data are available on the possible beneficial effects of high-dose statin treatment before stenting on long-term outcomes. Thus, the aim of this analysis was to investigate this issue performing a clinical follow-up of all these above-mentioned trials.

**Methods:** The overall population included 479 patients from ARMYDA, ARMYDA-ACS and ARMYDA-RECAPTURE trial; 237 patients received high-dose atorvastatin pre-treatment and 242 placebo. On long-term follow-up, the occurrence of major adverse cardiac events (MACE), defined as death, acute myocardial infarction, target vessel revascularization and coronary artery bypass graft, was evaluated. As secondary end point, we analyzed the incidence of clinically driven in-stent restenosis (ISR).

**Results:** Clinical follow-up (mean 78±18 months) was successfully completed in 396 patients (83%). The primary composite end-point occurred in 20% (48) of patients receiving statin treatment and in 31% (75) of those not pre-treated (p=0.007). The incidence of ISR was 8% in the atorvastatin group vs 18% in the placebo arm (p=0.0015). Furthermore, the Kaplan-Meier curves showed an event-free survival of 78% in patients undergoing statin therapy and 66% in controls (p=0.035).

**Conclusions:** According to the ARMYDA trials, high-dose atorvastatin therapy before PCI may be strongly suggested both in statin-naïve patients and those already on chronic statin use, in order to prevent peri-procedural myocardial damage. Moreover, for the first time, on the basis of the results of this analysis, an adjunctive improvement was observed also on long-term follow-up, with a reduced incidence of MACES and ISR. All these evidences should definitely influence clinical practice and warmly support early initiation of statin therapy before PCI.
Objective: The purpose of this study is to show the feasibility of the inside-out central venous access (IOCAV) method to gain vascular access in patients with complex central venous occlusions. Methods: Four patients with central venous occlusions were referred for device implantation. Inside-out central venous access (IOCAV) was obtained via a percutaneous femoral approach. A catheter-dilator system was advanced via the right atrium to the most central point of venous occlusion. The occluded vein segment was punctured with a directionally guided needle, which was advanced along intravascular or extravascular tissue planes to the subclavian region. A solid wire needle was oriented toward the skin surface and advanced through the soft tissues until it exits from the body. The wire was used to pull rigid dilators through the occluded segment. Standard transvenous leads were implanted through the newly created channel.

Results: From May 2013 till December 2013, 4 patients were implanted using the IOCAV technique. The mean age was 74 years, there were 3 males and 1 female. It was an initial implantation in all patients and all of them had a total central venous occlusion. They all had successful preoperative device implants on the left side (3 ICDs and 1 CRT-D). Fluoroscopy and procedural times were longer than average. No procedure related complications occurred. All patients had normal device function at follow-up of 5.5 months.

Conclusion: IOCAV is a feasible method to implant a transvenous lead for patients with ipsilateral central venous occlusions. Although taking more procedural time and using more fluoroscopy, this method avoids switching to a de novo implantation on the contralateral side or obviates the need for a thoracotomy approach.
Background: Transcatheter aortic valve implantation (TAVI) has been designed to treat patients affected by severe symptomatic aortic stenosis considered extreme or high risk for surgery. We report a single centre 5-year experience with Medtronic CoreValve implantation in patients affected by severe aortic stenosis.

Methods: Between May 2008 and December 2013 at our department 245 patients were treated with transcatheter aortic valve implantation, 204 patients (mean age 80.3±11.2 years, 92 male) underwent Medtronic CoreValve implantation. All patients were judged high risk for standard aortic valve replacement (mean Euroscore II 10.7±10.2%, mean STS Mortality 9.3±6.5%). Fifty six patient were redo at TAVI. 40 underwent prior CABB. Forty four patient suffered by severe renal failure; 63% of patients suffered of peripheral vasculopathy.

Results: All patients were evaluated and treated by a Heart Team composed by interventional cardiologist, hybrid cardiac surgeon, cardiac anesthesiologist and echocardiographist. 145 patients (71%) underwent trans-femoral TAVI and 51 patients were treated by a direct aortic approach. The CoreValve 26 and 29 were used in 92 and 94 patients respectively. Procedural mortality was 1 patient. Major vascular complication occurred in 27 patients (13.2%) and 34 patients experienced A bleeding complication. Forty patients required a permanent pacemaker implantation, 30-day mortality was 5.3% (11 patients). Mean follow-up was 24.66±17.5 months, 44 (22.7%) died during follow up with a 4-year survival of 63%.

Conclusions: Our experience confirms that a real heart team approach to valvular disease, having the possibility to offer our patients different alternative access site, is the best way to treat TAVI patients getting excellent short and long term results.

P5435 | BENCH
Immediate and midterm outcomes of repeat percutaneous mitral balloon commissurotomity for restenosis
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The increasing use of percutaneous mitral balloon commissurotomy (PMBC) has led to an increase in restenosis cases. Repeat PMBC may be a method of treatment for symptomatic patients with restenosis after successful initial one, but data regarding its outcomes are quite limited.

The aim of this retrospective study is to evaluate the immediate and midterm outcomes in patients who underwent a second PMBC for symptomatic mitral restenosis.

Methods: The study group consisted of 103 patients who have undergone a second PMBC, 4.5±3.3 years after a first intervention. All PMBC procedures were performed using the Inoue balloon system.

Results: The mean age of our patients was 28±11.2 years old and 78.8% were female. All patients present dyspnea with a poor functional capacity (New York Heart association [NYHA] III-IV). The wilkins score was between 8 and 12 in 60.2% of cases. The mitral valve area increased from 1.1±0.3 cm² and mean gradient decreased from 13±3.3 mmHg to 8±2.9 mmHg. An immediate good result (MVA > 1.5 cm², mitral regurgitation ≤ 2+) was obtained in 59 (57.28%) patients. There were no complications except for one case of pericardial tamponade requiring surgical evacuation (0.9%) and two cases (1.9%) of severe mitral regurgitation.

Conclusion: Repeat PMBC is a safe therapeutic option with good immediate and long-term results in patients with restenosis.

Repeat PMBC should be considered as the first strategy in suitable patients.

P5436 | BENCH
Mobile echogenic images during 3D-transoesophageal intraprocedural monitoring of transaortic valve implantation: incidence, characteristics, and clinical implications

Background: Transcatheter aortic valve implantation (TAVI) is an alternative to surgical valvular replacement in high-risk patients with aortic stenosis. Transoesophageal (TOE) intraprocedural monitoring is highly recommended to position appropriately the prosthetic valve.

Mobile echogenic images (MEI) may be visualized during the procedure, but information about this finding is scarce.

Material and methods: 104 consecutive patients undergoing TAVI (Edwards-Sapiens device) were included. All of them were monitored with 3D-TOE (Phillips). MEI were evaluated and correlated with clinical findings. All patients were fully anticoagulated (initially 100U/kg Sodic Heparin) and the procedure was performed following the standard protocol.

Results: MEI were visualized in 11 patients during the procedure (11%). In 7 cases (64%), MEI were seen during valve implantation and its main location was the aortic root (n=4; 36% Picture 1). Its size ranged between 3 and 30 mm, 45% of them had echocardiographic calcium density and 45% disappeared before procedural conclusion. The physician who performed TOE interpreted the MEI as thrombus in 55%, and as part of the former valvular structures in 45%. 3 of 104 patients had peri-procedural stroke, but MEI had been visualized in only one of them. No systemic embolisms occurred.

Conclusions: The visualization of MEI by 3D-TOE during TAVI is frequent, and in >50% of cases have echocardiographic characteristics of thrombus. The clinical implications of this finding is unclear.

P5437 | BENCH
TAVI: comparison of multislice computed tomography and rotational angiography based 3D reconstruction imaging for the measurement of the minimum annular diameter for transcatheter aortic valve prosthesis implantation
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Purpose: During transcatheter aortic valve implantation (TAVI) the valve has to be placed exactly in the annulus of the aortic valve to avoid paravalvular aortic insufficiency or even dislodgement from the annulus. As implantation is guided by projection images the angiographic view should be orthogonal to the plane of the aortic annulus. We evaluated if this view could be sufficiently predicted by multislice computer tomography (MSCT) carried out before TAVI.

Methods: In 100 consecutive patients receiving transcatheter TAVI using a Medtronic CoreValve, MSCT Siemens Somatom Sensation was performed before TAVI and rotational angiography based 3D reconstructions (Siemens Dynact) during TAVI. For both CT scans a plane was calculated which was perpendicular to the plane of the aortic annulus (defined as the plane through the most distal point of all three aortic cusps) and in which the noncoronary cusp was on the right, the left coronary cusp on the left, and the right coronary cusp in between.

Differences of the angles of the angiographic view in left anterior oblique (LAO)/right anterior oblique (RAO) and caudal/cranial were calculated as well as the angle between the two planes from the scalar product.

Results: All MSCT had a sufficient quality for analysis, 2 Dynact could not be analyzed due to artefacts from severe calcification of the aortic annulus and breathing artefacts. The angles of the projections were: LAO/RAO 6±1°, 20°±20°, 0°±20° and cranial/caudal 17°±17°, cranial 0°±20° and caudal 0°±20°. The correlation to MSCT was 0.76 for LAO/RAO (p<0.0001) and 0.77 for cranial/caudal (p<0.0001). The differences in the projection angles were on average small but showed large variations.

Conclusion: The angle between the planes calculated by MSCT and Dynact was 9.0±3.1° (R=0.14, 86). Considering an annulus of e.g. 25 mm, this angle is translated into a blurring of the annulus line using MSCT values for the projected image of 3.98 mm. This is half of the completely circular covered ring of the CoreValve which has a height of 8 mm.

Conclusions: The visualization of MEI by 3D-TOE during TAVI is frequent, and in >50% of cases have echocardiographic characteristics of thrombus. The clinical implications of this finding is unclear.

P5438 | BENCH
Mitril regurgitation following percutaneous mitral balloon valvuloplasty: our experience
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Background and objective: Percutaneous mitral balloon valvuloplasty (PMBV) has revolutionized the treatment of patients with symptomatic mitral stenosis and is now established as the procedure of choice. Despite high technical expertise in PMBV using the Inoue balloon, mitral regurgitation (MR) remains a major procedure-related complication. We retrospectively analyzed our data of PMBV using the Inoue balloon with regard to the incidence of MR, its likely causative mechanism, and follow up of these patients.

Methods: During the past 15 years, PMBV was performed in 488 patients (me-
P5439 | BENCH
Increased genome instability in AZFc region on Y chromosome in interventional cardiologists exposed to chronic ionizing radiation
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Methods: A group of 45 interventional cardiologists (47±6.6 years) and 32 unexposed controls (48.9±8.2 years) were enrolled in the study. Interventional cardiologists were occupationally exposed to irradiation for 16.2±9.4 years (range 5–46 years). Two sex-determining region Y (SY) markers (SY1197 and SY579) in AZFc region and two housekeeping genes (GAPDH, β-globin) were assessed using genomic DNA extracted from leucocytes by quantitative Real-Time PCR. The copy number for each target was determined by the 2^−ΔCT method.

Results: Elevated levels of CNV in SY1197 were found in exposed when compared to controls (1.29±0.39 vs. 1.05±0.29, p<0.003). As shown in Figure, no significant difference was found for SY579 marker (1.44±0.48 vs. 1.3±0.66, p=0.27). The SY1197 marker did not show correlation with age (p=0.11) and smoking (p=0.8).

Conclusion: Y-chromosome instability was remarkably high in invasive cardiologists, suggesting that occupational exposure may predispose to spermatogenic impairment.

P5440 | BEDSIDE
Percutaneous left atrial appendage occlusion with Amplatzer devices in high risk patients with atrial fibrillation and a contraindication to oral anticoagulation
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Purpose: Percutaneous left atrial appendage occlusion (LAOO) is evolving as a device therapy for reduction of thromboembolic risk in atrial fibrillation (AF). Most available data for LAOO are related to AF patients who have a moderate stroke risk and no contraindication for long-term oral anticoagulation (OAC). We report our initial single-center experience on LAOO in AF patients with a high stroke risk and a contraindication to OAC.

Methods: In the period from 2010-2013 we performed 50 LAOO procedures using the Amplatzer Cardiac Plug (ACP, n=37) or the Amplatzer Amulet (n=13). All patients had a contraindication to OAC most of them because of a previous serious intracerebral or gastrointestinal bleeding. Cardiac CT and transesophageal echocardiography was performed at 6 weeks and 12 months after the procedure.

Results: The mean age was 73 (28-91) and 72% were men. The mean CHADS2-VASc score was 4.9 (predicted stroke rate 8.6%/y) and the HAS-BLED score was 4.8 (predicted bleeding risk 8%/y). Mean follow-up was 335 days (45.9 patient years). Antithrombotic treatment after LAOO was aspirin 75 mg daily for 6 months. The mean procedure time was 70 minutes. The LAA closure success rate was 100% (50/50). The peri-procedural complication rate (<7 days) was 3.7% (4/108). One patient had a device embolization. The device was easily snared and a new device was implanted without complications. Another patient with cerebral amyloid angiopathy suffered a small cerebral bleeding the day after the procedure. She recovered rapidly and completely. There were no episodes of perivalvular effusion or peri-valvular leaks. We observed antithrombin on the proximal disc of an ACP 3 weeks after implantation. It resolved after 3 weeks on warfarin. One stroke was observed 4 months after the procedure in a diabetic patient with late stage complications including severe carotid atherosclerosis. The observed annual stroke rate was 2.2% (67% reduction vs. predicted) and the observed bleeding rate was 4.3% (51% reduction vs. predicted).

Conclusions: LAOO using Amplatzer closure devices is a safe novel transcatheter therapy that reduces the risk of stroke and bleeding in patients with a high thromboembolic risk and a contraindication to OAC.
and vascular endothelial growth factor (VEGF) level were determined by corresponding ELISA kits in order to assess the endothelial function after scaffold implantation.

**Results:**

At the 28th day, no in-scaffold restenosis or scaffold thrombosis were found in both PLLA and PLLA/ACP group. Histological analysis from SEM indicated that the inflammation score in PLLA/ACP group was less than that in PLLA group (1.20 ± 0.42 vs. 1.70 ± 0.48, *P* < 0.05). Coniscaffold with that, the expression of NF-kB was lower in PLLA/ACP group (22.07 ± 1.38 vs. 28.59 ± 3.54, *P* < 0.05). The endothelialization score was higher in PLLA/ACP group than that in PLLA group (2.00 ± 0.47 vs. 1.40 ± 0.52, *P* < 0.05), even though no significant difference was found in neointimal area percentage between these two groups. The levels of VEGF and NO in PLLA/ACP group were significantly higher than those in PLLA group respectively (309.86 ± 55.16 pg/ml vs. 129.96 ± 9.52 pg/ml, *P* < 0.05). The primary endpoint was the relative change in stent length (length by MSCT dilation; 3) bifurcation techniques; 4) intravascular imaging techniques after stent implantation, MSCT was scheduled by protocol 9-12 months after the procedure. The primary endpoint was the relative change in stent length (length by MSCT divided by the stent length reported by the manufacturer).

**Results:**

Stents subject to catheter impairment were more frequently stainless-steel DES whereas those subject to post-dilation tended to be more frequently platinum-chromium DES. Stents subject to catheter impairment were shortened more than those that did not (mean difference 7.6%, 95% CI 3-12%, *P*<0.01). There were no differences in longitudinal deformation with the other studied mechanical actions (figure). After adjustment by stent-alloy type and nominal stent length, catheter impairment was the only mechanical action associated to longitudinal deformation. No stent fractures were observed.

**Conclusions:**

Guiding catheter impairment is the only mechanical action significantly associated to DES shortening. Therefore, it is of importance to avoid catheter impairment after stent implantation in coronary ostia independently of the stent type.

**Purpose:**

From October 1996 to March 2012, 164 patients underwent left main PCI at our institution. Twenty four patients who had both tissue Doppler imaging (TDI) echocardiography exams of pre and post LM PCI were included this study. We compared echocardiographic findings including TDI of pre and post LM PCI.

**Results:**

Time interval between PCI and post-PCI echocardiography was 85.9 ± 87.9 days.

Echocardiographic data pre and post PCI

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**Conclusions:**

Pre LM PCI | Post LM PCI
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<td>24.0 ± 7.1</td>
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<td>23.5 ± 6.2</td>
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<td>40.5 ± 22.3</td>
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Left ventricular ejection fraction (45.2 ± 16.3 vs. 49.3 ± 15.3%, *P* < 0.05) and septal systolic velocity (S) (measured by TDI (5.7 ± 2.1 vs. 6.9 ± 2.0, *P* < 0.01) were significantly improved after LM PCI (Table).

**Conclusions:** LM PCI improves LV systolic function not diastolic function assessed by TDI echocardiography.

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**Conclusions:**

Benefit of CABG over PCI in mortality and MI reduction seems uncertain. Although CABG was superior to PCI regarding repeat revascularization, the advantage of stent technology has narrowed the gap. Randomized trials comparing CABG vs. PCI with new generation DES.

**Purpose:**

Left main percutaneous coronary intervention (PCI) improves LV systolic function by tissue doppler imaging (TDI) echocardiography.

**Background:**

As the technology advances, new generation drug-eluting stents (DES) are reported to have better clinical outcomes than bare metal stents (BMS) or 1st generation DES. However, there has been no trial using new generation DES in comparing coronary artery bypass grafting (CABG) vs percutaneous coronary intervention (PCI). We performed indirect comparisons between CABG vs PCI with new generation DES.

**Methods:**

For the indirect comparison, we used Bayesian network meta-analysis. During systematic literature search, randomized trials comparing one intracoronary stents another were included as well as studies of CABG vs. PCI for treating left main or multivessel disease. (80,375 patients from 100 trials and 9,736 from 11 trials respectively). Comparisons were made for all-cause mortality, myocardial infarction (MI), repeat revascularization and stroke.

**Results:**

With respect to mortality and MI, superiority of CABG was not significant, especially compared to new generation DES (figure). Regarding repeat revascularization, CABG was better than PCI, regardless of stent types. However, the benefit decreased from odds ratio (OR) 6.7 with BMS to OR 1.9 with new generation DES in comparing coronary artery bypass grafting (CABG) vs percutaneous coronary intervention (PCI). We performed indirect comparisons between CABG vs PCI with new generation DES.

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Conclusion: In patients undergoing BES implantation for treatment of LMA stenosis the rate of 9-month strut coverage is high. The use of final kissing balloon reduces the risk of high uncovered stent segment length.

PS448 | BEDSIDE
Patient and operator radiation dose using a pelvic lead shield during trans radial angiography
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Background: Cardiac angiography using the radial access compared to the femoral approach, is associated with reduced complication rate and improved patient comfort but has significantly increased radiation dose to the patient and the operator. Improvements in radiation protection are needed.

Aims: To determine the efficacy of a 0.5-mm lead apron across the patient’s abdomen to reduce radiation on operator radiation exposure and to measure also patient radiation dose.

Methods: We randomly assigned 202 patients undergoing coronary angiography to a group with pelvic lead shielding and a group without. In each procedure 8 dosimeters were used to measure operator radiation dose [under the lead apron, outside the thyroid shield and at the left side of the head] patient dose at the level of the umbilicus [above and beneath the lead apron] and 2 on the acrylic shielding and one on the image intensifier to measure scattered radiation.

Results: Both groups were similar in BMI, procedures performed and number of sequences. Usage of lead shielding statistically significantly reduced the radiation dose of the operator at all 3 sites measured: under lead apron: 0.02±0.05 Vs. 0.06±0.17, on thyroid collar: 0.37±0.35 Vs. 0.64±0.79 and left side of head 0.24±0.21 Vs. 0.36±0.35. However the radiation for the patient was doubled 3.9±10.95 Vs. 1.51±2.65, p<0.001.

Conclusions: The use of a pelvic lead shield during radial angiography reduced the operator radiation exposure at multiple measurement sites. However there was an increased exposure to the patient. This balance has to be further investigated before the widespread of this method.

PS449 | BEDSIDE
The incidence, clinical outcomes, and risk factors of peri-contrast staining after second generation DES implantation
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Background: Several studies showed peri-contrast staining (PSS) after sirolimus-eluting stent was be associated with target-lesion revascularization (TLR) and very late stent thrombosis. However, the incidence and clinical sequela of PSS after second generation DES implantation are unclear, so we retrospectively evaluate the clinical outcomes.

Methods: This study consisted of de novo 2185 lesions in 1734 patients that were treated with second generation DES (zotarolimus-eluting stent: ZES, everolimus-eluting stent: EES, and biolimus-eluting stent: BES). They were evaluated by follow-up angiography within 12 months after stent implantation, from April 2009 to December 2012. We divided into PSS group and non-PSS group and compared the two groups in clinical and angiographical outcomes.

Results: We had obtained 1826 lesions follow-up angiography. (83.6%) The mean clinical follow up period was 786±15 days. Baseline clinical and angiographic characteristics were similar between the two groups. (N.S.) Late acquired PSS was observed in 19 lesions (0.87%) in 17 patients (0.98%). In these lesions, 3 lesions (0.73%) were observed in BES, 9 lesions (0.67%) were EES and 7 lesions (1.62%) were ZES. (N.S.) Stent fracture (SF), tortuosity, and lesions with severe angulation (>45°) were more frequently observed in lesions with PSS than in lesions without PSS (18.2% versus 0.61%, p<0.0001, 18.7% versus 0.85%, p<0.03, 0.85% versus 6.9%, p<0.03), Cumulative incidence of TLR and MACE in the PSS group was higher than that in the non-PSS group. (41.2% versus 0.0%, and 47.1% versus 9.6%, p<0.0001). There was no significant difference in late and very late stent thrombosis between the two groups. (N.S.) After multivariable analysis, CTO (OR: 4.07, 95% CI: 1.12 to 12.1, p<0.04), and reference diameter (>2.83mm) (OR: 4.17, 95% CI: 1.5 to 12.4, p<0.005) were independent predictors for PSS.

Conclusions: PSS after second generation DES was a rare phenomenon but appeared to be associated with subsequent TLR.
However complex lesions have been excluded in most clinical trials. The aim of this study is to analyse the mid-term follow up of a cohort of patients with complex lesions treated with BVS.

**Methods:** From January 2012 to January 2014, 306 patients having 394 coronary lesions were treated with BVS in our institutions. From them, we analyse the subset of patients (n=187) with complex lesions (n=233).

**Results:** The mean age was 57±9.1 years;168 patients were male (85%). In 81 (42%) the clinical presentation was an acute coronary syndrome. The location of the lesion was as follows: Left anterior descending artery 127; Left circumflex 57; Right coronary artery 46; and Left main 5. The mean lesion length was 22.2±11 mm and the mean stenosis was 75±20%. Thirty-one lesions were chronic total occlusion, 151 bifurcations lesions, 9 restenosis lesions and 112 long diffuse stenoses (>22 mm). In 64 cases (27%), the lesion shared at least 2 types of complexities. Nighty seven lesions (42%) were studied at baseline condition by intravascular ultrasound (IVUS). After BVS implantation the geometry of the scaffold was analysed by optical coherence tomography in 80 lesions (34%) and with IVUS in 66 (28%). Direct BVS implantation was performed in 128 lesions (55%) and in the remaining 114 lesions pre-conditioning of the lesion by balloon angioplasty was carried out. The mean BVS diameter was 3.1±0.3 mm, and the mean scaffold length was 26.5±12 mm. Primary angiographic success was obtained in 233 lesions (100%). Ten patients (5%) had a peri-procedural myocardial infarction. Major cardiac events at follow up was 2.5%. After a mean follow-up time 11±5 months, 31 patients (scaffolded segments) were studied by scheduled angio-CT scan, documenting two restenoses of the scaffold. Angiographic reevaluation of the remaining 114 lesions preconditioning of the lesion by balloon angioplasty was carried out. The mean BVS diameter was 3.1±0.3 mm, and the mean scaffolded length was 26.5±12 mm. Primary angiographic success was obtained in 233 lesions (100%). Ten patients (5%) had a peri-procedural myocardial infarction. Major cardiac events at follow up was 2.5%. After a mean follow-up time 11±5 months, 31 patients (scaffolded segments) were studied by scheduled angio-CT scan, documenting two restenoses of the scaffold. Angiographic reevaluation driven by symptoms showed 3 additional restenoses. In all 5 restenotic lesions (2.5%) target lesion revascularization was performed. The remaining patients are symptom free.

**Conclusions:** Treatment of complex lesions with bioabsorbable vascular scaffold is safe with a low rate of major adverse cardiac events at mid-term follow-up.
Results: A total of 1,024 patients have been included with age 67.5 ± 10.6 years, 23.3% women, 41% diabetic and 25.8% with ACS. Among these 354 patients have already completed 12 months follow up. In this cohort the incidence of definite or probable thrombosis at 12 months was 0.57% (1 definite thrombosis at 2 months and 1 probable thrombosis at 7 months). The incidence of cardiac death and TLR at follow up at 6 months with 25%. Events reported between 6 and 12 months were 3 cardiac deaths (2 heart failure and 1 sudden death) and 2 non-ST elevated myocardial infarctions (one related with stent restenosis and the other without angiography considered a probable stent thrombosis). Using the ESTROFA-2 data (67.5 ± 10.6% patients treated with new generation DES, 4,355 of them with 12 months DAPT) we performed a propensity score matching with this registry. In ESTROFA-2 the incidence of definite or probable thrombosis at 12 months under 1 year DAPT was 0.7%.

Conclusions: A DAPT period of 6 months after non-first generation-DES implantation in selected population results safe with a very low rate of events between the 6th and 12th month. Final follow up for the whole cohort will be available at the time of the congress.

PS5456 | BEDSIDE
Long-term clinical impact of polymer-free sirolimus-eluting stents in unselected patients
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Purpose: The long-term clinical impact of polymer-free sirolimus-eluting stents (PF-SES) in unselected patients undergoing percutaneous coronary interventions (PCI) remains poorly investigated. We therefore sought to investigate the long-term clinical impact of PF-SES in a large cohort of unselected patients receiving PCI-therapy.

Methods: PCI-patients receiving PF-SES at two hospitals retrospectively studied. The primary endpoint was major adverse cardiac events (MACE; death/myocardial infarction – MI – or target lesion revascularization – TLR). The secondary endpoints were the subcomponents of the primary endpoint, cardiac death/MI and definite/probable stent thrombosis (ST). A subgroup analysis evaluated the occurrence of MACE, TLR and cardiac death/MI according to age, diabetes status, clinical presentation and multivessel disease.

Results: A total of 1,213 patients (males 83.8%, diabetics 31.8%) and 1,658 lesions (82.8% 52.5%) were studied. At a median follow-up of 1,160 days the incidence of MACE was 10.0% (119 patients, death 7.6% (92 patients), MI 3.2% (39 patients), TLR 2.2% (27 patients), cardiac death/MI 5.4% (65 patients) and definite/probable ST 1.9% (25 patients). MACE were more likely in patients aged ≥65 years (p = 0.004), diabetics (p = 0.004) and with unstable clinical presentation (p = 0.042) without impact of gender (p = 0.14) and multivessel disease (p = 0.18). No difference in the occurrence of TLR was found according to gender (p = 0.92), age (p = 0.28), diabetes (p = 0.47), clinical presentation (p = 0.19) or multivessel disease (p = 0.44). Cardiac death/MI was more likely in patients aged ≥65 years (p = 0.001), without impact of gender (p = 0.27), diabetes (p = 0.30), clinical presentation (p = 0.08) and multivessel disease (p = 0.13).

Conclusions: This study reported a sustained safety and efficacy at long-term follow-up in the largest cohort of unselected PCI-patients treated with polymer-free sirolimus-eluting stents studied so far.

PS5457 | BEDSIDE
Comparison of the safety and efficacy of bio-absorbable versus permanent polymer-platinum chromium everolimus-eluting stents in real-world Asian cohort

Objective: Drug-eluting stent (DES) with bio-absorbable polymer has the potential safety benefit of reducing stent thrombosis while maintaining efficacy. This study aims to compare the safety and efficacy of the permanent polymer-platinum chromium Everolimus DES with the newer generation bio-absorbable polymer DES, with respect to alloy and drug.

Methods and results: A total of 320 patients, who were implanted with either stents in our centre whilst undergoing percutaneous coronary intervention (PCI), were enrolled in this retrospective study. The primary endpoints were major adverse cardiac events (MACE, defined as all-cause death, myocardial infarction (MI) and target lesion revascularisation at 6 months. The baseline characteristics were similar with mean age of 59.3 ± 6.01 years, 85.3% males and 34.7% diabetics. Majority of the lesions (96%) treated were AHA/ACC Type B2/C and the mean length of lesion was 24.9 ± 10.7mm. The overall event rates were low at 6 months, with no significant difference in the overall MACE between the 2 groups. There was also no stent thrombosis.

Conclusions: The early experience with the new generation of bio-absorbable platinum-chromium DES suggests comparable efficacy to permanent polymeric DES with no safety concerns related to the biodegradable polymer.

PS5458 | BEDSIDE
Impact of metabolic syndrome on clinical outcome after new-generation drug-eluting stent implantation
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Purpose: Metabolic syndrome (MetS) has been reported to have negative impacts on the clinical outcome of patients who underwent percutaneous coronary interventions (PCI) with even drug-eluting stents (DES). Recently, new generation DES have improved clinical outcomes. However, their impact on patients with MetS is still unclear and data is limited. Because of the improvements of DES, there might be changes in the impact of MetS on the clinical outcome of patients in the era of new-generation DES

Methods: A single-center retrospective cohort study was performed from 2009 to 2013. Subjects undergoing PCI in at least one coronary artery using everolimus-eluting stents were included. A composite endpoint included target lesion revascularization (TLR), target vessel revascularization (TVR) and stent thrombosis. The recommendations of the Third Report of the National Cholesterol Education Program Expert Panel were used for MetS criteria.

Results: Total 909 subjects were observed for 4.9 years. Of the subjects, 613 (67.5%) were male, 551 (60.6%) had hypertension, 307 (33.8%) had diabetes and 571 (62.8%) were diagnosed with MetS. The mean age was 64.8 ± 10.7 years, total stent length (TSL) was 51.7 ± 31.7 mm and the number of intervened coronary arteries was 1.5 ± 0.7. All subjects took standard medical therapy including statin after the index procedures. Multi-vessel coronary artery disease (CAD) was more frequent and TSL was longer in subjects with MetS than those in subjects without MetS. Cardiac death and the composite endpoint occurred in 12 subjects (1.3%) and 88 subjects (9.7%), respectively. In Cox-regression analysis, the rate of cardiac death (1.4% vs. 1.2%, p = 0.61), TVR (0.2% vs. 0.5%, p = 0.61), TLR (9.3% vs. 7.4%, p = 0.63) and the composite endpoint (10.0% vs. 8.6%, p = 0.47) in subjects with MetS were not significantly different from those in subjects without MetS. After adjustment for age, sex and TSL, the rate of the composite endpoint in subjects with MetS was still different from that in subjects without MetS (10.5% vs. 8.1%, p = 0.73).

Conclusion: Although the extent of CAD was greater in subjects with MetS, the presence of MetS seems to have little impact on the outcome of patients undergoing PCI in the era of second-generation DES.

PS5459 | BEDSIDE
Readmission during the first year after percutaneous coronary intervention predicts long-term mortality

Background: Thirty-day readmission after percutaneous coronary intervention (PCI) is associated with higher mortality. However, little is known regarding the potential prognostic factor of hospital readmission beyond 30 days. We hypothesized that readmission within 1 year after PCI may also have prognostic significance.

Methods: A total of 746 consecutive patients were discharged alive after PCI for any reason between 2007 and 2011, and were followed-up during a mean of 27.2 ± 0.5 months (maximum 60 months). Of them, 389 patients (52%) were readmitted for any cause, 223 (29.9%) <1 year after discharge (<1yGroup). The remaining patients were used as reference group (RefGroup: no readmission or readmission >1 year after discharge). Only first readmission was taken into account. Survival was assessed by Kaplan Meier curves and log-Rank test for group comparison. Multivariable analysis was performed with a proportional-hazards Cox model.

Results: From the 223 patients, 139 (62.6%) were readmitted for cardiovascular causes, 109 (49.1%) for chest pain and 18.9% for a major adverse cardiovascular event (death, myocardial infarction, stroke, revascularization). Almost one half, 45 patients (24.5%) had a readmission due to a new or repeated catherization (61% new PCI). Patients in the <1yGroup had higher risk characteristics (higher age, creatinine level, number of diseased vessels, and need for hemodynamic support; also lower left ventricular ejection fraction and baseline haemoglobin) than the RefGroup.

There were 34 deaths (15.8%) in the <1yGroup compared to 18 (3.4%) in the RefGroup (p < 0.001). Only one third of deaths were from cardiovascular causes, with no differences between groups (35.3% vs. 38.9%; p = 0.8). Mean survival from all-cause death was 48.2 ± 1.1 months in the <1yGroup compared to 52.8 ± 0.4 months in the RefGroup (p = 0.001). Mean time to death was 27 months in the overall population, and it was shorter in the <1yGroup (25.6 vs. 27.9 months; p = 0.033).

The adjusted HR for mortality of the <1yGroup patients was 4.58 (95%CI 2.5 – 9.88).

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Conclusions: In an unselected population, nearly one third of the patients undergoing PCI needed to be readmitted during the first year after discharge. Readmission within 1 year identified a high-risk subgroup of patients and it was associated with a higher mortality risk. Most deaths occurred 2 or more years after discharge and had non-cardiovascular causes.

PS460 | BEDSIDE
Prevalence and outcomes of transradial vs transfemoral percutaneous coronary intervention in a high volume center

Background and purpose: Radial access reduces major bleeding complications and improves survival of STEMI undergoing primary percutaneous coronary intervention as compared to femoral approach. Our aim was to compare transradial (TR) versus transfemoral (TF) approaches in a non-selected cohort of patients undergoing percutaneous coronary intervention (PCI). We evaluated mortality and MACE at one-year follow-up. The clinical and angiographic data of 4672 consecutive patients treated who underwent PCI between 2007 and 2012 were evaluated retrospectively.

Results: Over the past 5 years, the use of TR in all-comers increased from 86% to 89%. PCI were performed using the TR in 88% of patients. There were no significant differences according to age (65 ± 12.5 vs 66 ± 12.5 years, p = 0.08) or body mass index (27.1 ± 13 vs 26.5 ± 5, p = 0.52) between TR and TF groups. Female gender (29% vs 21%, p < 0.001), cardiogenic shock (11% vs 2%, p < 0.001), cardiac arrest (6% vs 2%, p < 0.001), prior coronary artery bypass surgery (16% vs 7%, p < 0.001), dialysis (6% vs 2%, p < 0.001) were the most frequent reasons for using TF. One year follow-up was obtained in 97.9%. The rate of MACE was higher in TF versus TR (20.3% vs 10.2%, p < 0.0001) and cardiovascular mortality was increased by three-fold (15.1% vs 5.5%, p < 0.001). Target lesion revascularisation did not differ according to the vascular access site approach (6.5% vs 6.1%, p = 0.78). In multivariate analysis, TRI was associated with a lower adjusted risk of cardiovascular mortality (Odds Ratio OR: 0.654; 95% CI: 0.46 to 0.922; p = 0.0154).

Conclusions: In our center, which has been using radial access in PCI as default strategy for more than 10 years, the use of radial access for PCI continues to increase slightly. The radial approach was associated with a reduced one year cardiovascular mortality and MACE outlining a persisting selection bias and was associated with a similar target lesion revascularisation.

PS461 | BEDSIDE
Predictive value of LDL-C/HDL-C ratio on newly developed cardiac ischemia in patients with previous percutaneous coronary intervention beyond the early restenosis
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Purpose: LDL-C/HDL-C (L/H) ratio is considered as a sensitive risk factor for ischemic heart diseases, however, there is little information regarding the predictive value on newly developed cardiac ischemia in patients with previous percutaneous coronary intervention (PCI) after stabilization. We investigated predictive value of L/H ratio for secondary prevention.

Methods: We examined characteristics of 269 patients with previous PCI who underwent coronary angiography from January 2007 to December 2013 following recurrent cardiac ischemia beyond the early restenosis.

Results: Overall, during median follow-up period of 5.4 years, 61% patients underwent any late revascularization, and 28% and 17% underwent late target lesion revascularization and new lesion revascularization, respectively. Age, diabetes mellitus, T-chol, LDL-C, HDL-C, non-HDL, L/H ratio and HbA1c were detected as predictors of any late revascularization by univariate Cox proportional hazards analysis. Multivariate analysis identified that L/H ratio (HR, 1.32; p < 0.001) and HbA1c (HR, 1.13; p = 0.017) were independent predictors. Based on the median value of L/H ratio, subjects were classified into high and low L/H ratio groups. Kaplan-Meier estimation revealed significantly higher incidence of late revascularization in high L/H ratio group than in low L/H ratio group in patients with LDL-C > 100 mg/dl (median L/H ratio, 2.64; p = 0.017). However, in patients who could achieve LDL-C < 100mg/dl (median L/H ratio, 1.93), difference between the two groups was not significant (p = 0.224), and predictor of late revascularization tended to be LDL-C in diabetes mellitus.

Conclusions: L/H ratio was an important predictor of newly developed cardiac ischemia in patients with previous PCI after stabilization, particularly, in patients with LDL-C > 100 mg/dl.
both impaired HRR 1 min and impaired HR reserve was 9.6 without adjustment, and 9.4 with adjustment.

Conclusions: HR reserve in ETT could be a useful predictor for the MACE in the asymptomatic patients with successful revascularization.

P5464 | BEDSIDE
Differences in modes of dual antplatelet therapy (DAPT) cessation in the United States (US) v Europe: patterns of non-adherence to antplatelet regimens in stented patients (PARIS) registry substudy

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Purpose: The mode of DAPT cessation has been shown to impact differently on PCI outcomes. We sought to compare modes of DAPT cessation in patients undergoing PCI with stenting in the US vs Europe (EU).

Methods: The PARIS registry was a multicenter, prospective, observational study of patients who had PCI with stent implantation 2009 to 2010. Any cessation in DAPT following PCI was classified by an independent clinical events committee into 3 modes which included discontinuation (physician-deemed DAPT no longer required), interruption (temporary i.e. <14 days, of DAPT cessation due to surgical need) and 9.4 with adjustment (disruption (DAPT withdrawal due to bleeding or non-compliance).

Results: US patients (n=3660, 73%) were more often obese, more likely to have comorbidities and prior MI, to be smokers, to present with an acute coronary syndrome and to receive bare metal stents whereas EU patients (n=1358, 27%) received longer stents and were more likely to have government/insurance subsi-

dized medication. While EU patients had a greater rate of DAPT discontinuation, mainly after the first year (31.7% vs 55.6%), US patients had more interruption (13.8% vs 1.5%) and disruption (17.8% vs 5.1%) of DAPT at 2 years (Figure). US patients had higher unadjusted rates of death (5.5% vs 2.8%, p<0.001), MACE (7.7% vs 3.5%, p<0.001) and bleeding (8.9% vs 6.8%, p=0.02) compared to EU patients. After multivariate adjustment, MACE remained consistent with crude rates.

Conclusion: EU patients had greater rates of discontinuation whereas interruption and disruption were more frequent in the US. The differences in DAPT cessation modes may be attributable to baseline comorbidities, health insurance coverage, intercurrent adverse events or variability in PCI practice patterns between the US and EU.

P5465 | BEDSIDE
Risk stratification of stable patients undergoing fractional flow reserve guided percutaneous revascularization and multiple biomarkers assessment

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Purpose: Fractional Flow Reserve (FFR)-guided percutaneous revascularization (PCR) along with optimal medical therapy improves clinical outcome by targeting ischemia-inducing stenosis. Yet, plaque progression or stent failure may cause recurring cardiac events. We assessed the potential impact of inflammatory biomarkers, known to be associated with plaque progression or stent failure, on clinical outcome of patients undergoing FFR-guided PCR.

Methods: We prospectively enrolled 193 stable angina patients (pts) with intermediate coronary stenosis at angiography (i.e. with diameter stenosis 40-70%) undergoing FFR-guided PCR and: i.e. PCR in case of stenosis with FFR < 0.80, deferral in case of stenosis with FFR > 0.80. Serum levels of C-Reactive Protein (CRP), a sensitive marker of inflammation, and of Eosinophilic Cationic Protein (ECP), a sensitive marker of eosinophils activation, were assessed the day before FFR-guided PCR. Rate of major adverse cardiovascular events (MACE) as a composite of cardiovascular death, recurring myocardial infarction and PCR was evaluated.

Results: PCR was performed in 78 pts (46%) with FFR < 0.80 (mean age 69±10 years, male 73%) and deferred in 91 pts (54%) with FFR > 0.80 (mean age 64±11 years, male 53%). Average clinical follow-up was 31.2±11.5 months. Within the deferred group, CRP levels were significantly associated with higher MACE rate (H.R. [95%C.I.]: 1.04 [1.01-1.07], p=0.015) and pts with MACE (n=8 [9%]) had significantly higher CRP levels than those without [15 [6.5-3.19] vs. 1.6 [0.9-2.9] mg/L, p<0.001]. Within the PCR group, ECP levels were significantly associated with higher MACE rate (H.R. [95%C.I.]: 1.05 [1.01-1.09], p=0.021) and pts with MACE (n=14 [18%]) had significantly higher ECP levels than those without (14.4 [9.3-19.5] vs. 4.9 [2.8-10.9] mg/L, p<0.001).

Conclusions: Assessing inflammatory biomarkers allows identification of patients remaining at higher risk of MACEs after FFR-guided PCR.

P5466 | BEDSIDE
Dual antplatelet therapy over six months increases the risk of bleeding after biodegradable polymer- coated sirolimus eluting stents implantation: insights from the CREATE study

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Background: The optimal duration of dual antplatelet therapy (DAPT) after drug eluting stent (DES) implantation remains a controversy. The aim of the present study was to evaluate the impact of different DAPT duration on bleeding events between 6 to 12 months after biodegradable polymer coated DES implantation and to determine the predictors and prognostic implications of bleeding.

Methods: This study is a post hoc analysis of the CREATE study population. A total of 2040 patients survived at 6 months were enrolled, including 1639 (80.3%) received 6-month DAPT and 401 (19.7%) received DAPT > 6 months. Major bleeding events were defined according to the bleeding academic research consortium (BARC) definition and were classified as major/minor (BARC 2-5) and minimal (BARC 1). A left censored method with a landmark at 6 months was used to determine the incidence, predictors and the impact of bleeding on clinical prognosis between 6 and 12 months.

Results: At one year follow up, patient received prolonged DAPT of > 6 months had significantly higher incidence of overall (3.0% vs. 5.5%, p=0.021) and major/minor bleeding (1.1% vs. 2.5%, P=0.050) compared with the counterparts who received 6-month DAPT. Multivariate analysis showed that elderly (OR=1.882, 95% CI: 1.109-3.193, P=0.019), diabetes (OR=1.735, 95% CI: 1.020-2.952, P=0.026), history of coronary heart disease (OR=2.163, 95% CI: 1.029-4.266, P=0.026) and duration of DAPT > 6 months (OR=1.814, 95% CI: 1.064-3.091, P=0.029) were independent predictors of bleeding. Patients suffered from bleeding events had significantly higher incidence of death (7.0% vs. 0.4%, P<0.001), myocardial infarction (1.4% vs. 0.0%, P=0.035), target lesion revascularization (11.3% vs. 0.7%, P<0.001) and stent thrombosis (4.2% vs. 0.0%, P<0.001).
Conclusions: Prolonged DAPT (<6 months) after biodegradable polymer coated DES increases the risk of bleeding, which is associated with adverse cardiac events at 1-year follow-up.

**PCI LONG-TERM OUTCOME**

**PS469 | BEDSIDE**  
The clinical impact of borderline peripheral artery disease in patients undergoing percutaneous coronary intervention  

**Background:** Peripheral artery disease (PAD) is related to increased cardiovascular and cerebrovascular risk after percutaneous coronary intervention (PCI). However, there are little studies to investigate the impact of borderline ABI on clinical outcomes in patients who underwent PCI. This study aims to evaluate clinical implications of borderline PAD patients who underwent PCI.

**Methods:** A total 1,291 patients who underwent PCI and ankle-brachial index (ABI) between September 2009 and August 2012 were enrolled. Borderline ABI was defined as 0.91 to 0.99 of ABI. The primary outcome was the composite of all-cause death, cerebrovascular event, myocardial infarction or any revascularization (MACCEs).

**Results:** The median follow-up duration was 570 days (interquartile range 381 to 780). The patients with normal ABI was 1,065 (82%), borderline ABI 89 (7%), and PAD 137 (11%). Cox proportional-hazard analysis showed that the incidence of MACCEs in borderline ABI patients (12.4% vs. 6.1%, adjusted hazard ratio [HR] 1.91, 95% confidence interval [CI] 1.03-3.74, p=0.04) and PAD patients (25.5% vs. 6.1%, adjusted HR=3.19, 95% CI 2.05-4.97, P<0.001) were significantly higher than those with normal ABI.

**Conclusion:** Both borderline ABI and PAD in patients who underwent PCI is significantly associated with increased adverse clinical outcomes compared to those with normal ABI. The risk of adverse clinical outcomes of borderline ABI is lower than PAD.

**PS469 | BEDSIDE**  
Modes of dual antiplatelet therapy (DAPT) cessation in men and women: results from the patterns of non-adherence to antiplatelet regimens in stented patients (PARIS) registry  
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**Purpose:** Previous studies have demonstrated an association between female sex and unfavorable outcomes following PCI. However, the modes of DAPT cessation among women versus men have not been described.

**Methods:** PARIS was a multicenter, prospective registry of patients prescribed DAPT following PCI for any indication from 2009 to 2010. DAPT cessation included physician-guided discontinuation, interruption (<14 days for surgery) or disruption due to bleeding/non-compliance. We examined baseline characteristics, modes of DAPT cessation and clinical outcomes at 2 years in women (n=1279, 25%) versus men (n=3739, 75%). All events were independently adjudicated.

**Results:** Women were older, had more comorbidities, and were more likely to be treated with proton pump inhibitors whereas men were more likely to be smokers, have completed a higher level of education, have a history of prior MI or revascularization, and have PCI with longer stents. While there was no difference in DAPT interruption between women and men, women were significantly more likely to have DAPT disruption, and showed a trend toward increased DAPT discontinuation (Figure). Women had higher rates of death (6.5% vs 4.1%, p=0.0005), MACCE (7.8% vs 6.1% p=0.03) and bleeding (11.9% vs 7.1% p<0.001) at 2 years. The impact of DAPT cessation on ischemic events was similar between men and women (pint > 0.05).

**Conclusion:** Compared with men, women had higher rates of DAPT discontinuation and disruption. Although adverse events were more common among women, the impact of DAPT cessation on risk after PCI is non-differential by gender.

**Abstract PS469 – Figure 1. Modes of DAPT cessation women vs men. (a) Interruption (temporary discontinuation due to surgical necessity with reinstatement of DAPT on resuming hospital stay); (b) Disruption (cessation of DAPT due to bleeding or non-compliance); and (c) Discontinuation (recommended, physician-directed withdrawal of DAPT for patient considered no longer require DAPT).**
**P5471 | BEDSIDE**

Factors influencing clinical decision making for cessation of dual antiplatelet therapy within 1 year among patients undergoing PCI with drug eluting stents: results from the PARIS registry

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**Purpose:** Current guidelines recommend 6-12 months of dual antiplatelet therapy (DAPT) after PCI with drug eluting stents (DES). We sought to identify baseline factors that influence clinical decision-making for DAPT cessation within 12 months.

**Methods:** We performed a post-hoc analysis of the PARIS registry (n=5018), of whom 4,134 patients underwent PCI with DES. We compared baseline demographic, clinical and procedural characteristics between patients continuing DAPT beyond 12 months and patients with DAPT cessation within one year. Independent correlates of early DAPT cessation were identified using logistic regression.

**Results:** Compared to patients continuing DAPT beyond 1 year (n=3431, 83%) patients with any cessation within the first 12 months (n=703, 17%) were older, more often female, American and more likely to be discharge on warfarin with a lower prevalence of dyslipidemia and family history of coronary artery disease. These associations persisted after multivariable adjustment (Table) and were similar after excluding patients with adverse events in the first year. Presentation with an acute coronary syndrome and procedural parameters, such as stent length and vessel were not associated with DAPT duration.

**Predicators of early DAPT cessation**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio (OR) [95% CI]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>1.02 [1.01–1.03]</td>
<td>0.0001</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.23 [1.20–1.26]</td>
<td>0.0001</td>
</tr>
<tr>
<td>Region (USA vs. Europe)</td>
<td>1.54 [1.25–1.89]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.73 [0.59–0.88]</td>
<td>0.002</td>
</tr>
<tr>
<td>Family History of CAD</td>
<td>0.83 [0.69–1.00]</td>
<td>0.046</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0.78 [0.61–1.01]</td>
<td>0.06</td>
</tr>
<tr>
<td>Concurrent warfarin use</td>
<td>4.84 [3.58–6.55]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CAD: coronary artery disease; CABG: coronary artery-bypass grafting; DAPT: dual anti-platelet therapy.

**Conclusion:** Baseline clinical and demographic factors, rather than presentation or procedural parameters, are independent correlates of early DAPT cessation within 12 months. Table: Factors independently associated with DAPT cessation within 12 months

**P5472 | BEDSIDE**

Impact of stent fracture after sirolimus-eluting stent implantation on 8-year clinical outcomes

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**Purpose:** This study aimed to assess the impact of stent fracture (SF) after SES (sirolimus-eluting stent) implantation on 8-year clinical outcomes.

**Methods:** From 2002 to 2005, 1795 lesions (1119 patients) were treated exclusively with SES, in which follow-up angiography was performed within one year after index procedure. Excluding 165 lesions underwent target lesion revascularization (TLR) and 19 patients developed stent thrombosis (ST) within one year after SES implantation, 1630 lesions (1100 patients) constituted the study population. SF was defined as the separation of stent segments or stent struts at follow-up angiography. We defined the clinical endpoint as all-cause death, cardiac death, myocardial infarction (MI), definite ST, and TLR. TLR was evaluated on a per-lesion basis, whereas the other clinical endpoints were on a per-patient basis. Clinical endpoint rates were calculated by the Kaplan-Meier method and compared by the log-rank test.

**Results:** SF was observed in 92 lesions (5.6%). The median follow-up duration was 2975 days. The cumulative rates of MI, definite ST, and TLR were significantly higher in the SF group (10.2% versus 4.1%, p=0.01; 6.9% versus 1.7%, p=0.001; and 38.7% versus 9.4%, p<0.001). On the other hand, those of all-cause death and cardiac death did not significantly differ between the 2 groups (23.9% versus 27.6%, p=0.23 and 4.9% versus 8.6%, p=0.13). As the figure showed, those of TLR, which from 1 to 5 years and beyond 5 years, were also significantly higher in the SF group. That of definite ST from 1 to 5 years was significantly higher in the SF group, whereas that beyond 5 years showed no difference between 2 groups.

**Conclusions:** SF after SES implantation was associated with higher cardiac adverse events not only from 1 to 5 years, but beyond 5 years.

**P5474 | BEDSIDE**

Impact of Mehran contrast-induced nephropathy risk score for the prediction of clinical outcomes after percutaneous coronary intervention

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The Mehran Risk Score (MRS) has been demonstrated to be clinically useful for prediction of contrast-induced nephropathy (CIN) after percutaneous coronary intervention (PCI). We aim to investigate the association with MRS and clinical outcomes in patients who underwent PCI.

**Methods:** Study subjects consisted of 2198 consecutive patients treated with PCI from ICAS (Ibaraki Cardiovascular Assessment Study) multi-center registry, except for the patients who were receiving hemodialysis and died within seven days (n=34). We categorized them into 4 groups according to MRS (low-risk: ≤5, medium-risk: 6-10, high-risk: 11-16 and very high-risk: >16). We evaluated contrast-induced nephropathy (CIN) and major adverse coronary events (MACE), which were defined as all-cause death, myocardial infarction (MI), congestive heart failure, or cerebro-vascular accidents (CVA).

**Results:** A total of 192 patients (8.7%) developed MACCE. At multivariate analysis, MACCE in very high-risk group was more than 5-fold higher (HR 5.40, 95% CI: 2.96-9.28, p<0.001) when compared with low-risk group and was also increased in high-risk group (HR 3.72, CI: 2.59-5.32, p<0.001) and medium-risk group (HR 1.97, CI: 1.45-2.69, p<0.001). Kaplan-Meier analysis showed that increasing risk for MACCE was seen across the increasing MRS groups (p<0.001) (Figure). The odds ratio for CIN was 4.09 (95% CI: 1.72-9.17, p=0.002) in the very high-risk group, 1.49 (95% CI: 0.89-2.42, p=0.120) in the high-risk group, and 1.08 (95% CI, 0.74-1.54, p=0.693) in the medium-risk group, as compared with the low-risk group.

**Conclusions:** MRS might be potentially useful information for a prediction of CIN and clinical outcomes after PCI.

**P5474 | BEDSIDE**

A nationwide study on prognosis after percutaneous coronary intervention in persons with and without familial myocardial infarction

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**Purpose:** A family history of coronary artery disease is an independent risk factor for incident cardiovascular disease, and familial forms of cardiovascular disease can occur up to a decade before sporadic forms. However, it is unknown whether the prognosis after myocardial infarction (MI) in persons with a family history of MI differs from the post-MI prognosis in persons without such family history.

**Methods:** We linked data from national Danish registers and created a cohort of persons undergoing first-time percutaneous coronary intervention (PCI) without any prior revascularization in the period 2000-2010. We then identified the parents and siblings of all cohort members and determined whether these relatives had been registered with an MI before the cohort member’s PCI; based on this determination, we classified the PCI-cohort members as having or not having a family history of MI. We followed our cohort for re-PCI, CABG and death (all-cause mortality). Using Cox-regression with age at PCI as the underlying timescale, we estimated hazard ratios (HRs) for re-admission for a second PCI or a first cardiac bypass surgery (CABG) after PCI, and mortality ratios, by history of MI in a parent or sibling. All estimates were adjusted for previous or co-existing co-morbidities, sex, age at PCI in strata, calendar period and number of relatives.

**Kaplan-Meier curves for TLR and ST.**
Results: We included 63,077 persons with first-time PCI in the cohort, of whom 5,675 had a history of MI in a parent or sibling. We followed our cohort members for up to 10 years, with an average follow-up of 3.8 years, and found a 10% increased risk of second PCI or first CABG in those with a family history of MI, compared to those with no family history. There was no association between family history of MI and all-cause mortality, regardless of whether we looked at the whole cohort or stratified by sex (of either relative or cohort member), age of relative at MI, and age of cohort member at PCI.

Conclusions: Family history of MI appeared to have a modest impact on the post-MI prognosis as measured by re-admission for second PCI or CABG and mortality, which suggests that once coronary artery disease has developed, the familial forms have a good as a prognosis as the non-familial forms.

Interventional revascularization of coronary chronic total occlusions (CTO) represents a challenging field in cardiology with limited success and patency rates. Data on long-term prognosis after successful revascularization is conflicting and quality of life (QoL) remains unclear.

Methods:

- 796 patients (pt) treated for CTO at our institution from 2006 to 2009.
- A successful intervention for CTO decreases MACCE rate and in-spirate symptoms of pain.
- Conclusion:
  - Multivariate analysis revealed a benefit for Group A compared to Group C regarding the combined endpoint of death non-fatal myocardial infarction/hospitalisation for MI, and lipid plaque.
  - Compliance chart tiles of scaffold expansion were divided in tertiles of expansion (Actual Area/Predicted Area: <70%, 70%-80%, and >80%) and plaque components were quantified and compared among the tertiles. Bench test was also performed.
  - Results: A total of 28 patients (31 BVS) were included and 663 cross-sections were quantified and compared among the tertiles. Bench test was also performed.
  - Conclusion: Long-term RS after UPLMS PCI estimates were greatest for CSA compared with NSTEACS and STEMI. Only for NSTEACS was age a risk factor for long term excess mortality.
CHEST PAIN ASSESSMENT IN THE EMERGENCY DEPARTMENT

P5481 | BEDSIDE
Validation of the GRACE freedom from events score in an emergency department chest pain population

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Purpose: Risk stratification of patients with chest pain/acute coronary syndrome (ACS) is an important component of assessment and a driver of decision-making. The GRACE Freedom-From-Event score (GFFES) was developed to identify patients with a low risk of adverse in-hospital events. Our aim was to validate this score in an emergency department (ED) chest pain cohort.

Methods: A prospective cohort of adult patients attending a community teaching hospital ED and assessed for potential ACS. Defined major adverse cardiac events (MACE) were death, new MI, cardiac arrest or other life-threatening arrhythmia, high degree atrioventricular block, cardiogenic shock or new atrial fibrillation (AF) within 30 days of the index visit. The primary outcome of interest was the predictive performance of the GFFES for MACE by clinical performance and ROC analysis.

Results: 1076 patients were studied. There were 14 MACE (1.3%; 95% CI 0.8-2.2%). 721 patients (67%) were classified as low risk by the score (GFFES score ≥2817). 313 (7.6%) patients were classified as high risk. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the GFFES for MACE were 81.8%, 91.2%, 5.9% and 98.6% respectively. Sensitivity of GFFES for MACE was 81.8% (95% CI 64.2-99.6%), specificity 91.2% (95% CI 64.9-70.6%) and negative predictive value (NPV) 99.9% (95% CI 99.1-100%). Area under the ROC curve was 0.89 (95% CI 0.79-0.96). For the cohort assessed and then discharged from ED, sensitivity was 100% (46.3-100%) with NPV of 100% (99.2-100%).

Conclusion: In this large single site prospective validation study in ED chest pain patients, GFFES showed good discrimination, sensitivity and negative predictive value. It may be a useful tool for assigning patients to appropriate levels of care based on risk.

P5482 | BEDSIDE
Head to head comparison of risk stratification scores HEART vs TIMI score for patients with undifferentiated chest pain and correlating with frequencies of in-hospital major adverse cardiac events

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Purpose: Risk stratification of undifferentiated chest pain patients admitted to chest pain assessment unit (CPAU) according to HEART and TIMI risk score and correlating with in-hospital frequencies of major adverse cardiac events-MACE (Troponin positive MI, revascularisation percutaneous coronary intervention-PCI or coronary artery bypass grafting-CABG) and death.

Methods and material: Retrospective observational study. 1022 patients were prospectively enrolled in the CPAU from February 2011 to March 2013. 108 patients were excluded from study. Out of 1010 patients included 4 patients went back to home country, 7 patients left against medical advice, 10 patients were diagnosed with pericarditis and 89 patients had too limited data to evaluating a study group of 913. In a study group of 913 consecutives patients admitted with undifferentiated chest pain to (CPAU) were risk stratified according HEART and TIMI score. The patients were then divided in Low, Intermediate and High risk categories depending on their HEART score (0-3 low-risk, 4-6 Intermediate-risk, and 7-10 high-risk) and TIMI score (0-2-Low-risk, 3-4 Intermediate-risk, 5-7 high-risk). The frequencies of in-hospital adverse outcomes (MACE) were then compared in each risk category between HEART and TIMI scores.

Results: Troponin positive MI were noted in 1.5%, 10.2% and 72.2%; PCI in 1.7%, 12.2% and 36.1%; and CABG 0%, 2% and 0% in Low, Intermediate and High HEART risk score. In TIMI risk group troponin positive MI was noted in 4.5%, 17.5 and 75.5%, PCI in 5.9%, 15.9% and 25.0%; and CABG 0.48%, 1.9% and 2.5% respectively. Frequencies of admission outcomes significantly correlated well with HEART and TIMI risk score (p<0.001).

Conclusion: HEART and TIMI risk score correlate well with frequencies of in-hospital adverse outcomes (MACE) in term of troponin positive MI, PCI and CABG, however HEART risk score is found better in excluding MACE than TIMI risk score in Low and Intermediate category but comparable for predicting MACE in high risk group.

P5483 | BEDSIDE
Impact of the clinical introduction of high-sensitivity cardiac troponin T assay on rates of coronary angiographies and exercise stress tests in acute chest pain - Insights from an international trial

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Purpose: With the clinical introduction of more sensitive cardiac troponin (cTn) assays, concerns about potential higher rates of false positives leading to an increased number of clinically not indicated coronary angiographies and exercise testings.
stress tests arose. On the other hand, the increased sensitivity potentially improves the early rule out of acute myocardial infarction (AMI), decreasing the need for further stress tests.

Methods: We conducted a prospective, international diagnostic study to compare the incidence of coronary angiographies and exercise stress tests before and after the introduction of Roche high-sensitivity cTnT assay, replacing a less sensitive, conventional cTnT assay. A total of 2631 consecutive patients presenting with symptoms suggestive of AMI to the emergency department (ED) of three hospitals were included. Coronary angiographies and cardiac stress tests were only considered for this analysis if they were performed during the index visit or within the following three months.

Results: During the first phase using a conventional cTnT assay, 26% (387 out of 1513) of all patients underwent coronary angiography as compared to 25% (284 out of 1118) patients after the introduction of the hs-cTnT assay (p = 0.199 for comparison). The percentage of angiographic findings showing normal vesels (10% before vs. 7% after the introduction of hs-cTnT, p = 0.431) or just mild coronary sclerosis (4% vs. 6%, respectively) did not differ significantly between the two phases (p = 0.431). Cardiac stress tests were markedly less frequent after the introduction of the hs-cTnT assay in all three hospitals, with a median time of distress at discharge reduced significantly for out-patients after the introduction of hs-cTnT (359 minutes before vs. 277 minutes after hs-cTnT, p < 0.001).

Conclusions: At a first look to times using a conventional, less sensitive cTnT assay, the introduction of a hs-cTnT assay does not result in higher rates of coronary angiographies nor in an increased number of normal or just mild angiographic findings among patients presenting with acute chest pain to the ED. However, it reduces the median length of stay on the and seems to substantially improve the early rule-out of AMI by nearly halving the rates of subsequent exercise stress tests.

P5484 | BEDSIDE
Is high sensitivity troponin T a useful marker for ACS in advanced renal insufficiency?
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Purpose: Renal insufficiency (RI) is a well known limiting factor in the evaluation of coronary infarction (MI) with troponin T (TnT). Less data are available for high sensitivity-TnT (HS-TnT), in particular it is unknown in which amount the stage of RI influences HS-TnT level in the diagnostic workout for diagnosis of Acute Coronary Syndromes (ACS).

Methods: We included 533 pts coming to the emergency department for chest pain or symptoms suggestive of ACS. 449 were diagnosed with ACS and 84 with a diagnosis of ACS. In all pts we analyzed the HS-TnT level at the admission and at 3-6 hours; we consider positive a first measurement >14 ng/L and a relative delta >20 or 50% at the second sample, based on the admission level, according to literature. The population was classified according to the glomerular filtration rate (GFR) level: GFR ≥60 ml/min, GFR 30-60 ml/min, GFR <30 ml/min. We assessed the area under the curve (AUC) value by categorical values.

Results: 87 out of 533 pts had GFR <60 ml/min, among these pts 65 (75%) had HS-TnT ≥14 ng/L at first sample and 20 (31%) had diagnosis of ACS. HS-TnT at first sample had low diagnostic accuracy with increasing stage of RI, in particular in the group with GFR <30 ml/min (AUC 0.54). In these pts the use of relative delta led to an increase in AUC value from 0.54 to 0.85. The improvement was smaller and not significant in the other two groups.

Conclusions: Our study demonstrates that HS-TnT levels have a poor early performance in case of advanced RI, but in these pts, the use of an appropriate relative delta may increase diagnostic accuracy for ACS.

P5485 | BEDSIDE
Mechanical complications of acute myocardial infarction in the modern era of reperfusion: type, incidence, associated factors and prognosis

Introduction: The incidence of mechanical complications following acute myocardial infarction (AMI) has fallen with the provision of reperfusion therapies. Although, they remain life-threatening and need prompt detection and management. In the acute phase, these include ventricular septal rupture (VSR), free wall rupture (FWR) and acute mitral regurgitation (AMR).

Objective: To describe the type, incidence, associated factors and prognosis of AMI mechanical complications in the modern era of reperfusion.

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 (mean age 64 years, 77.2% male). The minimum follow-up performed was 6 months. The incidence of mechanical complications was 1.7% (41/2417) after the introduction of the hs-cTnT assay. Patients with mechanical complications were older (75 vs. 64 years, p < 0.001). At admission, they presented mainly with shock (20.0% vs. 6.2%, p = 0.001) and renal failure (65% vs. 27%, p < 0.001). NT-proBNP value (6962 vs. 2885 pg/mL, p = 0.004) and the risk scores GRACE (197 vs. 144, p < 0.001) and Crusade (51 vs. 29, p = 0.011) were higher. Time since symptom onset until reperfusion with primary angioplasty was superior in patients with mechanical complications (7h54min vs. 4h54min, p = 0.006) as was more frequent the absence of effective reperfusion after primary angioplasty (30.8% vs. 8.7%, p = 0.006). During hospitalization, these patients had higher peak creatinine (1.7 vs. 1.2 mg/dL, p = 0.002) and more rhythm disturbances, as new onset atrial fibrillation (25.0% vs. 9.4%, p = 0.019) and high degree atroventricular block (20.0% vs. 5.6%, p = 0.006). These patients were treated with more aggressive therapies, as the use of amions (40% vs. 6.7%, p = 0.001), ventilation support (29.4% vs. 5.5%, p < 0.001) or intra-aortic balloon pump (40% vs. 2.6%, p < 0.001). The prognosis was unfavorable at short and long term (mortality during hospitalization of 40% vs. 3.7% and during follow-up of 41.7% vs. 5.2%, p = 0.001). According to the mechanical complication type, the prognosis was better in AMR (global mortality of 20%) and worse in VSR and FWR (global mortality of 66.7% and 83.3%, respectively).

Conclusion: The definition of a clinical profile related to mechanical complications, including variables as shock at admission, iSthemia time or reperfusion success might be important to develop strategies to monitor more closely these patients.

P5486 | BEDSIDE
High sensitivity troponin T in managing patients with suspected acute coronary syndrome: comparison between two diagnostic algorithms
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Background: The universal definition of acute myocardial infarction (AMI) requires a rising/falling pattern of cardiac troponin with at least one value above the 99th percentile, but the actual A change between the serial measurements of troponin levels has not been defined yet. Herein we compared the algorithm published by White (WA) and that proposed by the European Society of Cardiology Working Group on Acute Cardiac Care (ESC-WG-ACC-A).

Methods: We enrolled 251 consecutive patients admitted to Emergency Department for suspected acute coronary syndrome (ACS) and for whom high-sensitivity Troponin T (hs-TnT) levels were determined in serial blood samples. We divided the study population into 3 subgroups according to the WA (positive for AMI, negative for AMI, adverse prognosis) and then we analyzed how the diagnosis changed according to ESC-WG-ACC-A within each such subgroup.

Results: A final diagnosis of AMI was made in 38 patients (15%) according to the WA, while unstable angina was diagnosed in 11% of cases. Among patients with hs-TnT curve positive for AMI according to the WA, we observed a difference in 6% of cases by using the ESC-WG-ACC-A (figure). In particular, the latter did not confirm AMI in those patients who had a falling pattern in troponin levels. Moreover, when hs-TnT was >14ng/L (99th percentile) without a positive curve for AMI (the so-called Adverse Prognosis subgroup according to the WA), the ESC-WG-ACC-A was discordant in 11% of cases. In these patients the final diagnosis was different from ACS in almost all cases (93%), meaning that ESC-WG-ACC-A would have diagnosed AMI in a larger number of patients.

Conclusion: The WA seems to be more specific in distinguishing patients with real AMI diagnosis from those with elevated troponin levels for reasons other than AMI.
Circumflex-related acute coronary syndrome: how to make an early diagnosis and treatment?

P5489 | BEDSIDE
Clinical presentation and outcome of patients with false-positive ST-segment elevation myocardial infarction
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Introduction: Activation of cardiac catheterization laboratory through regional code STEMI systems. Only admission values of non-trauma patients were analyzed. The diagnostic performance of a POC-test for TnT is compared with a "conventional" threshold value used is recommended to have a coefficient of variation of less than 10%. POC-systems do usually not meet these criteria at the 99th percentile. In this analysis, the diagnostic performance of a POC-test for TnT is compared with a "conventional" threshold value used is recommended to have a coefficient of variation of less than 10%. POC-systems do usually not meet these criteria at the 99th percentile. In this analysis, the diagnostic performance of a POC-test for TnT is compared with a "conventional" threshold value used is recommended to have a coefficient of variation of less than 10%. POC-systems do usually not meet these criteria at the 99th percentile.

Methods: All patients with routine TnT-testing in the ED were enrolled in two time-frames of 3 and 4 months. Double TnT-measurements were performed with a contemporary sensitive assay in EDTA whole blood on the AGT-90 (Radower) and a hs-TnT assay in heparin plasma on the Cobas-602 (Roche analysis systems). Only admission values of non-trauma patients were analyzed. The diagnostic performance of hsTnT for AMI in the prediction of outcome in patients with symptoms of non-STE ACS and non-conclusive ECG. The aim of the study is to investigate if copeptin provides additive information to hs-troponin in the prediction of outcome in patients with symptoms of non-STE ACS and non-conclusive ECG.

Results: Of all 3,396 patients, 7.9% had a final diagnosis of UAP (267), 3.7% NSTEMI (124) and 0.9% STEMI (32). A coronary angiography was performed in 11.5% (389) and PCI was required in 46.5% of these patients (181). The diagnostic performance of the respective TnT-assays is shown in table 1.

Table 1. Diagnostic performance of hsTnT and AQT-TnT at the 99th percentile and at the "conventional" threshold

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<th>hsTnT</th>
<th>AQT-TnT</th>
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<td>14ng/L</td>
<td>91.87</td>
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<td>50ng/L</td>
<td>66.67</td>
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<td>16ng/L</td>
<td>71.79</td>
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<td>30ng/L</td>
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Conclusions: In our cohort the diagnostic performance of conventional POC-testing was comparable to hsTnT. hsTnT in clinical routine provides information about slightly elevated Tn-values which might be of added value for further diagnostic evaluation. The implementation of a 99th percentile cut-off is accompanied by a major decrease in specificity, PPV and overall accuracy while NPV only increases slightly, thus questioning the routine clinical benefit.

P5490 | BEDSIDE
Prognostic role of copeptin in non-ST-elevation acute coronary syndrome
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Introduction: NSTEMI is defined as a rise or fall of cardiac troponin with at least one value above the 99th percentile of a healthy reference population. The cut-off value used is recommended to have a coefficient of variation of less than 10%. POC-systems do usually not meet these criteria at the 99th percentile. In this analysis, the diagnostic performance of a POC-test for TnT is compared with a "conventional" threshold value used is recommended to have a coefficient of variation of less than 10%. POC-systems do usually not meet these criteria at the 99th percentile.

Methods: First medical contact-to-balloon time. Paramedics achieved the 90 minutes first medical contact-to-balloon target compliance. Only admission values of non-trauma patients were analyzed. The diagnostic performance of the respective TnT-assays is shown in table 1.

Table 1. Diagnostic performance of hsTnT and AQT-TnT at the 99th percentile and at the "conventional" threshold

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Conclusions: In our cohort the diagnostic performance of conventional POC-testing was comparable to hsTnT. hsTnT in clinical routine provides information about slightly elevated Tn-values which might be of added value for further diagnostic evaluation. The implementation of a 99th percentile cut-off is accompanied by a major decrease in specificity, PPV and overall accuracy while NPV only increases slightly, thus questioning the routine clinical benefit.

P5488 | BEDSIDE
Circumflex-related acute coronary syndrome: how to make an early diagnosis and treat it?
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Purpose: This investigation points out the role of resting echocardiography in an Emergency Department (ED) as tool for the early diagnosis of left circumflex artery (LCx)-related acute coronary syndrome (AGS).

Methods: 451 (322 males) patients (pts) were observed in a cardiologist-run Chest Pain Unit because of a typical/atypical chest pain, negative ECC, normal T or ST elevation (12 pts, 19%), in the AQT-echo detection GROUP (23 pts), the culprit coronary lesion was on LCx in 15 pts (65,2%), on RCA=p<0.01). In other words, 15 out of 23 pts with normal ECG and T-Trop at presentation and echodetection of LCx in AQT-echo detection GROUP+culprit lesion on LCx (15 pts), the ECG remained NORMAL during hospitalization period in 11 patients (73,3%), compared to LAD-culprit lesion pts (0%) and RCA-culprit lesion pts (0%). LAD vs. RCA<p=0.001). LAD vs. RCA<p=0.001).

Conclusions: The ACS due to a culprit coronary lesion on the LCx may have a characteristic pattern defined by high percentage of 1)normal ECG; 2)LV wall motion abnormalities detected by resting echocardiography. Echocardiography could become an essential tool used to diagnose the LCx-related ACS.
peptide (NT-proBNP) and hs-troponin levels were measured. GRACE risk score was assessed at admission. Final diagnosis was set by two independent cardiologists based on current guidelines and available data. Copeptin was regarded as positive when > 18.5 pmol/l. Patients were evaluated after 6 months.

Results: In the cohort of 153 patients, there were 108 NSTEMI (70.6%), 28 UA (18.9%), 17 other causes of chest pain (11.1%). Median copeptin serum level was higher in NSTEMI than in UA and other patients (14.2: 7.9: 7.8 pmol/l, respectively; p=0.007). In the follow-up, copeptin was significantly correlated with GRACE score (r=0.27; p<0.001) and with mortality at 6 months (OR=4.0.2.29-7.32; p=0.0002) (figure). Levels of copeptin were higher in patients who died than in survivors (38.9 vs. 11.2 pmol/l, p<0.0014) while there was no difference in troponin levels (200.0 vs. 103.4 ng/ml, p=ns). Significant correlation of copeptin with NT-proBNP (r=0.23; p<0.0003) was aggravated by a tendency towards higher copeptin levels in patient with heart failure (NYHA - 1) at 6 month (p=0.06).

Conclusions: In a population of patients admitted to emergency department with chest pain and non-conclusive ECG copeptin is a valuable predictor of long-term prognosis of mortality. Therefore copeptin can be regarded as a co-efficient marker in the management of patients with non-STE ACS.

P5494 | BEDSIDE
Diagnosis of acute myocardial infarction in patients with complete left bundle branch block: prospective evaluation of the Sgarbossa criteria

Purpose: Patients with suspected acute myocardial infarction (AMI) and complete left bundle branch block (LLBB) in the ECG present a unique diagnostic challenge to clinicians. The Sgarbossa criteria were established to identify patients with AMI with acute coronary occlusion, but have not been validated in unselected patients with acute chest pain after the introduction of the universal definition of AMI. This was the aim of our study.

Methods: We included 2938 unselected patients presenting with acute chest pain to the emergency department in a prospective multicentre diagnostic study. Patients with complete LLBB at presentation were included in this subgroup analysis. The ECGs were reviewed by two independent cardiologists blinded to the adjudicated diagnosis for the presence or absence of the Sgarbossa criteria. The final diagnosis of AMI was adjudicated by two independent cardiologists according to the universal definition of AMI using all information becoming available during the work-up including coronary angiography, echocardiography and serial high-sensitivity cardiac troponin T testing.

Results: 83 patients (2.8%) had a complete LLBB at presentation, of whom AMI was the adjudicated diagnosis in 32 patients (39%). Applying the Sgarbossa criteria only four patients (12.5% of all patients with LLBB and AMI) could be correctly identified as having an AMI. 28 patients with AMI were missed (sensitivity 13%, negative predictive value 65%). There were no falsely positive results with the Sgarbossa criteria, therefore both specificity and positive predictive value were significantly lower (65%). There were no falsely positive results with the Sgarbossa criteria, therefore both specificity and positive predictive value were significantly lower (65%). There were no falsely positive results with the Sgarbossa criteria, therefore both specificity and positive predictive value were significantly lower (65%).

Conclusion: The Sgarbossa criteria are highly specific for AMI according to the universal definition, but have a very low sensitivity. Absence of the Sgarbossa criteria should not be interpreted as absence of AMI in patients presenting with acute chest pain. Our findings may help to better manage patients with complete LLBB in the future.

P5495 | BEDSIDE
Mode of presentation of patients with ST-segment elevation myocardial infarction in Singapore and its impact on door-to-balloon time and clinical outcome

Purpose: In the management of patients with ST-segment elevation myocardial infarction (STEMI), the timeliness of reperfusion via primary percutaneous coronary intervention (PPCI) is important in determining the morbidity and mortality. The timeliness of PPCI is estimated by the door-to-balloon (D2B) time which has become a key performance measure. Current guidelines recommend a D2B of ≤90 minutes. Given that most STEMs occur out of hospital, the mode of presentation, whether by emergency medical service (EMS) or by self-presentation (SP) is an important factor influencing the timeliness of treatment and possibly clinical outcomes.

Methods: From January 2009 to December 2011, 957 patients (86% male, mean age of 58 ± 12 years) presented to our hospital for STEMI and underwent PPCI. We evaluated the relationship between the 2 different modes of presentation with median door-to-balloon (D2B) time and in-hospital mortality. Data were collected retrospectively on baseline clinical characteristics, angiographic findings, therapeutic modality and hospital course.

Results: The majority of STEMI patients (64%) utilized EMS with the remaining 36% being SP. The percentage of patients achieving D2B < 90 minutes was 84%. The median D2B time was significantly shorter in patients presenting via EMS (57 minutes vs 66 minutes in the SP group; p=0.001). Despite shorter D2B time, the EMS group had a significantly higher in-hospital mortality rate than the SP group (6.4% vs 2.9%, p=0.02). Patients in the EMS group had a higher incidence of hypertension and hyperlipidaemia and were more often on 2-T therapy than patients in the SP group (p=0.001). In the EMS group, triple vessel and obstructive left main disease on coronary angiography were more common (9.4 vs 4.4%, RRR 41.4%, 95% CI 16.2-59.1, p=0.003), women (18.2 vs 10.6%, RRR 41.9%, 95% CI, 4.1-64.8, p=0.031), patients with diabetes (53.5%, 95% CI, 4.4-77.3, p=0.032) and women aged ≥65 years (22.1 vs 11.9%, RRR 46.0%, 95% CI, 7.6-86.5, p=0.022). In the 2-T group factors that significantly increased hospital mortality were: age ≥65 years (p=0.001), female gender (p=0.003), diabetes (p=0.034) and noninvasive treatment (p=0.003) in 1-T group only ≥65 years (p=0.001).

Conclusions: The introduction of tele-ECG and replace the two-stage transport system by direct transport was associated with a reduction in hospital mortality in STEMI.

P5496 | BEDSIDE
Clinical characteristics and outcome of STEMI patients with early (3 hours) presentation treated by primary PCI or fibrinolysis therapy
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Background: It is well known that prognosis of STE-AMI is worse in STEMI patients (pts) treated by fibrinolysis than by primary PCI. However, the choice of type of RT, primary percutaneous coronary intervention (p-PCI) or fibrinolysis (FT) depends on many factors, but both methods are suitable for STEMI-related PCI. The aim of this study was to compare clinical characteristics and outcomes of STEMI pts p-PCI is more suitable and with better prognosis than FT. In spite of that, in real life, p-PCI is the preferred therapy for low risk patients. There are not enough
The Timing of Intervention in acute Coronary Syndrome (TIMACS) trial. Patients not already on antplatelet therapy received aspirin and clopidogrel according to the current guidelines for management of non-STEMI.

Results: Median time to angiography in the immediate group was 1.3h and 61.8h in the delayed group (p < 0.001). Baseline clinical characteristics were similar, except for a higher rate of diabetes in patients undergoing delayed intervention (33% vs. 22%, p = 0.024). There was a trend for higher in-hospital bleeding rates in the immediate compared with the delayed intervention group (9.9% vs 4.3%, OR 2.41, 95%CI 0.96-6.02, p = 0.06). The observed difference was mainly due to minor non-major bleeding events. The extent of bleeding was analyzed in two cases in the delayed and in one case in the immediate intervention group. There was one intracranial bleeding in a patient randomized to the immediate invasive strategy.

Conclusion: Occurrence of in-hospital major bleeding in non-STEMI patients is similar in immediate versus delayed invasive strategy. Immediate intervention is associated with higher rates of minor bleeding events.

P5497 | BEDSIDE
Comparison of transradial versus transfemoral approach for primary PCI in diabetic patients with ST-elevated acute myocardial infarction
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Purpose: The aim of the study is to compare the outcome of transradial access (TRA) vs. transfemoral approach (TFA) in primary percutaneous coronary intervention (PCI) for ST elevation myocardial infarction (STEMI) in diabetic patients.

Methods: Data of diabetic patients (n=364) who underwent PCI to STEMI patients that underwent PCI for STEMI during that period. Interventions were successfully done in 236 with TRA artery access and 128 with TFA. The 30 days and 1 year mortality rates were lower in TRA compared to TFA (6.4% vs 17.2%, p < 0.001, and 8.5% vs 18.8%, p=0.004, respectively). The 30 days and at 2 years follow-up, MACE rates were favorable for TRA vs TFA group (9.7% vs 18.8%, p=0.021 and at 2-5 years vs 35.2%, p=0.034 respectively). The major bleeding and non-CABG bleeding rates were more favorable for TRA than TFA (3.4% vs 13.3%, p<0.001, and 13% vs 9.4%, p=0.001, respectively). The unfavorable and stepwise multivariable Cox-regression analysis was performed, adjusted hazard ratio was calculated and adjusted Kaplan Meier curves were created.

Results: There were 364 diabetic patients (age range 43 to 86 years) out of 1808 patients that underwent PCI in STEMI during that period. Interventions were successfully done in 236 with TRA artery access and 128 with TFA. The 30 days and 1 year mortality rates were lower in TRA compared to TFA (6.4% vs 17.2%, p < 0.001, and 8.5% vs 18.8%, p=0.004, respectively). The 30 days and at 2 years follow-up, MACE rates were favorable for TRA vs TFA group (9.7% vs 18.8%, p=0.021 and at 2-5 years vs 35.2%, p=0.034 respectively). The major bleeding and non-CABG bleeding rates were more favorable for TRA than TFA (3.4% vs 13.3%, p<0.001, and 13% vs 9.4%, p=0.001, respectively). The unfavorable and stepwise multivariable Cox-regression analysis was performed, adjusted hazard ratio was calculated and adjusted Kaplan Meier curves were created.

Conclusion: Transradial access strategy for primary coronary intervention is associated with significant early and two years mortality and MACE rate reduction compared to transradial access strategy for primary coronary interventions in diabetic STEMI patients.

P5498 | BEDSIDE
Effects of immediate invasive strategy on occurrence of in-hospital bleeding in non-STEMI patients

Methods: We interrogated the database of a register of all acute coronary syndrome cases presenting to a PCI tertiary care centre in the southern region of Ireland from 2006 to 2013 inclusively. All cases classified on referral or admission as STEMIs were identified. The diagnostic ECG was used to confirm the presentation of LBBB and the Sgarbossa criteria were applied: ST elevation > 1mm in a lead with a positive QRS complex, (5 points), ST depression in a lead with a negative QRS complex (2 points). The diagnostic ECG was used to confirm the presence of LBBB and the Sgarbossa criteria were applied: ST elevation > 1mm in a lead with a positive QRS complex, (5 points), ST depression in a lead with a negative QRS complex (2 points). STEMI was diagnosed by angiographically confirmed acute occlusion of an epicardial artery with a significant elevation of cardiac troponin T.

Results: Thirty eight patients were registered as STEMI with LBBB as a referral or admission diagnosis. LBBB was confirmed in 30/38 (79%). Of these patients, 83% (5/6) had STEMI, 3 confirmed angiographically, 2 dying before angiography. Fifty seven percent (17/30) of patients with LBBB had a Sgarbossa score of 0. Four of these 17 (24%) patients were diagnosed with STEMI.

Conclusion: True aLBBB-STEMI was found in a very small number of cases presenting for PPCLI. Over half of cases referred as aLBBB-STEMI were false positives. An elevated Sgarbossa score was specific in diagnosing aLBBB-STEMI but restricting PPCLI only to those with an elevated Sgarbossa score risks missing true aLBBB-STEMI cases. TRA continues to pose an operational challenge in PCI protocols and further work is warranted to determine the best approach to these patients.

P5499 | BEDSIDE
Spontaneous coronary artery dissection; an uncommon consequence of acute coronary syndrome
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Background and aims: Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome more frequently diagnosed in women and sometimes related with peripartum period. The diagnosis is usually made by coronary angiography. Due to its not well-known pathophysiology and low incidence, clinical features, prognosis and treatment of this patients remain unknown. The purpose of the present study was to analyze clinical, angiographical characteristics and prognostic of patients with confirmed SCAD.

Methods: This is a prospective registry of patients with SCAD diagnosed in our institution from October 2009 to January 2014. All patients were diagnosed with coronary angiography and were regularly followed in the outpatient clinic or by telephone contact. In most of the cases a follow-up coronary CT was performed to evaluate coronary artery patency. After initial diagnosis a conservative approach

Data about mortality and the type of applied RT in STEMI patients hospitalized during first three hours in Serbia as transition country.

Results: Data were used from the hospital registry for Acute Coronary Syndrome in Serbia (HORAKS) and observed STEMI pts during three years, from 2007 to 2009, hospitalized in 52 Coronary Care Units. In 13534 consecutive STEMI pts, mean age 63.6±12.0 years, m/f 85/38, RT was done in 8502 (56.4%) pts. The most of repertused pts, 4986 (58.6%) arrived during first three hours; mean age 59.6±11.4 and more received fibrinolysis (FT) 3277 (65.7%) pts than pPCI 1709 (34.3%) pts. The pts in FT group were older (60.1±11.3 vs 58.6±11.5, p<0.000) than pts in p-PCI group, with higher prevalence of diabetes (20.1%, vs. 17.6%, p<0.004), with higher prevalence of renal failure (4.3% vs. 3.1%, p<0.035) and heart failure (27.9% vs. 18.5%, p<0.000). Doctors decision to choose the p-PCI or FT (HL test, y2=10.421, p=0.023, c-statistic 0.699, SE 0.006, 95% CI 0.657-0.740) was dependent on pts ages, age<45, the time from symptoms onset (>120 minutes), the anterior localization, pts without heart failure, non-diabetes pts, non-previous myocardial infarction and with previous PCI; additional factors were gender, previous CABB, stroke, anemia, ages <75 years. The mortality in whole repereused group of pts was 7.5%; in p-PCI group was 4.3% and FT group was 8.7%. However, the time from symptom onset to hospital arrival was longer in p-PCI group 92.4±36.4mm vs. FT group 80.9±37.4mm, p<0.000.

Conclusion: The STEMI high risk patients with early (<3 hours) presentation and possibility for on-time reperefusion were more often reperefered by fibrinolysis, compared to STEMI pts with positive QRS complex. STEMI decision should be treated with p-PCI in order to better prognosis. In our study, the morality of these patients was statistically better in p-PCI (4.3%) than in FT (8.7%) group.
was mandatory in all cases. Only patients with persistent angina and severe coronary flow disruption were revascularized.

Results: Thirty patients with SCAD were recruited (from a total of 3905 acute coronary syndromes). Most of them were female (97%), ST-elevation myocardial infarction was the most frequently observed clinical presentation (53.3%) followed by non ST-elevation myocardial infarction and unstable angina. A low prevalence of cardiovascular risk factors was observed: smoking (63.3%), hypertension (17%) and dyslipidemia (17%). Over 17% of the cases were in periapertum period. Eight patients (26.6%) were treated with PCI and only one (3.3%) underwent coronary artery bypass graft. All other patients were treated conservatively. No differences between both groups were found, in part due to the small sample size. Overall mortality rate was 6.6%, one patient that required cardiac TC and one death, both included in revascularized group. Patients in the conservative group presented a low rate of major cardiac events during the follow-up period (611 days; IQR 852) 13.4% of readmissions, 4.5% reinfarction and only one patient required revascularization after the first episode. Follow-up coronary CT (performed in 53.3% patients) showed no evidence of residual lesion or persistent coronary dissection in 93.7% patients. Coronary aneurism was observed in 12.5% patients. Coronary aneurism was observed.

Conclusions: In our experience SCAD is more frequent in female with low cardiovascular risk factors. Conservative medical treatment was the most common used and seems to be appropriate with an excellent prognostic and good angiographic evolution. PCI should be restricted to cases of persistent angina or compromised coronary flow.

P5501 | BEDSIDE

Long term-prognostic value of multivessel or culprit-only revascularization in patients with ST-elevation myocardial infarction and multivessel coronary disease


Objective: Many ST-segment elevation myocardial infarction (STEMI) patients have multivessel disease. There is still controversy in treatment strategy in STEMI patients with multivessel disease. We compared clinical outcomes between multivessel revascularization and culprit-only revascularization in this setting.

Methods: We performed a retrospective analysis in 600 patients (67.4±12.7 years; 25.2% Female) admitted by STEMI in our department between 2004 and 2012, with multivessel coronary disease underwent percutaneous coronary intervention (PCI). Using Cox proportional hazards regression analysis, we evaluate the long-term value of complete revascularization.

Results: 42.7% of patients underwent culprit-only PCI. 105 patients (17.5%) died during the follow-up (4.2±2.8 years) and 32 patients presented reinfarction (5.3%). Multivessel PCI was not associated with lower rates of mortality (HR 0.81, CI 95% 0.54-1.20, p=0.291), HF and reinfarction (HR 1.22, CI 95% 0.61-2.46, p=0.575). Stratifying by GRACE risk score groups, we also did not find differences between multivessel revascularization and culprit-only revascularization.

Conclusion: Our findings support the current guidelines recommendation to perform culprit-only PCI in STEMI patients with multivessel coronary artery disease without hemodynamic compromise.

P5502 | BEDSIDE

Impact of multivessel coronary artery disease on reperfusion success in patients with ST-elevation myocardial infarction - insights from cardiac magnetic resonance imaging

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Background: A significant portion of patients with ST-elevation myocardial infarction (STEMI) display multivessel coronary artery disease (MVD). However, data on the association of MVD and reperfusion success are scarce. Thus, we thought about the impact of MVD on infarct size, microvascular obstruction (MO) and myocardial salvage index (MSI) assessed by cardiac magnetic resonance imaging (CMR) in a large unselected cohort of patients with STEMI reperfused by primary percutaneous coronary intervention (PCI).

Methods: STEMI patients reperfused by primary PCI (n=1074) within 12 hours after ST-elevation infarction and STEMI from CMR (interrater range IQR 2.4). Infarct size and MO were measured 15 min after gadolinium injection. T2-weighted and contrast-enhanced CMR were then used to calculate MSI. Severity of coronary artery disease was graded as single- vessel disease compared to patients with MVD. Further, we detailed set of clinical, angiographic and electrocardiographic parameters was recorded. The primary endpoint was defined as a composite of death, non-fatal myocardial infarction and congestive heart failure (MACE). Clinical follow-up was conducted after 12 months.

Results: MVD was present in 48.5% (n=521) of patients. Patients with MVD were older (66 [IQR 55-73] vs. 60 [IQR 50-70] years, p<0.001) and more often diabetics (26.3 vs. 17.5%, p=0.001) in comparison to those with single- vessel disease. Angiographic reperfusion success defined as TIMI-flow III post-PCI (87.6 vs. 88.1%, p=0.92) and ST-segment resolution (60 [IQR 25;80] vs. 60 [30;80]%, p=0.18) were similar between both groups.

Patients with MVD displayed no significant differences in infarct size (17.5 [IQR 8.4-26.4] vs. 16.0 [IQR 8.5-24.4] %L V; p=0.15) and extent of MO (0.4 [IQR 0.01; 6] %L V, p=0.71) as well as MSI (52 [IQR 33-74] vs. 53 [IQR 36-72], p=0.48 in comparison to patients with single-vessel disease.

Finally, the presence of MVD was significantly associated with the time-dependent occurrence of MACE (log-rank comparison p=0.004).

Conclusion: MVD is not associated with impaired reperfusion success assessed by CMR. However, the adverse clinical outcome of patients with MVD might thus rather be explained by more advanced coronary artery disease itself and unfavourable baseline characteristics.

P5503 | BEDSIDE

Feasibility and efficacy of zotarolimum-eluting stent in the patients with acute coronary syndrome: optical coherence tomography analysis


Background: Drug-eluting stent in the lesions with acute coronary syndrome (ACS) is one of the major predictors of late stent thrombosis. The purpose of this study is to evaluate feasibility and efficacy of zotarolimum-eluting stent (ZES; Resolute-integrity or Endeavor stent) in the ACS lesions, using optical coherence tomography (OCT) in vivo.

Methods: OCT was performed at 9-month follow-up in 40 ACS patients treated with ZES (14 Resolute-integrity and 26 Endeavor). Every observed stent were analyzed at intervals of 1mm. Neointimal coverage of struts, stent apposition, and neointimal thickness (NIT) were evaluated.

Result: In total, 2737 struts in 14 Resolute-integrity stents and 5576 struts in 26 Endeavor stents were analyzed. Frequencies of exposed stents and of incompletely apposed struts were 3.2±3.5% / stent and 1.2±1.6% /stent in Resolute-integrity stent, 0.5±0.9% / stent and 0.05±0.1% /stent in Endeavor stent (p<0.001, p<0.001, respectively). The mean thickness of neointima was 0.1±0.09 mm and 0.3±0.10 mm (p<0.001). Thrombus was not detected in all patients.

Conclusion: These data would suggest feasibility and efficacy of ZES in the lesion of ACS. However, stent coverage is better in Endeavor stent than in Resolute-integrity stent in those lesions.

P5504 | BEDSIDE

Higher in-hospital-mortality of NSTEMI as compared to unstable angina despite higher rate of invasive therapy in clinical practice - results of the EHS ACS Registry

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Background: About half of ACS present without ST-segment elevation. Current ESC guidelines for the management of NSTE-ACS recommend risk stratification to decide about the appropriateness of invasive treatment. This risk stratification also includes troponins which define the diagnosis of NSTEMI. Little is known about treatment and outcome differences between NSTEMI unstable angina pectoris (UAP) in clinical practice.

Methods: Between Oct 2006 and Oct 2008, 21,872 consecutive patients with ACS were enrolled into the Euro-Heart-Survey ACS-Registry to document treatment and hospital complications. We examined the differences in treatment and outcome of patients with NSTEMI and UAP in Europe.

Results: A total of 13,018 patients (59.5%) presented with NSTEMI, 7,688 (59.1%) had NSTEMI, 5,330 (40.9%) had UAP. NSTEMI patients were older and more often suffered from diabetes, peripheral artery disease and renal failure. They were more likely to undergo an invasive strategy with early PCI as compared to patients with UAP. Despite the more aggressive treatment, NSTEMI had...
a significantly higher in-hospital mortality and MI-rate. After correction for differences in baseline characteristics as well as in treatment strategy patients with NSTE-ACS had a more than 4-fold increased risk to die during the index hospital stay (HR 4.19, p < 0.001).

**Conclusions:** Patients presenting NSTE-ACS and troponin release are known to be at high risk. These NSTEMI-patients were more often treated by coronary intervention. However, NSTEMI was an independent predictor of hospital mortality in the patient population with NSTE-ACS with a more than 4-fold increased rate of death.

**P5505 | BEDSIDE**

Relative prognostic significance of self-reported frailty components in non-ST-segment elevation acute coronary syndromes: men and women are not the same

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**Purpose:** Frailty is associated with worse morbidity and mortality in CVD; however, the prognostic value of self-reported frailty components is unclear. In the TRILOGY ACS trial of medically managed ACS patients, elderly participants (> ≥ 65 y) were asked if they had experienced any Fried Frailty Index component in the last 12 mos: unintentional weight loss (WL); decreased grip strength (GRIP); increased fatigue/lethargy (F-L); slower 5-m walking pace (WALK); or decreased physical activity (PA). We examined 1) contributions of individual frailty components to risk of all-cause mortality and 2) whether this association is modulated by age and sex.

**Methods:** Cox proportional models were used to examine associations between frailty components and time to death. The impact of age and sex on Fried categorization (not frail; pre-frail [1-2 components]; and frail [≥3 components]) was examined.

**Results:** Of 4996 elderly patients, 89 (1.8%) had WL, 211 (4.2%) had GRIP, 523 (10.5%) had F-L, 489 (9.7%) had WALK, and 975 (19.9%) had PA. Overall, 3612 (72.3%) were not frail, 1147 (23%) were pre-frail, and 237 (4.7%) were frail. The distribution of frailty and its components was similar between sexes and increased with age. HRs for association of self-reported frailty components with mortality was: WL, p = 0.01; WALK, 1.78; p = 0.01; PA, 1.64; p = 0.01; F-L, 1.53; p = 0.01; GRIP, 1.29; p = 0.20. However, the components did not offer additive prognostic power. The association between frailty categorization and mortality was modulated by age and sex (Fig. 1).

**Conclusions:** A simple frailty self-assessment offers important prognostic information on mortality. Equal weighting of frailty components deserves reexamination. Self-reported frailty may offer more prognostic information in men than in women.

**THROMBOSIS AND ANTICOAGULATION – I**

**P5507 | BEDSIDE**

Betaesian meta-analysis of the efficacy and safety of the novel oral anticoagulants for treatment of venous thromboembolism

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**Purpose:** Traditional extended treatment of venous thromboembolism (VTE) has relied on the use of vitamin K antagonism for prevention of recurrent VTE after initial diagnosis. The use of warfarin in this patient population has challenges including risk of significant bleeding, drug interactions, and frequent monitoring. While new oral anticoagulants have been tested as alternatives to warfarin, the extent of longitudinal benefit and safety remains unclear. We sought to examine this controversy by performing a Betaesian meta-analysis.

**Methods:** A literature search was performed which identified a total of 16,117 patients from 5 randomized controlled trials comparing the novel oral anticoagulants (apixaban, rivaroxaban, edoxaban, dabigatran) to warfarin. Frequentist and Betaesian random effects models were utilized to evaluate the primary efficacy endpoints of recurrent VTE and mortality, VTE related death and mortality, in addition to safety endpoints of major bleeding and clinically-significant minor bleeding.

**Results:** For the primary combined endpoint of recurrent VTE and mortality, there was a 62% probability of benefit, with a posterior odds ratio of 0.6593 (Bayesian credible interval 0.51-2.51). The combined safety endpoint of major bleeding and clinically relevant minor bleeding was found to have a 42% probability of benefit, with posterior odds ratio of 1.35 (Bayesian credible interval 0.61-2.51). Additional clinical and safety endpoints did not demonstrate significant differences, though a trend towards benefit with the novel oral anticoagulants was seen.

**Conclusions:** Sequential Bayesian meta-analysis of the novel anticoagulants versus warfarin in treatment of venous thromboembolism supports the safety and efficacy of using the novel oral anticoagulants as primary therapy for VTE. There is a non-significant trend towards increased efficacy of the novel oral agents, though this is tempered by a non-significant trend towards increased bleeding events.

**P5508 | BENCH**

Macrophages and platelets are the major source of the Factor Seven Activating Protease (FSAP) in human atherosclerotic plaques: a possible crosslink between inflammation and coagulation

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**Purpose:** Factor VII activating protease (FSAP) activates FVII as well as pro-urokinease, thus regulating local proteolysis-, hemostasis- and remodeling associated processes in the vasculature. In order to define the role of FSAP in vascular pathophysiology we have investigated the expression of FSAP protein in atherosclerotic plaques with defined clinical features.

**Methods:** 36 carotid atherosclerotic plaques were harvested during carotid endarterectomy, immunohistochemically and semi-quantitatively examined for the presence of macrophages (CD68), platelets (CD41) and FSAP. Patients' demographics were recorded and blood samples were stored. Human macrophages were isolated and stimulated with defined concentrations of oxLDL and several statins. Stimulated and non stimulated human platelets underwent further analysis and FSAP signals were ascertained at both messenger- and protein levels.

**Results:** FSAP protein was found to be associated with CD68 expressing cells in macrophage-rich shoulder regions in early uncomplicated plaques. A stronger FSAP signal was observed in advanced symptomatic lesions, focally surrounded in intraplaque hemorrhage-related structures within the necrotic core of atherosclerotic plaques. Platelets were identified as the main sources of FSAP within atherothrombotic material. Unstimulated platelets, isolated from healthy subjects, showed a small amount of FSAP mRNA and protein and ADP, but not TRAP, induced expression expression in activated platelets. Interestingly, agonist-induced FSAP expression was partially inhibited by aspirin. Furthermore, human foam cells expressed FSAP in vitro and this was further induced by different statins.

**Conclusions:** Platelets and monocytes macrophages are a major source of FSAP in human atherosclerotic plaques. Human foam cells and human platelets expressed FSAP in vitro. These findings suggest that FSAP could serve as a molecular link between lipid metabolism, inflammation, and thrombus formation, which are all features of atherosclerotic plaques.
The presence of type 2 diabetes increased P AI-1 expression 3.2-fold, while int-PA was 2.2-fold, u-PA 5.8-fold, P AI-1 8.7-fold, PTX3 1.7-fold, CXCL9 3-fold, the relative reduction of P-selectin was 0.7-fold, while the relative increase (all plaque instability (MMP-2 and TIMP-1) correlated positively to the ischemic time (t-PA, u-PA, P AI-1), inflammation (PTX3, CXCL9, MCP-1, IL-1B, 7-Hanska University Hospital-Osstra, Department of Medicine, Gothenburg, Sweden; 8 Brigham and Women’s Hospital, Cardiovascular Division, Boston, United States of America; 4 Thrombosis Research Institute, London, United Kingdom; 5 Bellevue Hospital, Department of Vascular Pathology, St Eilene, France; 6 Municipal Hospital Friedrichstadt, Medical Division 2, Dresden, Germany; 7 Boehringer Ingelheim GmbH & Co KG, Ingelheim am Rhein, Germany; 8 Friedman Consulting, Portland, United States of America

*Subset of VTE/VTE related deaths.

**Conclusions:** Several pro-inflammatory markers and mediators were genetically expressed in aspirated coronary thrombi from patients with acute myocardial infarction. The genetic expression profile changed according to the ischemic time with a decrease in expression of genes related to platelets and an increase in expression of genes related to fibrinolysis, inflammation and plaque instability, respectively. Expression of PAI-1 was significantly higher in patients with type 2 diabetes, possibly confirming the particular role of impaired fibrinolysis in type 2 diabetes.

The presence of hypertension seemed to be associated with plaque instability.

**P5511 | BEDSIDE**

Markers of thrombin generation are associated with myocardial necrosis and left ventricular impairment in patients with ST-elevation myocardial infarction

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**Introduction and aim:** Thrombin generation and fibrin formation play an important role in intracoronary thrombus formation, which may lead to an acute myocardial infarction.

**Aim of the present study was to investigate whether D-dimer, pro-thrombin fragment 1+2 (F1+2) and endogenous thrombin potential (ETP) as markers of in vivo and ex vivo thrombin generation, respectively, are associated with myocardial necrosis as assessed by Troponin T (TnT), and left ventricular impairment assessed by left ventricular ejection fraction (LVEF) and NT-proBNP.

**Methods:** Patients with ST-elevation myocardial infarction (STEMI) from a cross sectional cohort study (n=993) referred for primary percutaneous coronary intervention (PCI) were included. Median age was 61 years (range 24-94), 80% male. Blood samples were drawn the first morning after admission at a median time of 24 hours after onset of symptoms. D-dimer and F1+2 were determined by ELISA and ETP by the CAT-assay. Patients on warfarin were excluded from analysis.

**Results:** The total population levels of D-dimer, F1+2 and ETP (median (25,75 percentiles)) were 456 ng/l (287,796), 246 pmol/l (178.356), 1564 nm (1386,143).

Significant correlations were found between both peak TnT and D-dimer (r=0.260, p<0.0001) and F1+2 (r=0.364, p<0.001) and between NT-proBNP and D-dimer (r=0.243, p<0.001) and F1+2 (r=0.120, p=0.0001). When dividing TnT and NT-proBNP levels into quartiles there were significant trends for increased levels of both markers across quartiles (all p<0.001). No significant associations between TnT, NT-proBNP and ETP were found. When adjusting for relevant covariates (age, gender, BMI and NT-proBNP), both D-dimer and F1+2 remained significantly associated with peak TnT (both p<0.0001).

D-dimer remained significantly associated with NT-proBNP after adjustments (p=0.001), whereas the association between NT-proBNP and F1+2 was no longer statistically significant (p=0.301). A weak, but statistically significant inverse correlation was found between LVEF and D-dimer (r=0.160, p=0.0001) and F1+2 (r=0.090, p=0.011). When dichotomising LVEF levels at 40%, we observed significantly higher levels of both D-dimer (p=0.000) and F1+2 (p=0.014) in the group with low EF (r=0.147). No difference in ETP levels was found.

**Conclusion:** In a large cohort of STEMI patients, levels of D-dimer and F1+2 were significantly associated with the extent of myocardial necrosis assessed by peak TnT, the high levels of these coagulation markers in patients with low LVEF and high NT-proBNP may indicate a hypercoagulable state in patients with impaired myocardial function.

**P5512 | BEDSIDE**

The management of patients with atrial fibrillation undergoing percutaneous intervention with stent implantation (ACFAS); triple therapy with warfarin bridging is associated with higher risk

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**Purpose:** Bridging treatment with low-molecular-weight heparin (LMWH) has been the standard recommendation for patients at high risk for thromboembolic events if VKA were interrupted, but this strategy seems questionable in the light of recent findings indicating that bridging increases the risk of haemorrhage with- out lowering the risk of peri-procedural thromboembolism. Therefore, we prospectively assessed the effect of LMWH-bridging on thrombotic and bleeding events in patients with AF undergoing stent implantation with an indication for percutaneous coronary intervention.

**Methods:** ACFAS is an observational, multicenter, prospective registry including patients with AF who are referred for percutaneous coronary interventions with stent implantation (PCI-S). The primary endpoints were a composite of cardiac
and cerebrovascular events (MACCE) and bleeding complications as defined by the BARC-definition from discharge to 1-year follow-up period.

**Results:** Of the 975 consecutive patients enrolled, 663 were discharged on triple therapy, either VKA-triple therapy (VKA-TT, n=498) or LMWH-triple therapy (LMWH-TT, n=165). Male gender (70.7% VKA-TT vs. 72.7% LMWH-TT), age (73.0 ± 7.9 years of age LMWH-TT, vs. 72.5 ± 7.9 years of age LMWH-TT), BMI (28.4 ± 4.5 VKA-TT vs. 28.7 ± 4.9 kg/m² LMWH-TT) and other risk factors with the exception of diabetes (32.3% VKA-TT vs. 50.9% LMWH-TT, p<0.001) and hypertension (79.7% VKA-TT vs. 95.3% LMWH-TT, p<0.001) were not different in both groups.

The rate of MACCE was significantly elevated in patients discharged on LMWH-TT compared with VKA-TT (OR 0.58, 95% CI 0.49 to 0.72) and TIMI minor bleeding (OR 0.52, 95% CI 0.41 to 0.69).

**Conclusions:** In our large, prospective, real-world population of patients with AF undergoing PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT. Our study further supports the idea that bridging therapy with LMWH may be harmful for patients with an indication for PCI-S under oral anticoagulation.

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**P5515 | BEDSIDE Impact of dabigatran and phenprocoumon on clopidogrel mediated ADP induced platelet aggregation in patients with atrial fibrillation (T (DAB) AF who underwent PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT. Our study further supports the idea that bridging therapy with LMWH may be harmful for patients with an indication for PCI-S under oral anticoagulation.**

**Results:** We identified 585 patients with AF (74.8% male, 73.11±4.5 years old) who underwent PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT (HR 1.6, 95%CI 1.05-2.45, p=0.028). Moreover, severe bleedings (BARC ≥2) were more often but not significantly associated with LMWH-TT during the one year follow-up period (13.3% LMWH-TT vs. 9.2% VKA-TT, p=0.140).

**Conclusions:** In our large, prospective, real-world population of patients with AF undergoing PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT. Our study further supports the idea that bridging therapy with LMWH may be harmful for patients with an indication for PCI-S under oral anticoagulation.

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**Objective:** To assess the impact of dual antiplatelet therapy (DAPT: clopidogrel and a GP IIb/IIIa inhibitor) with warfarin (triplet therapy, TT) compared with unfractionated heparin or enoxaparin plus GP IIb/IIIa inhibitors. An antithrombotic effect of TT was further investigated.

**Methods:** A prospective multicenter study was conducted from 2007 to 2011 to include 1080 AF patients who underwent PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT (HR 1.6, 95%CI 1.05-2.45, p=0.028). Moreover, severe bleedings (BARC ≥2) were more often but not significantly associated with LMWH-TT during the one year follow-up period (13.3% LMWH-TT vs. 9.2% VKA-TT, p=0.140).

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**P5514 | BEDSIDE Blood clot formation for acute coronary syndromes and percutaneous coronary intervention: a meta-analysis of randomized trials**

**Background:** A variety of antithrombotic medications are used in the management of patients with acute phase of coronary syndrome (ACS) undergoing early use of percutaneous interventions (PCI) which attempt to reduce death, myocardial infarction and periprocedural ischemic events, recurrent revascularization and stent thrombosis. The efficacy of ADP on induced platelet function may be influenced by concomitant antithrombotic therapies. The impact of the direct thrombin inhibitor dabigatran etexilate as compared to phenprocoumon on platelet function in patients with concomitant clopidogrel therapy is unknown.

**Methods:** The “Impact of DABIgatran and phenprocoumon on the clopidogrel mediated ADP induced platelet aggregation in patients with atrial fibrillation” (DABI ADP 2) study was a randomized trial performed at Deutsches Herzcentrum Munich, Germany, which enrolled patients with atrial fibrillation who also required dual antiplatelet therapy (DAT). Patients were randomly assigned to receive either dabigatran (n=22) or the vitamin K antagonist phenprocoumon (n=24) in addition to DAT for a 2 week period. The primary endpoint was ADP-induced platelet aggregation (in AU x min) assessed with multiple electrode platelet aggregometry at 14 days after randomization.

**Results:** There was no significant difference regarding the primary endpoint between both groups, dabigatran 326 [266 - 462] AU x min and phenprocoumon 350 [214-535] AU x min, p=0.70. Furthermore, no significant differences were observed regarding the secondary endpoints, ADPs (P=0.70), TRAP- (P=0.17) and platelet aggregation scores (P=0.68). Conclusion: For all agonists studied here, dabigatran as compared to phenprocoumon has no impact on the ex vivo-measured platelet aggregation in patients with concomitant aspirin and clopidogrel therapy.

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**P5516 | BEDSIDE The association of deep venous thrombosis with atherosclerosis depends on a concomitant history of pulmonary embolism**

**Background:** A variety of antithrombotic medications are used in the management of patients with acute phase of coronary syndrome (ACS) undergoing early use of percutaneous interventions (PCI) which attempt to reduce death, myocardial infarction and periprocedural ischemic events, recurrent revascularization and stent thrombosis. The efficacy of ADP on induced platelet function may be influenced by concomitant antithrombotic therapies. The impact of the direct thrombin inhibitor dabigatran etexilate as compared to phenprocoumon on platelet function in patients with concomitant clopidogrel therapy is unknown.

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**P5515 | BEDSIDE Impact of recommendations of guidelines in patients with atrial fibrillation submitted coronary stenting**

**Objective:** To assess the impact of dual antiplatelet therapy (DAPT: clopidogrel and a GP IIb/IIIa inhibitor) with warfarin (triplet therapy, TT) compared with unfractionated heparin or enoxaparin plus GP IIb/IIIa inhibitors. An antithrombotic effect of TT was further investigated.

**Methods:** A prospective multicenter study was conducted from 2007 to 2011 to include 1080 AF patients who underwent PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT (HR 1.6, 95%CI 1.05-2.45, p=0.028). Moreover, severe bleedings (BARC ≥2) were more often but not significantly associated with LMWH-TT during the one year follow-up period (13.3% LMWH-TT vs. 9.2% VKA-TT, p=0.140).

**Conclusions:** In our large, prospective, real-world population of patients with AF undergoing PCI-S patients discharged on LMWH-TT had a significantly higher risk for the 1-year incidence of MACCE in comparison to patients discharged on VKA-TT. Our study further supports the idea that bridging therapy with LMWH may be harmful for patients with an indication for PCI-S under oral anticoagulation.
pathophysiology is however not fully clarified, although a number of possible explanations have been suggested, such as coexisting acute coronary artery disease or a neurogenic cardiac damage due to sympathetic activation. In our ongoing study (The Impact of Stroke on Heart Function) we seek to identify possible mechanisms behind troponin elevation in AIS.

Methods: The study is based on diagnostic methods ranging from clinical assessment and radiology to laboratory methods including flow cytometry and histopathological investigation to seek underlying mechanisms behind unexplained high levels of plasma troponin.

Results: We have identified a previously not recognized mechanism; a malignancy associated hypercoagulative state, presenting with ischemic stroke and high levels of plasma troponin T. Autopsy with histopathology in two cases revealed adenosarcomas with cerebral and myocardial microthrombosis (fig a). Analysis of the serum of cancer associated thrombosis with tissue factor in both metastases (fig b) and thrombi. We could also show, to the best of our knowledge for the first time in human, microvesicles staining positive for the tumour marker CK18, and citrullinated histone H3, markers of the recently described cancer associated procoagulant DNA-based neutrrophil extracellular traps (NETs) in thrombi in the heart (fig c), lung and brain (fig d).

Conclusion: Our results identify cancer associated microthrombosis as a previously unrecognized contributing factor to high levels of troponin in AIS. We believe that unexplained high levels of troponin in acute stroke deserve special attention in terms of possible occult malignancy.
autoimmunity, but uncertainty is still present about the most important predictors of cardiovascular events.

**Objectives:** Aim of our work is therefore to perform a collaborative systematic review on incidence and predictors of cardiovascular events in SLE patients.

**Methods:** PubMed, Cochrane was systematically searched for eligible studies on SLE cardiovascular event between January 2008 and December 2012. Study features, patient characteristics, and incidence of stent thrombosis were abstracted and pooled, when appropriate, with random-effect methods (point estimate [95% confidence intervals]), and consistency of predictors was formally assessed.

**Results:** A total of 17187 patients were included; of those, 93.1% were female, and the median age was of 39 years. After a median follow-up of 8 years, cardiovascular events presented in 25.4%, including acute myocardial infarction (4.1%), stroke (7.3%). The most important predictors may be divided into traditional risk factors, like male gender (OR 6.2, CI 95% 1.49 – 25.9), hyperlipaemina (OR 3.9, CI 95% 1.57 – 9.71), familiar history of cardiac disease (OR 3.6, CI 95% 1.15 – 3.12) and hypertension (OR 3.5, CI 95% 1.65 – 7.54), and SLE-related features, like the presence of auto-antibodies (OR 5.8 and 5.0, CI 95% 3.28 – 7.78) and neurological disorders (OR 5.2, CI 95% 2.0 – 13.9). A low correlation was shown for importance of organ damage and SLE activity (respectively OR 1.4, CI 95% 1.09 – 4.44 and OR 1.2, CI 95% 1.2 – 1.2), as well as for the age at diagnosis (OR 1.1, CI 95% 1.07 – 1.17).

**Conclusions:** Cardiovascular events in SLE patients are caused by a multifactorial mechanism, including both traditional and disease-specific risk factors. A global valuation with an individual risk-stratification based on both these features is important to correctly manage these patients in order to reduce negative outcomes.

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**P5524 | BENCH**

No signal for higher risk of myocardial infarction with apixaban: meta-analysis of randomized controlled trials

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**Purpose:** The coagulation system contributes greatly to the evolution of myocardial infarction (MI). Anticoagulation may reduce the occurrence of MI as monotherapy or with concomitant use of aspirin. Activated factor X antagonists (anti-Xa) and direct thrombin inhibitors have promising results in various indications in multiple non-inferiority trials. However, heterogeneous results were found regarding their cardiovascular safety. We systematically evaluated the risk of MI and mortality in patients receiving the new-generation oral anti-Xa agent apixaban.

**Methods:** Electronic databases were searched to find prospective, randomized, controlled clinical trials (RCT) that evaluated the clinical impact of apixaban. Efficacy measures included frequency of MI, cardiovascular and overall mortality. Outcome parameters of RCTs were pooled with a random-effects model.

**Results:** Between January 2000 and December 2013, twelve RCTs comprising 54,054 patients were identified. Based on the pooled results, there was no increase in the risk of MI in patients treated with apixaban (Odds Ratio (OR): 0.90; 95% Confidence Interval (CI) 0.78-1.04; p=0.17) compared to different controls. Cardiovascular and overall mortality with apixaban was comparable to the control groups (OR: 0.88; 95% CI 0.72-1.06; p=0.18, OR: 0.89; 95% CI 0.77-1.03; p=0.11, respectively). The pooled risk of major bleeding was lower in the apixaban groups (OR: 0.64-1.12; p=0.24), however, this reached significance only in subgroup analysis of trials with anticoagulant regimens in the control (OR: 0.68; 95% CI 0.53-0.88; p=0.003).

**Conclusions:** In a broad spectrum of patients and compared to different controls apixaban treatment was not associated with an increase in myocardial infarction or mortality.

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**P5525 | BENCH**

Comparison of fondaparinux and enoxaparin for non ST elevation acute coronary syndromes - an evaluation in a real world population

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**Introduction:** In the clinical trials setting, fondaparinux was more effective than enoxaparin in patients with non-ST elevation acute coronary syndromes (NSTEACS). However, few observational studies were done to assess the effect of fondaparinux in routine clinical practice.

The aim of this study was to evaluate the effect of fondaparinux, in comparison with enoxaparin, in the in-hospital outcome of an unsélected population of NSTEACS patients.

**Methods:** We performed an observational study of all NSTEACS patients treated with fondaparinux or enoxaparin included in a nation-wide registry, since October 2010. Eighteen patients treated with both fondaparinux or enoxaparin were excluded and data from 3298 patients treated with enoxaparin and 875 with fondaparinux was analyzed. The incidence of in-hospital death, re-infarction, stroke and major bleeding was compared in the two groups of patients. A combined efficacy endpoint of death, re-infarction and stroke was considered. Adjusted odds ratio (OR) for the combined endpoint were computed using logistic regression models.

**Results:** Fondaparinux treated patients were younger than patients in the enoxaparin group (66±12 vs. 68±13 years, p<0.001). Coronary angiography was performed in 75.6% of patients in the fondaparinux group and 63.3% in enoxaparin group (p<0.001); percutaneous coronary intervention (PCI) was done in 47.3% of fondaparinux group patients and 50.9% of the enoxaparin group (p=0.056).

Comparing with enoxaparin group, fondaparinux group had a lower rate of in-hospital death (1% vs. 0.9%, p=0.07) and death (1.1% vs. 2.7%, p=0.008). No significant differences were found in the incidence of re-infarction (1.4% vs. 2.0%, p=0.24) or major bleeding (1.0% vs. 1.4%, p=0.43). In multivariate analysis, adjusting for age, admission systolic blood pressure, ST-segment changes, use of glycoprotein IIb/IIIa receptor blockers and platelet aggregation and PCI risk of the combined endpoint was significantly lower in fondaparinux treated patients (OR: 0.43, 95%CI: 0.25-0.74, p=0.003).

**Conclusions:** In this “real world” population of NSTEACS patients, fondaparinux
was associated to a significantly lower risk of death and ischemic complications, without an increase in major bleeding events.

P5526 | BEDSIDE
Novel oral anticoagulants (NOAC) show the anticoagulant action without excess suppression of thrombin

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Background: NOAC acts the effects of anticoagulant without the adverse effects. Objectives: The aim was to compare NOAC (rivaroxaban; R, dabigatran; D) with warfarin, anticoagulant benchmark; LMWH, tissue factor pathway inhibitor; TM-D, thrombin-antithrombin complex; TAT, prothrombin fragment 1+2; PT F1+2.

Subjects: The blood concentration of benchmarks were measured in 28 cases taking R, in 76 cases taking W, in 60 cases taking dabigatran and in 477 cases as control.

Method: During the administration of the R, the TM (TM-R) was measured in 28 cases (total 69 samples). The TM (TM-N) was able to be measured without any anticoagulants in 8 out of the 28 cases (25 samples), and in 13 out of the 28 cases (84 samples) while taking W (TM-W). In 60 cases taking D, who belonged another group, the TM (TM-D) was measured.

Result: TM-N (mean ± SD, 3.20±0.82 FU/ml) was higher in patients with antithrombin (AF) than the control (TM-C: 2.97±0.74). That means that AF might impair the antithrombin endothelium due to remodeling. Furthermore, TM-R (3.22±0.92 FU/ml) was the highest compared with W (2.93±0.69) and TM-D (2.95±0.85). Significantly good relationships were observed between TM-N and TM-R (R=0.701), and between TM-W and TM-R (R=0.779), but TM-R was higher than both TM-N and TM-C (1.3 and 0.73 FU/ml higher). In addition, the TM-W was high during the pre-treatment period, but decreased with W and R and became within nearly normal range. After administration of W, D was also within normal range. The TAT decreased with W and D. These findings suggest that the higher TM-R may be related to active TM and not the degradation of TM. PT-F1+2 (171±111) to almost the same level by R. However, W suppressed it strongly compared to R and D. These findings suggest that W, R and D suppressed the coagulation equally, but if PT F1+2 reflects the amount of thrombin, R and D may not suppress it completely. These findings suggest that R and D show the anticoagulant action as W equally without release of the effect accounting for the absence of suppression of thrombin by W. Furthermore, that suggests R may have an anticoagulant action in addition to thrombin suppression which may be due to the TM-thrombin complex because of the elevation of the TM.

Conclusion: NOAC has certainly the anticoagulant action without adverse effects of bleeding because avoiding excess suppression of thrombin.

P5527 | BEDSIDE
Apixaban for the treatment of venous thromboembolism in cancer patients: data from the AMPLIFY trial

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Purpose: Using data from AMPLIFY, a phase III trial comparing apixaban with conventional anticoagulant treatment in patients with venous thromboembolism (VTE), we performed subgroup analyses to compare the efficacy and safety of these regimens in patients with and without active cancer at baseline. Active cancer was defined as cancer that was diagnosed or treated within the past 6 months.

Methods: Patients with symptomatic VTE were randomized to a 6-month course of apixaban (10 mg BID for 7 days followed by 5 mg BID) or conventional treatment consisting of enoxaparin (1 mg/kg BID for at least 5 days) followed by dose-adjusted warfarin (target INR 2-3). Cancer patients for whom long-term anticoagulation was contraindicated (LMWH was planned were excluded. The primary efficacy outcome was symptomatic VTE or VTE-related death. The intent-to-treat efficacy analysis included all randomized subjects with a non-missing primary endpoint. The primary safety outcome was ISTH-defined major bleeding up to 2 days after starting the study drug in all randomized subjects who received at least one dose of study medication. All outcomes were adjudicated by an independent committee blinded to treatment assignment.

Results: Of the 5395 patients randomized, 169 (3.1%) had active cancer. Baseline characteristics in these patients were similar between the two treatment groups. The median duration of treatment was 167 and 168 days in the apixaban and warfarin groups, respectively. In patients with active cancer at entry, recurrent VTE occurred in 3 of 81 (3.7%) patients in the apixaban group and in 5 of 81 (6.2%) patients in the warfarin group (relative hazard ratio 1.81, 95% CI: 0.38 to 8.94, p=0.46). In the apixaban group, major bleeding occurred in 2 of 87 (2.3%) and 4 of 80 (5.0%) patients, respectively (RR, 4.05; 95% CI, 0.08 to 2.54). In the warfarin group, due to recurrent VTE occurred in 56 of 2528 (2.2%) and in 66 of 2557 (2.6%) patients in the apixaban and warfarin group, respectively (RR, 0.86; 95% CI, 0.60 to 1.22), whereas major bleeding occurred in 13 of 2589 (0.5%) and in 45 of 2609 (1.7%) patients in the apixaban and warfarin group, respectively (RR, 0.29; 95% CI, 0.16 to 0.54).

Conclusions: Although the number of cancer patients was small, the results in this pre-specified subgroup were consistent with the overall findings and suggest that apixaban is as effective as conventional therapy in VTE patients with active cancer, and is associated with less bleeding. Additional studies are needed to compare the efficacy and safety of apixaban and LMWH for VTE treatment in cancer patients.

P5528 | BEDSIDE
Direct acting oral anticoagulants are more effective than Vitamin K-antagonists for the resolution of established left atrial thrombi in patients with atrial fibrillation

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Background: Left atrial appendage thrombus formation (LAAT) occurs in a relevant subset of patients with atrial fibrillation (AF), despite oral anticoagulation (OAC) with Vitamin K antagonists (VKA). LAAT is associated with a 5-fold increase in risk of stroke. The objective of this study was to assess resolution rate of LAAT if treated with direct acting OAC (DOAC) in a patient cohort with therapeutic failure of VKA.

Methods and results: In this prospective registry 37 patients (age 73±7.5 years, 62% male) were enrolled who were treated with conventional OAC (VKA). LAAT was a frequent complication (37/2609, 1.7%). VKA showed a higher failure rate, however, than DOAC treatment (n=18) with dabigatran (n=5), rivaroxaban (n=8), or apixaban (n=5). LAAT resolved under DOAC therapy including clinical examination and transesophageal echocardiography (TEE). Overall VKA showed a poor capability for mid-term thrombus resolution after six weeks of intensified anticoagulant treatment. We identified only three cases (8.1%) with LAAT disappearance, and one patient experienced massive LAAT expansion (2.7%). After switching anticoagulant treatment to DOAC, LAAT resolution was observed in 11 out of 24 patients (48%) treated with W (23.1±13.6 cm3). In a first step all patients received intensified VKA therapy with targeted INR ranging between 2.3-5.6 for six weeks. In cases with persistent LAAT after this follow-up (FU) period, alternative therapeutic options were discussed with the patient, and if consented, VKA was switched to DOAC (n=18) with dabigatran (n=5), rivaroxaban (n=8), or apixaban (n=5). FU was performed after at least 2 weeks under DOAC treatment including clinical examination and transesophageal echocardiography (TEE) Overall VKA showed a poor capability for mid-term thrombus resolution after six weeks of intensified anticoagulant treatment. We identified only three cases (8.1%) with LAAT disappearance, and one patient experienced massive LAAT expansion (2.7%). After switching anticoagulant treatment to DOAC, LAAT resolution was observed in 11 out of 24 patients (48%), including six patients out of eight, which were treated with rivaroxaban (75%), three out of five under anticoagulant therapy with dabigatran (60%), and in three out of five patients under apixaban (60%). When comparing the absolute LAAT resolution rates of W versus other OAC (P5529), this difference reached statistical significance (p<0.05). We observed no major bleeding complication during FU in patients treated with either VKA or DOAC.

Conclusion: These preliminary results of a single-centre registry give interesting insights in promising characteristics of all three so far available DOACs. These substances might enable effective anticoagulant treatment of patients with therapeutic failure of VKA therapy.

P5529 | BENCH
Rivaroxaban inhibits angiostatin II-induced cardiac fibrosis via reduction of inflammatory cytokines production through the growth stimulating signal pathway

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Purpose: It is known that the proliferation and migration of cardiac fibroblasts (CFs) lead to cardiac fibrosis which is dependent on cardiac remodeling cause heart failure. Recently, factor Xa (FXa)-dependent proteinase-activated receptor (PAR)-1 and PAR-2 cleavage has been reported play a role in tissue fibrosis and remodeling. However, there has been few evidence to substantiate the pleiotropic effects of direct FXa inhibitors. In this study, we aimed to investigate the local action of rivaroxaban, which is an oral approved direct FXa inhibitor, attenuates cell proliferation and migration in angiostatin (Ang II) induced mouse CFs.

Materials and methods: Confluent fibroblasts derived from myocardium of mice were cultured with or without rivaroxaban of various concentrations for 3 hours. Proliferation assays using MTT assay method and cell migration were performed after 24 hours of Ang II (10-8M) stimulation. Comprehensive cytokine and chemokine chemiluminescence reactions were evaluated by mouse cytokine/chemokine kit. Cell viability and proliferation was assessed using the MTS assay method and caliper assay method.


Results: After Ang II stimulation, rivaroxaban inhibited cell proliferation by 72.5% in 0.01 μg/ml, 95.1% in 0.1 μg/ml, 85.0% in 1 μg/ml and 77.5% in 5 μg/ml, respectively. Cell migration was decreased by 73.4% in rivaroxaban induced cells. In mouse cytokine array measuring 40 cytokines, we observed various chemiluminescence reactions by Ang II stimulation, including interleukin-1, TIP-1 and tumor necrosis factor-α. The productions of those 3 cytokines were significantly reduced with rivaroxaban pretreatment. TIP-1 production was decreased in rivaroxaban induced CFs in various concentrations (49% decrease in 0.01 μg/ml, 51% in 0.1 μg/ml, 55% in 1 μg/ml and 46% in 5 μg/ml). In dual reporter assay analysis, rivaroxaban also inhibited various inflammatory signal pathways, including nuclear factor-kappa B pathway, cyclic adenosine monophosphate pathway and mitogen-activated protein kinase pathway.

Conclusions: These data suggest that rivaroxaban inhibits proliferation and migration responses of various major inflammatory signal cascades involved in cardiac fibrosis.

THROMBOSIS AND ANTITHROMBOTIC THERAPY: MISCELLANEOUS

P5531 | BEDSIDE
A study of platelet inhibition, using a “point of care” platelet function test, following primary percutaneous coronary intervention for ST-elevation myocardial infarction (PINPOINT-PPCI)

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Background: Bivalirudin and prasugrel are well recognized for their efficacy in the treatment of ST-elevation myocardial infarction (STEMI) but their use in combination has not been well tested. Bivalirudin has a superior bleeding profile compared to heparin but is associated with a higher rate of acute stent thrombosis (ST). We aimed to test whether potential oral anti-platelet therapy provides early protection against ST.

Methods: The study of platelet inhibition, using a ‘point of care’ platelet function test, following primary percutaneous coronary intervention for st-elevation myocardial infarction (PINPOINT-PPCI) trial (ISRCTN22575414) enrolled 108 patients presenting with STEMI treated with pre-procedural oral loading of Prasugrel 60mg & peri-procedural Bivalirudin (as per the HORIZONS-AMI protocol, stopping the infusion at the end of the procedure). Patients underwent Multplate platelet function testing (adenosine diphosphate (ADP), aspirin & thrombin assays) on arrival at hospital, at the completion of the procedure, 1, 2 and 24 hours post-procedure, with measurement of thromboxane receptor baseline at 24 hours. In-hospital and 30-day major adverse cardiac event (MACE) rates, bleeding and stent thrombosis events were recorded.

Results: Radial access was used in 101 patients (93.5%) with a median door to balloon time of 45 mins [interquartile range (IQR) 40.2, 70.2] and a median bivalirudin infusion duration of 30 mins [IQR 19.8, 42.0]. Patients demonstrated high baseline platelet reactivity, with a mean baseline ADP-induced platelet aggregation (M) of 54.7±19.6% and a median ADP-induced platelet aggregation (P2Y12) of 12% (IQR 0-23%). 179 patients were studied, 108 patients were included in the study. Prasugrel 100 mg over 60 mg LD significantly reduced the percentage of ADP-induced platelet aggregation and the urine 11-dehydro-thromboxane B2 level be- descriptionally. Platelet aggregation in T-allele patients was not only significantly higher than that of the C-allele patients (p<0.001), but also it was higher than 20%. This is the criterion for functional AR. There were no statistically significant difference between C-allele patients and T-allele patients. In dual reporter assay analysis, 11-dehydro-thromboxane B2 in urine as a criterion for biochemical AR was deter- mined by ELISA. Functional AR was identified by ADP- and arachidonic acid-induced light transmittance aggregometry. Genotyping was performed using poly- merase chain reaction followed by restriction fragment length analysis.

Results: In the patient group the frequency of individual genotypes was: 86.7% with wild CC genotype, 12.7% - heterozygous genotype CT and 1 patient (0.6%) - mutant genotype TT. Distribution of genotypes in the control group was as follows: CC – 85.7%, CT – 14.3%, mutant homozygotes have not been identified. No statistically significant difference of C and T alleles frequency between studied and control groups (p>0.05) was found. The total level of arachidonic acid-induced platelet aggregation in T-allele patients was not only significantly higher than that of the C-allele patients (p<0.001), but also it was higher than 20%. This is the criterion for functional AR. There were no statistically significant difference between C-allele patients and T-allele patients. In dual reporter assay analysis, 11-dehydro-thromboxane B2 in urine as a criterion for biochemical AR was deter- mined by ELISA. Functional AR was identified by ADP- and arachidonic acid-induced light transmittance aggregometry. Genotyping was performed using poly- merase chain reaction followed by restriction fragment length analysis.

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than the standard LD of prasugrel results in earlier, greater and more consistent platelet inhibition (23.4% vs 51.4%; p<0.01).

Conclusions: In STEMI patients treated with primary PCI a higher (100 mg) platelet inhibition (23.4% vs 51.4%; p=0.01).

Methods: HPR and LPR were prospectively identified in 624 patients exposed to a maintenance dose of aspirin and clopidogrel for at least 7 days having at least 2 different PFT techniques performed simultaneously. HPR and LPR were defined as WASSP PRI ≥50% / ≤15%, P2Y12 reaction units (PRU) ≥208 / ≤86 (VerifyNowP2Y12 assay) or a residual platelet aggregation (RPA) ≤56% / ≤10% (light transmission aggregometry), respectively. The primary composite end point of all-cause mortality, non-fatal myocardial infarction, stent thrombosis, sudden cardiac death, urgent revascularization, and stroke was analyzed according to agreement between PFT. Bleeding complications were categorized according to BARC.

Results: Mean follow up on-treatment was 476±325 days. HPR was identified in 278 (45%) patients of whom 142 (23%) according to one PFT only, B6 (14%) and 20 (8%) according to two and three PFT, respectively. Independent predictors of HPR, defined as at least one positive PFT, were diabetes status and carriage of the loss-of-function allele CYP2C19*2. The primary endpoint occurred in 3.8% of the patients with good response as compared to 9.0% of the patients with HPR defined as at least one positive PFT (OR 2.53, 95% CI 1.27-5.05, p=0.007). There was a stepwise increase in the rate of the primary endpoint according to the number of PFT demonstrating HPR (7.7% vs. 7.0% vs. 16.0% according to 1, 2 and 3 concordant tests, respectively, p for trend = 0.0054). The presence of 3 concordant tests remained independently associated with the occurrence of the primary endpoint during follow up after multiple adjustments (adjusted OR 3.62, CI 1.49-8.81). The primary safety endpoint did not differ significantly according to LPR status and according to the number of PFT demonstrating LPR.

Conclusions: Multiple testing may reflect better the complexity of platelet function, improving the specificity of HPR and prediction of future cardiovascular ischemic events. This finding should deserve consideration in future clinical trials of personalized antiplatelet therapy.

Methods: Impact of dabigatran and phenprocoumon on ADP induced platelet aggregation in patients with atrial fibrillation (The Dabi-ADP-1 trial) N. Sarafoff1, A. Martischewing, J. Pollack1, D. Sibbing1, S. Massberg1, J. Mehilli1, A. Kastrati1, Ludwig-Maximilians University, Medizinische Klinik und Poliklinik I, Munich, Germany; 2 German Heart Center of Munich, Klinik für Herz- und Kreislaufkrankungen, Munich, Germany

Background: Thrombin plays a major role in hemostasis through fibrin formation as well as platelet activation and aggregation. Both low and high on-treatment platelet reactivity are associated with adverse clinical events. The impact of the direct thrombin inhibitor dabigatran etexilate on platelet function in patients in need of oral anticoagulation is unknown.

Methods: The "Impact of DABIGatran and phenprocoumon on the ADP induced platelet aggregation in patients with atrial fibrillation" (DABI ADP 1) study was a randomized trial performed at Deutsches Herzzentrum Munich, Germany, which compared the ADP-induced platelet aggregation (in AU x min) assessed with multiple electrode platelet aggregometry at 14 days after randomization.

Results: There was no significant difference regarding the primary endpoint between both groups, dabigatran 846 [650 - 983] AU x min and phenprocoumon 839 [696 - 1038] AU x min, p=0.90. Furthermore, no significant differences were observed regarding the secondary endpoints, ADPThrombin receptor agonist (P<0.06), TRAP-1 (P=0.45) and COL-1 (P=0.55) induced platelet aggregation at 14 days. There was no death, myocardial infarction, TIMI major or minor bleeding during the study period.

Conclusion: Dabigatran as compared to phenprocoumon has no impact on the ex vivo measured platelet reactivity in patients with atrial fibrillation ClinicalTrials.gov identifier: NCT01339819.

P5537 | BEDSIDE Impact of dabigatran and phenprocoumon on ADP induced platelet aggregation in patients with atrial fibrillation (The Dabi-ADP-1 trial) N. Sarafoff1, A. Martischewing, J. Pollack1, D. Sibbing1, S. Massberg1, J. Mehilli1, A. Kastrati1, Ludwig-Maximilians University, Medizinische Klinik und Poliklinik I, Munich, Germany; 2 German Heart Center of Munich, Klinik für Herz- und Kreislaufkrankungen, Munich, Germany

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Conclusion: Dabigatran as compared to phenprocoumon has no impact on the ex vivo measured platelet reactivity in patients with atrial fibrillation ClinicalTrials.gov identifier: NCT01339819.


Background: Although postprandial hyperglycemia may affect profiles of platelet reactivity through multiple mechanisms, whether or not insulin resistance (IR) contributes to differences of platelet reactivity profiles following hyperglycemia remains explored.

Objectives: To investigate the impact of IR on platelet reactivity profiles in patients with stable coronary artery disease (CAD) who are treated with standard dual antiplatelet therapy.

Methods: A 75g oral glucose tolerance test was performed in 70 stable CAD patients treated with maintenance aspirin (100mg/day) and clopidogrel (75mg/day) therapy. Blood samples were collected before and 1 and 2 hours after glucose load. The degree of IR was estimated by the homeostasis model assessment (HOMA) according to standard definitions (HOMA-IR ≥2.5). Maximum platelet aggregation was assessed by light transmittance aggregometry using 5 and 20 μmol/L ADP stimuli.

Results: There were 15 (21%) subjects who had IR. Following a glucose load, profiles of platelet reactivity varied according to IR status (Figure). In particular, following 20 μmol/L ADP stimuli, there were with minimal changes over time in patient with IR (P for trend < 0.79), while there was a significant reduction in the no-IR group of patients (P for trend < 0.001). Consistent findings were observed following 5 μmol/L ADP stimuli. After adjustment for baseline platelet reactivity, there were significant differences in profiles of platelet reactivity according IR status (Fig. 1).

Conclusions: In patients with stable CAD who are treated with standard dual antiplatelet therapy, IR is associated with differences of platelet reactivity profiles following glucose load.
antiplatelet therapy, the presence of IR is associated with variations in pharmacodynamic response profiles following hyperglycemia.

**P5539 | BEDSIDE**

**Efficacy of aspirin in aspirin-based versus non-aspirin based RCTs in the secondary prevention of MI: can we skip aspirin?**

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**Background:** Aspirin prevents reinfarction. Several newer and more effective antithrombotic therapies have been added on top of aspirin. They show, however, significantly increased bleeding, but have not been extensively tested without background aspirin.

**Methods:** We summarized results of the RCTs of aspirin versus antithrombotic therapy without aspirin in the secondary prevention of MI, carried out in 18,464 patients in 8 trials between 1980 and 2013.

**Results:** Reinfarction was seen in 4.4% on aspirin versus 4.1% on non-aspirin based therapy (OR 0.91, 95% CI 0.79 - 1.05, p<0.20, figure), whereas major bleeds occurred in 242/12,961 pts (1.9%) on aspirin versus 284/1,972 pts (2.2%) on non-aspirin based therapy (OR 1.10, 95% CI 0.99 - 1.40, p=0.06). When warfarin was the non-aspirin based comparator, reinfarction was seen in 223/3,131 pts (7.1%) on aspirin versus 203/3,122 pts (6.4%) on non-aspirin based therapy (OR 0.91, 95% CI 0.78 - 1.05, p=0.20), whereas major bleeds occurred in 60/3,131 pts (1.9%) on aspirin versus 134/3,122 pts (4.3%) on non-aspirin based therapy (OR 2.30, 95% CI 1.67 - 3.16, p<0.00001). When clopidogrel was the non-aspirin based comparator, reinfarction was seen in 187/6,127 pts (3.1%) on aspirin versus 172/6,084 pts (2.8%) on non-aspirin based therapy (OR 0.92, 95% CI 0.74 - 1.15, p=0.46), whereas major bleeds occurred in 192/6,830 pts (1.9%) on aspirin versus 150/9,850 pts (1.5%) on non-aspirin based therapy (OR 0.82, 95% CI 0.66 - 1.03, p=0.07).

**Conclusion:** In the secondary prevention of MI antithrombotic treatments without aspirin are at least as effective as those with aspirin strongly suggesting that aspirin can be skipped when other antithrombotic strategies are applied. This may lead to less bleeding, but only when clopidogrel is used.

**P5541 | BEDSIDE**

**Fixed-dose aspirin-clopidogrel combination enhances compliance to aspirin after acute coronary syndrome**

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**Purpose:** The purpose of this retrospective study was to compare observance with antithromplate therapy in stented ACS patients treated with the same doses of aspirin and clopidogrel administered in the FDC form or separately.

**Methods:** Consecutive patients admitted to our institution for ACS were considered eligible if they had undergone successful stent implantation and demonstrated good in-hospital response to aspirin. Biological assessment criterion for aspirin good-response is arachidonic acid–induced aggregation (AA-agar):>30%. To avoid any observation issue due to association with the daily 75 mg dose of clopidogrel, a daily 75 mg dose of nonsteroidal-coated aspirin was administered under nurse control. Aspirin response was re-evaluated on day 3. Patients with AA-agar:<30% before discharge were considered as poor responders and excluded from study. Patients were treated at discharge with an antithromate therapy using 75mg doses of aspirin and clopidogrel administered separately (A+C) or in the FDC form. At one month clinical follow up, patients with AA-agar:<30% were considered as non-observant. The primary endpoint was detection of a difference in treatment observance between the FDC and A+C groups.

**Results:** Between 2011 and 2013, a total of 390 patients were enrolled in study including 106 in the FDC group and 284 in the A+C group. (table 1) At the time of discharge, 10 patients in the A+C group were classified as aspirin resistant and excluded. No significant difference between the two cohorts was reported. At one month the non observance rate was 7% (n=7) in the FDC group versus 17% (n=49) in the A+C group (OR [95%CI]: 0.32 [0.14 – 0.74]; p=0.01).

**Conclusion:** A fixed combination of aspirin clopidogrel significantly improves drug observance, crucial end point after a stented ACS.

**P5540 | BENCH**

**Comparison of blood loss reducing efficacy of the antifibrinolytics tranexamic acid and aprotinin in a canine model of cardiopulmonary bypass**

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**Purpose:** Anti-haemorrhagic drugs are being used to prevent and treat haemorrhagic complications in cardiac surgery. The serine-protease-inhibitor aprotinin is an antifibrinolytic agent that had been used in clinical practice for decades. In 2008, the BART-study revealed its unfavourable effects on postoperative mortality, which led to its withdrawal from the market. Today, the lysine-analogue tranexamic acid (TA) is available for the clinical routine. We compared the effects of aprotinin and TA on postoperative blood loss, hemodynamic, hemostaseologic and inflammatory parameters, using a canine model of cardiopulmonary bypass (CPB).

**Methods:** Beagle dogs were randomized into three groups (n=8/group). Control dogs received placebo, treated groups were given aprotinin or TA. All animals received heparin and underwent 90min of CPB. The weaning from the heart-lung-machine was followed by administration of protamine and 130min of observation.

**Results:** TA reduced blood loss to 39±12% (p<0.01) vs. 69±15% in the control group. Similar results were seen in TA-treated animals (42±11%, p<0.01). Aprotinin showed a stronger reduction of blood loss compared to TA (31±16%, p<0.01) but has a stronger anti-inflammatory effect. Our work points out the need for the comparison of blood loss reducing efficacy of the antifibrinolytics aprotinin and TA in a canine model of CPB.

**Conclusion:** Tranexamic acid is available for the clinical routine. We compared the effects of aprotinin and tranexamic acid in a canine model of cardiopulmonary bypass.

**P5542 | BENCH**

**Compound 21, a selective angiotensin II type 2 receptor agonist, downregulates LPS-stimulated tissue factor expression in human peripheral blood mononuclear cells**

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**Purpose:** Intricate interrelationships connect Tissue Factor (TF), the principal initiator of the clotting cascade, to inflammation, a cross-talk amplified by locally active angiotensin (ang) II, a proinflammatory agent with direct TF stimulating properties mediated by the ang II type1 receptor (AT1R). However, ang II also stimulates ang II type 2 receptor (AT2R)s and they may as well contribute to TF expression. We investigated the effect of C21, a specific AT2R antagonist, on TF expression. We studied the effect of C21, a specific AT2R antagonist, on TF expression.

**Methods:** PBMCs were obtained from healthy volunteers through a discontinuous Ficol/Hyastopaque density gradient. C21, PD123319, a selective AT2R antagonist, and Olmesartan (OLM), a selective AT1R antagonist were added at log-doses from 10-7M to 10-3M. PBMCs were obtained from healthy volunteers through a discontinuous Ficol/Hyastopaque density gradient.

**Results:** Between 2011 and 2013, a total of 390 patients were enrolled in study including 106 in the FDC group and 284 in the A+C group. (table 1) At the time of discharge, 10 patients in the A+C group were classified as aspirin resistant and excluded. No significant difference between the two cohorts was reported. At one month the non observance rate was 7% (n=7) in the FDC group versus 17% (n=49) in the A+C group (OR [95%CI]: 0.32 [0.14 – 0.74]; p=0.01).

**Conclusion:** A fixed combination of aspirin clopidogrel significantly improves drug observance, crucial end point after a stented ACS.
expression, n=5 each, p<0.001. LPS-induced TF mRNA (from 0.82±0.07 to 0.24±0.13 normalized fold expression, n=5 each, p<0.001), a 3.5-fold inhibition. PD123,319 preserved in the presence of PD123,319. BAY 11-7082, a specific NF-κB inhibitor, abolished at a 10⁻⁵M concentration.

Conclusions: C21, a selective AT2R agonist downregulates the transcriptional expression of TF in LPS-activated PBMCs, a finding consistent with the existence in PBMCs of AT2Rs whose stimulation attenuates inflammation-mediated procoagulant responses. The data open insofar unexplored and potentially relevant facets to our understanding of the complex links connecting ang II to inflammation and coagulation.

ACUTE CORONARY SYNDROME: COMORBIDITIES AND PROGNOSIS

P5544 | BEDSIDE
Is GRACE risk score a useful tool to predict stroke after an acute coronary syndrome?

Background: The risk of stroke after an acute coronary syndrome (ACS) is increased. The aim of this study was to do a comparative validation of 6-month GRACE risk score and CH2DS2VASc score to predict the risk of post-ACS stroke.

Methods: This is a retrospective study carried out in a single center with 4,229 ACS patients discharged from 2004 to 2010 (66.9±11.8 years, 27.9% women, 64.2% underwent PCI). The primary endpoint of this study was the occurrence of an ischemic stroke during follow-up (median 4.6 years, IQR 2.7-7.1 years). Cumulative stroke rates were analyzed by the method of Kaplan-Meier for the different risk groups, evaluating hazard ratios with a Cox Analysis. We also calculated the discriminative and the predictive values of both scores. The risk reclassification was analyzed with Penalino's method.

Results: 184 (4.4%) patients developed an ischemic stroke; 153 (83.2%) had sinus rhythm and 31 (16.9%) has atrial fibrillation. The HR for CH2DS2VASc was 1.38 (CI 95% 1.27-1.48, p<0.001) and for GRACE was 1.02 (CI 95%, 1.01-1.03, p<0.001). Both risk scores showed adequate discriminative ability (c-statistics 0.63±0.02 for CH2DS2VASc, and 0.60±0.02 for GRACE). By reclassification method there was not difference between GRACE and CH2DS2VASc risks scores (NRI 1.98%, p=0.69). Comparing moderate-high risk patients with low-risk patients, both risk scores showed very high negative predictive value (99.5% for CH2DS2VASc, 98.1% for GRACE). The sensitivity of CH2DS2VASc was higher than GRACE risk score (95.1% versus 87.0%), whereas specificity was lower (14.4% versus 30.2%).

Conclusions: GRACE risk score has a discrimination and a negative predictive value similar than CH2DS2VASc to predictive post ACS stroke. In this way, our study shows a new utility for GRACE risk score.

P5545 | BENCH
Decreased levels of circulating natural regulatory T cells after ST-segment elevation myocardial infarction
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Background: Contribution of natural regulatory T cells (Treg) to the pathogene-
sis of acute myocardial infarction (MI) remains elusive. Treg cells are thought to play a protective role in atherosclerosis, and, in concert with this notion, previous reports demonstrated decreased levels of Treg cells in the course of ST-segment elevation MI (STEMI). However, much less is known whether alterations of Treg cell numbers could persist for longer periods of time.

Aim: To investigate whether levels of natural Treg cells are subject to long-term quantitative changes within first months following STEMI.

Methods and results: A flow-cytometric analysis of frequencies of natural Treg cells delineated by CD4+CD25+CD127- phenotype in eighteen patients (mean age 65±12 years, 55% males) at the time of admission for the first STEMI and after four to six months was performed. All patients were successfully treated with primary percutaneous coronary intervention. At the time of MI, natural Treg cells comprised 10.66% [7.42-13.69] of all CD4+ T cell population. Quite surprisingly, after six months, the frequencies of CD4+CD25+CD127- T cells significantly decreased and reached the level of 6.16% [5.22-8.07] (p<0.001). Consistently, at four to six months following STEMI, significant decrease in mean fluorescence intensity of CD25 expression on circulating CD4+ T cells was found (p=0.0003).

Conclusions: The recovery from STEMI is associated with the decrease in numbers of putatively protective Treg cells.

P5546 | BEDSIDE
How reliable is the EKG in detecting stent thrombosis after successful primary PCI in acute ST elevation myocardial infarction
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Purpose: Stent thrombosis (ST) is one of the most feared complications of PCI presenting as recurrent acute myocardial infarction sometimes leading to cardio- genic shock, life-threatening arrhythmias or sudden death. We sought to deter- mine the sensitivity, specificity and the predictive value of EKG alone, and EKG in combination with clinical evaluation, for diagnosis of suspected ST.

Methods: We retrospectively reviewed the records of patients who presented with STEMI to our hospital between Jan 1, 2007 and Dec 31, 2012. Records of patients who had urgent repeat coronary angiography within 30 days of the index primary PCI for STEMI were analyzed. EKG's done just prior to the urgent angiography were reviewed without knowledge of the presenting symptoms or the results of the repeat angiogram. We also reviewed the medical records of these patients to see if ST was being considered by the treating cardiologist.

Results: A total of 963 STEMI patients underwent primary PCI with stent implantation, of which 44 (4.57%) had repeat urgent coronary angiography within 30 days. The age range was 43-86 years (mean 62.6 yrs.) with 68% males. Of these 44 patients, 19 patients had ST on angiogram. EKG was suggestive of ST in 17/44 patients but only 12 were found to have ST on angiogram. EKG was not suggestive of ST in the other 27/44 patients, yet 7 of these patients were found to have ST. Combined EKG and clinical evaluation was suggestive of ST in 26/44, of which 18 patients had ST on angiogram, and the combination did not suggest ST in 18/44 patients, of which only 1 patient had ST on angiogram. The sensitivity, specificity and predictive values of the above diagnostic tools are detailed in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Diagnostic tool</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>EKG alone</td>
<td>63.2% (38.4-83.7)</td>
<td>80.0% (59.3-93.1)</td>
<td>70.6% (44.0-89.6)</td>
<td>74.1% (53.7-88.8)</td>
</tr>
<tr>
<td>Combined EKG and clinical evaluation</td>
<td>94.7% (73.9-99.1)</td>
<td>69.0% (46.5-85.0)</td>
<td>69.2% (48.2-84.6)</td>
<td>94.4% (72.6-99.0)</td>
</tr>
</tbody>
</table>

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

Conclusion: Although EKG remains an important tool to diagnose ST, it missed ST in almost one third of our patients. Combining EKG and clinical evaluation improved the sensitivity and negative predictive value at the cost of specificity. We suggest that even in the absence of significant EKG changes, a high index of clinical suspicion for ST should lead to emergent coronary angiography, as significant proportion of these patients will be found to have ST.
P5547 | BEDSIDE
Impact of occluded culprit arteries on the long-term outcomes of patients with non-ST-elevation myocardial infarction. Could they be true STEMI-equivalents?
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Background: Recent studies have suggested that a subset of patients with non-ST-elevation myocardial infarction (NSTEMI) who had occluded culprit arteries had worse outcomes compared to those with non-occluded culprit arteries. Therefore, they have been regarded as "STEMI-equivalents". We aimed to compare the clinical characteristics and the long-term prognostic between these "STEMI-equivalents" and STEMI patients.
Methods: A total 5025 patients with acute MI from 9 centers of 2 universities were retrospectively registered in COREA-AMI (Convergent REGistry of catholic and chonmnn university for Acute MI registry). Out of these, the patients who had a total occlusion (TIMI 0 or I) of "culprit" left anterior descending artery (LAD) on the baseline angiography were selected as study subjects. They were classified into two groups by initial electrocardiographic findings: the "NSTEMI" group (n=253) and the "STEMI" group (n=800). The clinical, angiographic findings and the incidences of adverse events including in-hospital death (IHD), in-hospital death (IHD), cardiac death (CD), recurrent nonfatal MI (RFMI), and target vessel revascularization (TVR) were compared between two groups. The median follow-up duration was 47.3 months (IQR 32.7–66.2).
Results: The patients in the STEMI group were younger and had lower left ventricular ejection fraction (LVEF). The peak levels of CK-MB and cardiac troponin were significantly higher in the STEMI group. While the NSTEMI group had complex angiographic lesion (B2C), multi-vessel disease, and smaller stenosis of the culprit artery, the incidence of IHD was significantly higher in the STEMI group than in the NSTEMI group (4.1% vs 1.2%, p=0.027). In the multivariate logisitic regression, age (adjusted HR 1.161; 95% CI [1.104-1.221], p=0.035), LVEF (0.938 [0.894-0.985], p=0.010), and peak level of troponin (1.102 [1.100-1.104], p=0.016) were revealed as the independent predictors for IHD. During the 48-month follow-up period, however, CD (10.6% vs 9.1%), RI (6.3% vs 7.9%), and TVR (4.5% vs 3.2%) occurred at similar rates in both groups (all p>0.05). Furthermore, in the 12-month landmark analysis, the risk of all adverse events was not significantly different between both groups up to 12 months (p=0.05).
Conclusions: Patients with NSTEMI who had an occluded "culprit" LAD demonstrated the similar rates of adverse cardiovascular events during 48 months, compared with the patients to STEMI. These patients in the NSTEMI group may represent true "STEMI-equivalents". Thus, the precise early risk stratification followed by an early intervention should be considered for these high risk patients.

P5548 | BEDSIDE
Is the obesity paradox present in the extreme Body Mass Index groups of patients with Acute Coronary Syndrome? Data from a national registry
A.T. Timoteo, M. Nogueira, R. Cruz Ferreira on behalf of ProACS investigators. Hospital Santa Marta, CHLC, Lisbon, Portugal
Background: In the general population, obesity has an important prognostic impact. However, in patients with cardiovascular disease it is described a paradoxical relationship between patients with overweight and obesity and good clinical outcome. Some authors also describe a U-shaped risk, with the more extreme categories of patients to a given treatment using a naturally occurring characteristic, e.g. age, gender, cardiovascular and non-cardiovascular co-morbidities, Killip-Kimbball class at admission, performance of coronary angiography, coronary anatomy, ejection fraction (EF) and pharmacological in-hospital treatment.
Results: Overall, the presence of Re-AMI was found in 99 (1.4%) patients with MI in the overall cohort (87 patients more prevalent in STEMI (32 patients – 1.0%), p=0.006. In both groups Re-AMI was an independent predictor of in-hospital mortality [STEMI - OR: 4.78 (1.07 to 21.2), p=0.04 and NSTEMI – OR: 11.67 (2.92 to 46.51), p<0.001]. By multivariate analysis, left main stenosis >50% and EF <50% were identified as independent predictors of Re-AMI in both groups. We identified some specific predictors of Re-AMI according to the type of AMI. In STEMI the presence of in-hospital treatment with ibllib/lipaglycoprotein inhibitors [OR: 2.96 (1.27 – 6.86), p=0.01] was identified as an independent predictor of Re-AMI in NSTEMI, age [OR: 1.05 (1.02 – 1.08), p=0.001] and previous peripheral arterial disease [OR: 3.27 (1.50 – 7.08), p=0.003] were identified as independent predictors of Re-AMI. On the other side, performance of coronary angiography appears to be a protective factor against development of Re-AMI in NSTEMI (OR: 0.22 [0.10 – 0.46], p<0.001).
Conclusions: Re-AMI is a rare complication in both STEMI and NSTEMI, although more prevalent in NSTEMI. Left main stenosis >50% and EF <50% were identified as predictors of Re-AMI in both in STEMI and NSTEMI. There are some specific predictors of Re-AMI according to the type of AMI.

P5550 | BENCH
Increasing the use of an early invasive strategy in acute coronary syndromes reinfarction rate: an instrumental variable approach to administrative health data
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Purpose: An early invasive strategy compared to a conservative strategy in acute coronary syndrome (ACS) reduces mortality and myocardial infarctions in randomized trials. We investigated whether this benefit can be retrieved in an unselected population of ACS patients using instrumental variable (IV) analysis.
Methods: We identified all patients hospitalized with a first ACS in 2005–11 from the Danish national registries including data on the entire population of 5.5 mio. An early invasive strategy was defined as receiving a diagnostic coronary angiography within 3 days of admission. IV analysis was applied to address the inherent treatment selection bias of observational comparisons. An IV randomizes patients to a given treatment using a naturally occurring characteristic, e.g. place of residence, thus offsetting measured and unmeasured confounders and providing unbiased estimates of the treatment effect. We used quartiles of CAG rates in 29 hospital catchment areas as IV to estimate the effect of early versus conservative invasive strategies on mortality and reinfarctions at 60 days. We estimated absolute risk reductions (ARR), which in an IV context are interpreted as the effect of increasing the use an early invasive strategy in hospital catchment areas of the lower quartiles to that of higher quartiles.
Results: We included 52,615 patients. Our IV allocated patients with similar characteristics to different levels of treatment as required (Table). An early invasive strategy reduced reinfarctions with ARR: -10.8% (-13.9% to -7.7%; p<0.001)
Table 1. Characteristics according to IV

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low quartile</th>
<th>2nd quartile</th>
<th>3rd quartile</th>
<th>High quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>67 (58–77)</td>
<td>67 (58–77)</td>
<td>68 (58–78)</td>
<td>68 (58–78)</td>
</tr>
<tr>
<td>Females, %</td>
<td>35.6</td>
<td>37.6</td>
<td>35.7</td>
<td>35.4</td>
</tr>
<tr>
<td>Non-ST-elevation myocardial infarction*</td>
<td>0.95 (0.85–1.05)</td>
<td>0.95 (0.85–1.05)</td>
<td>0.95 (0.85–1.05)</td>
<td>0.95 (0.85–1.05)</td>
</tr>
<tr>
<td>CAG within 3 days, %</td>
<td>37.2</td>
<td>37.2</td>
<td>37.2</td>
<td>37.2</td>
</tr>
<tr>
<td>Revascularization within 3 days, %</td>
<td>30.2</td>
<td>32.7</td>
<td>35.1</td>
<td>42.9</td>
</tr>
<tr>
<td>Median (interquartile range); r</td>
<td>(Median (interquartile range)); r</td>
<td>(Median (interquartile range)); r</td>
<td>(Median (interquartile range)); r</td>
<td>(Median (interquartile range)); r</td>
</tr>
</tbody>
</table>

Acute coronary syndrome: comorbidities and prognosis 999

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compared to a conservative invasive approach. Mortality was unchanged, ARR: -2.6% (-5.5% to 1.3%; p=0.20).

**Conclusions:** In unselected ACS patients, an early invasive strategy reduced reinterventions at 60 days by almost 11% compared to a conservative strategy. No significant effect on mortality was found. Instrumental variable analysis is a promising analytical approach to administrative health data.

**P5551 | BEDSIDE**
The presence of in-hospital atrial fibrillation is associated with mortality in patients with chronic kidney disease complicated with acute myocardial infarction


**Purpose:** Chronic kidney disease (CKD) is an important predictor for mortality after acute myocardial infarction (AMI). Atrial fibrillation (AF) often coexists with CKD and AMI. However, the impact of AF on mortality and morbidity in CKD patients complicated with AMI remains unclear.

**Methods:** A total of 4738 patients with AMI were consecutively enrolled between 2004 and 2009 from 9 hospitals. CKD was defined as eGFR < 60 mL/min/1.73m². Patients were divided into CKD (n=1181) and non-CKD (n=3607) groups, and then were analyzed to investigate the association with mortality and morbidity according to presence of AF. The primary endpoint was a composite of MACCE including death from any cause, recurrent non-fatal MI, ischemic stroke or re-hospitalization for heart failure.

**Results:** The prevalence of in-hospital AF in CKD group was significantly higher than in non-CKD group (6.77% vs. 3.27%, P<.001). During a mean follow-up period of 3.5±1.7 years, a total of 1107 (23.4%) composite MACCE occurred after the index PCI: 34.8% in CKD group, 19.6% in non-CKD group (P<.001). In both CKD and non-CKD groups, the cumulative event rate of MACCE was significantly higher in patients with AF than in patients without AF at the 5-year follow-up (CKD: 68.5% vs. 41.2%, P<0.001, non-CKD: 42.7% vs. 26.2%, P=0.001). Especially, a prevalence of AF was independently associated with mortality in CKD group (adjusted HR, 1.87; 95% CI, 1.15-3.06; P=0.01), while not in non-CKD group (adjusted HR, 0.74; 95% CI, 0.34-1.64; P=0.16).

**Conclusions:** In patients with CKD, the presence of in-hospital AF is significantly associated with increased mortality and morbidity. In patients with non-CKD, the presence of in-hospital AF is not associated with increased mortality and morbidity.

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**P5553 | BEDSIDE**
In-hospital case-fatality and one-survival after acute myocardial infarction in Chile, 2002-2011: a national trends analysis

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Age-standardised myocardial infarction (MI) mortality rates have declined during the past decades in many countries. Part of this decline is due to an increase in survival. During the last decade a health care reform was implemented in Chile to provide effective preventive and curative services for priority health conditions, in which MI was included. Aim: to estimate trends in hospital case-fatality rates and long-term survival from MI in Chile between 2002 and 2011.

**Methods:** Population based study using person unique identification number linked hospital and mortality data. Data was obtained from the national Hospitalizations and Mortality Databases from the Ministry of Health, which covers 100% of hospitalizations (public and private) and deaths registered in Chile. International classification of disease codes I21-I22 were used to identify MI cases. All-cause mortality was the main outcome in this analysis. We estimated in-hospital case-fatality and one-year survival after discharge among all patients who were admitted to hospital due to a first MI in Chile. We used Kaplan-Meier method to estimate survival and Pris-Winsten (PW) regression to evaluate trends expressed as percentage change per year (IC 95%). Separate analyses of in-hospital case-fatality and one-year after discharge survival were done.

**Results:** During 2002-2012 a total of 65,225 fatal and nonfatal hospitalized first MI occurred (STEMI and non-STEMI). 31.4% were women. Women were significantly older than men (68.6±13.5 vs. 61.6±13.1; p<0.0001). Vital status information at one-year was available for 92.4% of patients (there were no differences in age or sex between cases with and without vital status information). In-hospital case-fatality was reduced from 16.8% in 2002 to 10.0% in 2011. In-hospital survival increased at an average annual rate of 0.68 percentage points (IC 95% 0.57-0.80) during this period. After discharge, one-year survival improved from 88.8% to 91.1% (PW: 0.23 percentage points/year; IC95% 0.14 to 0.33). In men, in-hospital case-fatality declined from 13.1% to 7.7% (PW: -0.52; IC95% -0.68 to -0.35) and one-year survival increased from 90.4% to 92.1% (PW: 0.19; IC95% 0.04 to 0.36). In women the corresponding values were 25.0% to 15.1% (PW: -1.04; IC95% -1.21 to -0.88) and 84.9% to 88.4% (PW: 0.31; IC95% 0.21 to 0.42) respectively.

**Conclusions:** Asymptomatic post-ACS patients have fairly stable NT-proBNP during 400 days, in a range that is compatible with heart failure according to ESC guidelines. Interpatient variability is substantial.

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**P5555 | BEDSIDE**
Circulating NT-proBNP in post ACS patients who remained asymptomatic and event free during 400 day follow-up

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**Method:** BIOMArCS is an observational study of ACS patients in 18 hospitals in our country Treatment is left to the discretion of the physician. During 1 year follow-up, 20 repeat blood samples are taken at preset time intervals. Serum and plasma are separated and stored on site at -80°C within 2h, until batch analysis in the central laboratory of the Erasmus MC. This abstract describes 103 patients who remained free of death, ACS-readmission, revascularisation and angina until 400 days. We determined NT-proBNP with the Roche STAT on Cobas e system in their repeated samples.

**Results:** Mean age was 65 (SD 5) years, 79% were men, 64% had STE-ACS. Patient profile was typical for an ACS population. Discharge medication included antiplatelet therapy (99%) and statins (97%). Median peak NT-proBNP within 30 days was 568 (IQR 220 to 1195) pg/mL. During 30 to 400 days 1574 repeated blood samples were collected, with a median of 16 (IQR 15 to 17) for each patient. NT-proBNP -125 pg/mL (heart failure threshold in ESC guidelines) was observed in 50% of samples; levels >3125 were found in 16% of samples (in 49% of patients). The within-patient variability explained 19% of total variation, and was much smaller than the between-patient variability (figure). Mean change in NT-proBNP between 30 and 400 days was -2.2 pg/mL.

**Conclusions:** NT-proBNP in asymptomatic patients who remained stable for a MI in Chile. These results are useful for the evaluation of public policies implemented during this period.

Purpose: Fibrinogen genetic variability plays a significant role in atherogenesis. However, the role of specific polymorphisms (rs1800790, rs2070011) remains unclear. We examined the combined effects these polymorphisms on the coagulation process and endothelial function in Caucasian subjects.

Methods: We enrolled 422 patients with coronary artery disease (CAD) and 277 controls. The rs1800790 (G455A) and the rs2070011 (G58A) polymorphisms were estimated by PCR and appropriate restriction enzymes (HaeIII and AcI respectively). Fibrinogen and D-Dimer levels, as well as factors (f) V, X activity were measured by standard coagulometry techniques. Flow-mediated dilation (FMD) was assessed by brachial ultrasound.

Results: 58A A subjects had lower fibrinogen levels in controls (p<0.038). Importantly, the G55A homozygosity was associated with enhanced fibrinogen levels in both groups (p=0.003 controls and p<0.001 CAD). Both the 58A (p=0.027) and 455A homozygotes (p=0.022) had higher levels of D-Dimer in the CAD group. Interestingly, the 455A homozygotes had increased IV activity in the CAD group (p=0.048). However, no significant effects were observed on IX activity and FMD. Further analysis revealed that fibrinogen levels were strongly associated with CAD (1.005 [1.003-1.007], p<0.001) as well as the presence of MI (1.003 [1.001-1.005], p<0.001). Similarly, D-Dimer levels were also strong predictors of CAD (1.005 [1.001-1.007], p<0.001), but not of MI (1.001 [1.001-1.001], p=0.83). With respect to clinical manifestations, we found that IV activity was associated with increased number of diseased vessels (1.016 [1.001-1.030], p=0.037), while IX activity was strongly related to MI (0.985 [0.973-0.997], p=0.013).

Conclusion: The rs1800790 variant increases fibrinogen and D-Dimers levels as well as IV activity, therefore contributing to the initiation and progression of atherosclerosis. Also, we have shown that fibrinogen and D-Dimers levels were strong predictors of CAD and MI. Importantly, our results highlighted a new role for IV and IX regarding to the number of diseased vessels and the risk of MI respectively.

P5557 | BEDSIDE
Evaluation of clinical risk factors to predict high on-treatment platelet reactivity and outcome in patients with stable coronary artery disease (PREDICT-STABLE)
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1 Charite Universitary Hospital of Tübingen, Department of Cardiology and Cardiovascular Medicine, Tübingen, Germany; 2 Dr Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany; 3Medical University of Vienna, Vienna, Austria

Purpose: The role of clinical risk factors on high on-treatment platelet reactivity (HPR) in patients with stable CAD undergoing elective PCI has been poorly understood. This study was designed to identify clinical risk factors that are easily available from patient data to predict HPR and 12 months major adverse events under treatment with aspirin and clopidogrel in patients undergoing non-urgent PCI.

Methods: 739 consecutive patients with stable CAD were recruited. On-treatment platelet aggregation was tested by light transmittance aggregometry. Major cardiovascular events (MACE) were recorded during one-year follow-up.

Results: Degree of on-treatment platelet aggregation was influenced by different clinical risk factors. In multivariate regression analysis older age, diabetes mellitus, elevated body mass index, renal function and left ventricular ejection fraction were independent predictors of HPR. After weighing these variables according to their estimates in multivariate regression model, we developed a score to predict HPR in stable CAD patients undergoing elective PCI (PREDICT-STABLE Score). Patients with a high score had a significantly more likely to develop MACE within one year of follow-up. This association was confirmed in a validation cohort of 591 patients.

Conclusions: In conclusion, variability of on-treatment platelet function and associated clinical outcomes of patients with stable CAD may largely be explained by the aggregation score. Further analysis should be re-assessed.
The current use of direct oral anticoagulants (DOACs) for the treatment of VTE in Europe-PREFER in VTE

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Purpose: The conventional treatment of venous thromboembolism (VTE) in Europe has been use of heparin and vitamin K antagonists (VKA), and although effective, they have numerous limitations. Direct oral anticoagulants (DOACs) are promising alternatives with the potential to overcome these limitations. All DOACs have shown similar efficacy as compared with heparins and VKA and they have a better safety profile. The PREFER registry is the first large study to investigate the management and the use of DOACs in VTE.

Methods: The PREFER registry has enrolled patients starting in January 2013 until March 2014. A total of 338 centres in France, Germany, Switzerland, Austria, Italy, Spain and UK (33.2% office-based and 66.7% hospital-based) are participating. We collect patient’s characteristics and history as well as medical management information related to the VTE index event (pulmonary embolism (PE) and deep vein thrombosis (DVT)) at the time of diagnosis, at baseline and at 1, 3, 6 and 12 months follow-up. We report the first data of the use of DOACs. Enrolment in countries is ongoing.

Results: DOACs were used more frequently in younger patients (22.7% vs 11.1% in patients with CRCL levels ≤60 ml/min), diabetes (22.9% vs 13.5% in patients without/with diabetes), and those at risk of bleeding (HAS-BLED low 27.1%, medium 17.8%, high 12.5%). There was great variation in use related to region, which is related to the different time of approval of these agents. Use in PE patients was as frequent as use in DVT patients (Table 1).

Table 1. Use of DOACS (percentage) by VTE for country, indication and inhibitor type

<table>
<thead>
<tr>
<th>Country</th>
<th>France</th>
<th>Germany/Austria</th>
<th>Italy</th>
<th>Spain</th>
<th>UK Total</th>
<th>Total (N=248)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=616)</td>
<td>(n=199)</td>
<td>(n=15)</td>
<td>(n=183)</td>
<td>(N=565)</td>
<td></td>
</tr>
<tr>
<td>Use of DOACS (mono or in combination)</td>
<td>Overall VTE</td>
<td>91 (36.7%)</td>
<td>264 (46.7%)</td>
<td>26 (3.2%)</td>
<td>16 (8.0%)</td>
<td>6 (40.0%)</td>
</tr>
<tr>
<td></td>
<td>PE</td>
<td>55 (36.9%)</td>
<td>55 (43.7%)</td>
<td>8 (2.7%)</td>
<td>8 (7.7%)</td>
<td>5 (60.0%)</td>
</tr>
<tr>
<td></td>
<td>DVT</td>
<td>36 (36.4%)</td>
<td>209 (47.8%)</td>
<td>18 (3.5%)</td>
<td>8 (8.7%)</td>
<td>6 (50.0%)</td>
</tr>
</tbody>
</table>

Conclusions: DOACs are used frequently throughout Europe for VTE treatment, but usage varies greatly from country to country and is also associated with patient characteristics.

P5560 | BEDSIDE
Triple antithrombotic therapy is not associated with long-term cardiovascular events and bleeding complications after drug-eluting stent implantation


Triple antithrombotic therapy increases the risk of bleeding events in patients undergoing drug-eluting stent (DES) compared with dual anti-platelet therapy (DAPT). However, it is uncertain whether warfarin control is associated with reduced cardiovascular events and bleeding events in patients undergoing DES with triple antithrombotic therapy.

Methods: We investigated clinical outcomes in 1207 consecutive patients (82.8% men, mean age 67.0 years) of our institute PCI database between 2004 and 2011. Baseline clinical characteristics and MACCE and bleeding complication were compared between triple antithrombotic therapy and DAPT group. MACCE was defined as death, myocardial infarction, stroke, target vessel revascularization, and bleeding complications. Results: 95 (7.9%) patients received triple antithrombotic therapy. The comorbidities with hypertension (81.1%) and diabetes (54.7%) were more common in triple antithrombotic therapy. The mean INR at the time of PCI was 1.8. The target PT-INR levels was set between 1.6 and 2.5 and calculated the percent time in the therapeutic range (TTR). The median TTR was 78.4% (interquartile range 67.4-87.6%). By Kaplan-Meier survival analysis, warfarin therapy was not associated with MACCE (P=0.98) and bleeding (P=0.74). Multivariable Cox regression analysis revealed that triple antithrombotic therapy was also not the independent predictor for the MACCE and bleeding (HR 1.12, 95%CI 0.76-1.73; P=0.58).

Conclusions: Triple antithrombotic therapy did not have a predictive value for the occurrence of MACCE and bleeding complications as long as warfarin was controlled tightly with lower INR value.

P5561 | SPOTLIGHT
Coffee reduces death risk after acute myocardial infarction: a meta-analysis

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Purpose: It has been shown that habitual coffee consumption is protective against coronary heart disease in women however it is not clear whether such cardio-protection is conferred upon those who have already experienced an acute myocardial infarction.

Methods: We conducted a dose-response meta-analysis of prospective studies which probing the relationship between coffee intake and mortality in those who had experienced an acute myocardial infarction. Using a defined-search strategy, electronic databases (MEDLINE, EMBASE, and Embase) were searched for papers published between 1946 to July 2013. Two eligible studies that investigated post acute myocardial infarction mortality risk against coffee consumption were identified and appraised using set criteria. Combined, these studies recruited a total of 3,271 patients for which 604 deaths were observed. The hazard ratios for the following experimental groups were defined: Light coffee drinkers (1-2 cups/day) versus non-coffee drinkers, heavy coffee drinkers (>2 cups/day) versus non-coffee drinkers and heavy coffee drinkers versus light coffee drinkers.

Results: A statistically significant inverse correlation was observed between coffee drinking and mortality; all three groups demonstrated a significant reduction in relative risk. Light coffee drinkers versus non-coffee showed a risk ratio of 0.79 (95% confidence interval (CI)=0.66-0.94, p=0.008); heavy coffee drinkers versus non-coffee drinkers showed a risk ratio of 0.54 (95% CI=0.45-0.65, p=0.00001) and heavy coffee drinkers versus light coffee drinkers showed a risk ratio of 0.69 (95% CI=0.58-0.83, p=0.0001)

Conclusions: Drinking coffee habitually following an acute myocardial infarction was associated with a reduced risk of mortality.

P5562 | BEDSIDE
Plaque debris embolization than thrombus embolization was the higher risk of slow flow in the patients with or without acute coronary syndrome during percutaneous coronary intervention

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Background: Slow flow or no re-flow phenomenon (slow/no flow) during coronary intervention is mainly caused by distal embolization of thrombus and plaque debris, and is associated with unfavorable long-term clinical outcomes. Slow/no flow occurs in both acute coronary syndrome (ACS) and non-ACS patients during percutaneous coronary intervention (PCI). However, the contribution of thrombus and plaque debris for slow/no flow was unknown. Therefore, we examined the association of thrombus and plaque debris embolization with slow/no flow.

Methods: Consecutive patients who received PCI with filter-type distal protection device (Filterap) (n=520, 291 ACS and 229 non-ACS patients) from August 2008 to May 2012. We evaluated the distal embolization of thrombus and plaque debris by the captured material in Filterap. Filter slow/no flow was defined angiographically.

Results: Filter slow/no flow occurred more frequently in ACS than in non-ACS patients (36% vs. 17%, P<0.001). Distal embolization of plaque debris with or without thrombus was detected in 103 (35%) ACS and 42 (18%) non-ACS patients. Distal embolization of thrombus alone was detected in 181 (55%) ACS and 103 (45%) non-ACS patients. Filter slow/no flow occurred more frequently in the patients with plaque debris embolization than in the patients with thrombus embolization alone both among ACS (91% vs. 6%, P<0.001) and non-ACS (83% vs. 2%, P<0.001) patients groups.

Conclusion: Plaque debris embolization was the higher risk of slow/no flow compared with thrombus embolization both in ACS and non-ACS patients.

P5563 | BEDSIDE
Cardiac troponin I, NT-proBNP and galactin-3 are elevated in patients with unrecognized myocardial infarction detected by cardiac magnetic resonance imaging

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Purpose: To determine the association between levels of cardiac biomarkers and...
an unrecognized myocardial infarction (UMI) in patients with suspected stable coronary artery disease (CAD) with or without significant stenosis in the coronary artery supplying the infarcted area.

Methods: A total of 234 patients (median age 65 years; 66% men) with suspected stable CAD without previously known myocardial infarction (MI) were examined with late gadolinium enhancement magnetic resonance imaging and coronary angiography. For each patient with an UMI, the status of the coronary branch supplying the infarcted area was independently determined; a stenosis ≥70% was regarded as significant. Blood samples were drawn at enrolment and high sensitivity cardiac troponin I (hs-cTnI) (Abbot), NT-proBNP (Roche) and Galectin-3 (BioMerieux) were analyzed.

Results: UMI was detected in 58 of the 234 patients (24.8%), 39 (67%) of the UMIs were located in an area supplied by a coronary branch with a significant stenosis. The median levels of hs-cTnI, NT-proBNP and Galectin-3 were higher in patients with UMI compared to those without: 5.4 vs. 3.7 ng/L (p<0.001); 172.5 vs. 93.5 ng/L (p<0.005); and 11.1 vs. 10.0 ng/L (p=0.028), respectively. There was no significant difference in levels of the biomarkers among UMI patients with or without significant stenosis in the coronary artery supplying the infarcted area (p=0.99; p=0.48; and p=0.22). There were significant correlations between the volume of the infarcted area and hs-cTnI (Rho= 0.40; p=0.002) and NT-proBNP (Rho= 0.41; p=0.001). In a linear regression model comprising presence of UMI, age and the degree of the most severe coronary stenosis, the level of hs-cTnI was independent of age and stroke. The association between the hs-cTnI level and UMI was independent of age and degree of coronary stenosis.

Conclusions: The levels of hs-cTnI, NT-proBNP and Galectin-3 were elevated in patients with UMI. The association between the hs-cTnI level and UMI was independent of age and degree of coronary stenosis.
Survival in patients with cardiomyopathy and duchenne muscular dystrophy in use of an angiotensin-converting enzyme inhibitor and a beta-blocker during long-term follow-up

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Purpose: All Duchenne muscular dystrophy (DMD) patients in the middle of second decade of life display cardiomyopathy. One of the major problems for clinicians dealing with the cardiomyopathy of DMD patients is unsuccessful treatment since appearing of congestive heart failure symptoms.

Methods: A progressive long-term follow-up (from 6 up to 18 years) of 68 patients with DMD (all with verified mutations of dystrophin gene). Mean age in the start of follow-up was 8.8 years. Cardiac examination was made in all patients (ECG routine, ECG monitoring, ECHO, Doppler).

Result: During the follow-up, all the patients were found to have indications for treatment of an ACE inhibitor (captopril or in a dose of 0.5 mg/kg/day) and a beta-blocker (metoprolol by individually adjusting its dose). Despite recommendations, Group 2 patients (n=33) were not treated with the above drugs. Mortality in this group might lead to the follow-up period was 37% (13 patients), in group 2 – 60% (20 patients). In group I mean death age was 21.15 years (standard deviation 2.70 years; mediania: 25 percentile – 17 years; 75 percentile – 19.5 years; moda – 18 years; mode frequency – 5; min age 17 years, max age 25 years). In group II mean death age was 18.25 years (standard deviation 1.55 years; mediania: 25 percentile – 20 years; 75 percentile – 23.5 years; moda – 20 years; mode frequency – 3; min age 16 years, max age 21 years). No significant difference were found in mean death age. The part of survived patients to the age of 21 years was significantly higher in group I than in group II; related frequency 0.77 (95% CI 0.5983...0.94) versus 0.39 (95% CI 0.19...0.5974).

Conclusion: Early started long-term treatment by angiotensin-converting enzyme inhibitor and a beta-blocker in patients with Duchenne muscular dystrophy significantly increased the part of survived patients to the age of 21 years.

Table 1

<table>
<thead>
<tr>
<th>PHASE</th>
<th>LV systolic function</th>
<th>RV systolic function and SPAP</th>
<th>2D EF (%)</th>
<th>3D EF (%)</th>
<th>S (%)</th>
<th>GLS (%)</th>
<th>3DGLS (%)</th>
<th>FAS (%)</th>
<th>TAPSE</th>
<th>RVMPVI</th>
<th>RVGVS (%)</th>
<th>SPAP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS1</td>
<td>55±6</td>
<td>53±7</td>
<td>5.9±1.1</td>
<td>19.5±2.6</td>
<td>-14.7±3.1</td>
<td>40.7±7.9</td>
<td>22.7±2.2</td>
<td>0.6±0.1</td>
<td>-22.3±3.5</td>
<td>22.8±8.5</td>
<td>49.0±15.2</td>
<td></td>
</tr>
<tr>
<td>MS2</td>
<td>56±5</td>
<td>52±6</td>
<td>6.0±1.2</td>
<td>-20±1.8</td>
<td>-13.3±1.5</td>
<td>44.6±6.7</td>
<td>23.0±2.5</td>
<td>0.6±0.1</td>
<td>-22.8±3.1</td>
<td>27±12</td>
<td>50±17.8</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>56±4.2</td>
<td>64±2</td>
<td>7.3±0.8</td>
<td>-22±1.8</td>
<td>-20.3±1.8</td>
<td>53.1±9.5</td>
<td>26.3±2.2</td>
<td>0.4±0.1</td>
<td>-25.8±4.0</td>
<td>15±6</td>
<td>49±17.5</td>
<td></td>
</tr>
</tbody>
</table>
Results: Patients were divided in 4 ventilatory classes (VC) according to the mean ejection fraction (VEF; >40%), including 81 with AHF and 44 with CHF. Clinical status and L V diastolic function were determined using air–acetylene flame atomic absorption spectrophotometry. Serum Zn was significantly lower in AHF vs. CHF (B= -1.093, 95%CI: -2.009 to -0.177, p=0.020) were independent predictors of rest E/e’ ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity (E/e’) (r: -0.349, p=0.001), NT-proBNP (r: -0.297, p=0.004), cTnTMAX (r: -0.336, p<0.001) were negatively correlated with serum Zn. In multiple linear regression, only NYHA class (B= -11.05, 95%CI: -16.740 to -5.469, p<0.001) and E/e’ ratio (B= -1.093, 95%CI: -2.090 to -0.177, p=0.020) were independent predictors of serum Zn.

Conclusions: Serum Zn was decreased both in AHF and CHF patients compared to controls and seems to be lower in AHF vs. CHF. Furthermore serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Moreover, serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure. Serum Zn was significantly lower in AHF vs. CHF and chronic (CHF) heart failure.
no dynamic MR may impact on cardiopulmonary and echocardiographic related phenotypes.

Methods: 80 HF patients (age 65±12; male 75%; ischemic etiology 67%; NYHA class I, II, III and IV 20, 36, 34, 10) with reduced ejection fraction (LVEF 33±9%) underwent cardiopulmonary exercise test (CPET) on tilttable cycle-ergometer (standard incremental ramp protocol) combined with exercise-echocardiography. The population was studied according to the degree of functional MR.

Results: Population was divided into three groups according to functional MR: Group A (rest MR<1/4, no dynamic MR), GroupB (rest MR>1/4, dynamic MR) and Group C (dynamic MR+). The latter group was taken as control group and well defined had higher resting and peak exercise pulmonary pressure and impaired right ventricular (RV) function. Interestingly, Group B patients exhibited a worsening pattern of exercise response (lower peak VO2, O2 pulse and workload) and high dynamic MR (Type 3) to Group A (Type 1a, Type 1b) with similar LVEF, and exercise was the key physiological tool to unlock the worse clinical condition.

Conclusions: In HF patients the severity of rest functional MR is associated with the most unfavorable RV performance and pulmonary hemodynamic response. Among patients without significant MR at rest, development of dynamic MR transmutes into a worse exercise phenotypes and very likely more rapid clinical deterioration.

P5576 | BEDSIDE
Myocardial ventricular adaptation to pulmonary hypertension in non-ischemic dilated cardiomyopathy: a study performed by cardiac magnetic resonance imaging

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Pulmonary hypertension (PH) is a prognostic factor in heart failure (HF) in terms of increased mortality and hospitalization. The prognostic impact of PH in HF suggests an important role for preclinical detection of signs indicating an ongoing RV dysfunction due to its remodeling. Several studies highlighted the utility of cardiac magnetic resonance (CMR) in patients with arterial pulmonary hypertension in terms of early detection of late gadolinium enhancement (LE) in the RV junctional insertion point of the interventricular septum. The aims were to evaluate the presence of junctional LE in patient with non-ischemic dilated cardiomyopathy (NICD), to evaluate the relationship between this specific LE pattern and CMR parameters, to evaluate its prognostic impact.

Methods: All consecutive patients admitted to our clinic with diagnosis of NICD. All subjects underwent a diagnostic work-up including CMR and cardiac catheterization.

Results: 118 patients fulfilling the enrollment criteria. 38 patients (32%) showed functional LE: in 29 patients, junctional LE was associated with midwall septal or posterior free wall LE. In 8 LGE was confined only to the junctions points, and 1 had junctional LE associated with a stria on free wall LE. In the patients with the patients had increased RVEDV (p<0.03) and reduced RVEF (p<0.01). Patients with junctional LGE showed a worse hemodynamic profile in terms of PH (p<0.03) and LVEDP (p=0.02); moreover, this group showed an increased value of 6MWT distance. In the patients with junctional LE the mean value of 24h ambulatory BP monitoring was significantly higher than in the control group. During a follow-up of 37 months Kaplan Meier analysis revealed a correlation between junctional LE and occurrence of episodes of HF (p=0.03). On univariate analysis, all right catheterization parameters indicating a worse hemodynamic profile were associated with junctional LE. On multivariable analysis, only the increased LVEDP showed a trend for prediction of HF (p=0.079).

Conclusions: Junctional LE in the RV insertion points is a frequent CMR finding in NICD, up to 32% in our population. The strict relationship with all hemodynamic parameters indicating the presence of PH complicating the NICD with junctional LE makes this peculiar pattern not specific for pre-capillary PH as herein demonstrated. The junctional LE pattern on follow-up was able to identify the patients at risk for developing HF, assuming the role of an imaging marker of ventricular remodeling in NICD complicated by PH.

P5577 | BEDSIDE
Effects of low dose dopamine infusion on ventriculoarterial coupling, ventricular efficiency and renal function in patients with acute decompensated systolic heart failure

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Our purpose was to assess the effects of the combination of low dose dopamine and furosemide on optimising ventriculoarterial coupling (VAC), ventricular efficiency and renal function. The combination therapy was compared to control therapy (the dopamine group) and the combination group. The primary endpoint was the VAC and renal function and “zero” coronary calcium (controls, referred for a CT coronary angiography).

Methods: A total of 42 patients were randomised to one of the following groups: high dose furosemide (20mg/hr), low-dose dopamine (5mg/hr) and low dose furosemide alone (5mg/hr). Protocol duration was 8 hours and all patients received standardised treatment until further assessment (40mg furosemide iv q12 hours). Renal function was assessed by means of serum creatinine and creatinine clearance at 0 and 24 hours. Patient groups did not differ significantly regarding their baseline status, VAC and ventricular efficiency status at 0 and 24 hours post protocol initiation. Each patient was randomised to one of the following groups: treatment in ADHF patients.

Results: Mean LVEF was slightly lower in CAD and CABG (63±10%) than in controls (68±5%), but LVEDV were comparable (147±37 vs 135±29ml), and LVM significantly higher (158±42 vs 122±25±5), as expected. In patients with ischemic HF all traditional parameters were most abnormal (32±12%, 263±70ml and 205±50g, resp.). The PER reached 412±98 in controls, 384±102 in CAD, 382±98 in CABG and 325±113 in HF (p<0.001 ANOVA). The PER/V*M (established in controls log10 -0.43) was observed in 58 out of 185 CAD-pts (31%) and 41 out of 101 CABG-pts (40%), and in all HF patients, while low LVEF (<50%) was observed in 15 (8%), 11 (11%) and 25 (96%) patients, resp.

Conclusions: Cardiac CT allows for determination of volume-ejection rate based parameters indicating the presence of PH complicating the NIDC with junctional LE in the RV insertion points is a frequent CMR finding in NICD, up to 32% in our population. The strict relationship with all hemodynamic parameters indicating the presence of PH complicating the NICD with junctional LE makes this peculiar pattern not specific for pre-capillary PH as herein demonstrated. TREATING VENTRICULAR DYSFUNCTION
P5580 | BEDSIDE
Intra-aortic balloon pump effects on macrocirculation and tissue microcirculation in cardiogenic shock patients supported by venoarterial extraorporeal membrane oxygenation
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Aims: This study was designed to assess the effects on macrocirculation and tissue microcirculation of adding an intra-aortic balloon pump (IABP) to peripheral venoarterial–extraorporeal membrane oxygenation (VA-ECMO) in patients with severe cardiogenic shock and little/no residual left ventricular (LV) ejection.

Methods and results: Clinical, Doppler echocardiography and pulmonary artery-derived hemodynamic parameters, and cerebral and thenar eminence tissue oxygenation (StO2) and side-stream dark-field (SDF) imaging of sublingual microcirculation were evaluated in 12 consecutive patients before, and 30 minutes after interrupting and restarting IABP. Stopping IABP was associated with higher pulmonary artery-occlusion pressure (PAOP) (19±1.0 vs. 15.8±3.6 mmHg, P=0.01), increased LV end-systolic (51±13 vs. 50±14 mm, P=0.05) and end-diastolic (55±13 vs. 52±14 mm, P=0.003) dimensions and decreased pulse pressure (15±13 vs. 29±22 mmHg, P=0.02). Maximum PAOP reduction when the IABP was restarted was observed in the 7 patients whose PAOP was >15 mmHg when IABP was off (–6.6±2.3 vs. +8.6±3.4 mmHg, respectively). Thenar eminence and brain StO2 and SDF-assessed sublingual microcirculation were unaltered by stopping and restarting IABP.

Conclusion: Restoring pulsatility and decreasing LV afterload with IABP was associated with smaller LV dimensions and lower pulmonary artery pressures, but did not affect microcirculation parameters in cardiogenic shock patients with little/no residual LV ejection while on peripheral VA-ECMO. IABP might prevent severe hydrostatic pulmonary edema in this context.

P5581 | BEDSIDE
A phase II randomized, double-blind, placebo controlled study to evaluate the safety and efficacy of an endomyocardial injection of hSDF-1 alpha to restore left ventricular function in patients with symptomatic chronic heart failure
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Purpose: Stromal cell-derived factor-1 (SDF-1) promotes tissue repair by increasing cell survival, endogenous stem cell recruitment and vasculogenesis. In an open-label Phase I study, endomyocardial injection of a non-viral DNA plasmid encoding human SDF-1 in ischemic heart failure (HF) patients led to improved clinical status. The purpose of STOP-HF, a Phase II multi-center double blind randomized placebo-controlled trial, is to study the effects of a single-dose of SDF-1 plasmid delivered via endomyocardial injection on clinical parameters and outcomes.

Methods: 93 IHF subjects on stable medical therapy with reduced LV function (EF ≤40%), New York Heart Association Class III or IV, and New York Heart Association Class I or II Heart Failure Questionnaire scores (MLWHFQ = 20 points) and limited six minute walk distances (6MWD < 400 meters) were randomized 1:1:1 to receive 15 or 30 mg of SDF-1 plasmid or placebo via 15 injections through the BioCardia Helical Infusion Catheter. The primary efficacy endpoint is a composite change in MLWHFQ and 6MWD at 4 months. Additional efficacy assessments included NYHA class, biomarkers, echocardiographic parameters and exercise capacity.

Results: Enrollment was completed in October of 2013. Profile of subjects at baseline (mean ± SD): age 65±9 years, LVEF 29±7%, MLWHFQ 50±20 points and 6MWD 289±199 meters. All subjects received injections with 96% of patients receiving all 15 injections. To date, 761 follow up months have been completed, all subjects beyond 1-month are free of unanticipated serious adverse events related to study drug. Four-month efficacy results will be available in April 2014.

Conclusions: STOP-HF continue to demonstrate the strong safety profile of SDF-1 plasmid delivery. Primary efficacy endpoint data will be presented.

P5582 | BEDSIDE
Application of novel hemodynamic subsets in predicting the need for inotropic support in congestive heart failure
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Purpose: We aimed to elucidate the best hemodynamic parameter to propose novel hemodynamic subsets in predicting the need for inotropic support in patients with congestive heart failure (CHF).

Methods: We performed right heart catheterization (RHC) in 197 consecutive HF patients (67±15 years old, 129 males) on hospital admission. Left ventricular stroke work index (LVSWI) was estimated by the formula: (mean blood pressure – mean pulmonary capillary wedge pressure (PCWP)) × stroke volume index 0.0136 (g/m²/beat/m²).

Results: Sixteen (8.1%) patients required inotropic support during hospitalization. Among hemodynamic variables including cardiac index, stroke volume index, mean PAOP, and left ventricular stroke work index, LVSWI was identified as the best predictor of inotropic need with an area under the receiver operating characteristic (ROC) curve (AUC) of 0.85 (95% CI: 0.76-0.95, P<0.01), and the best cutoff value was 29.8 g/m²/beat with sensitivity of 94% and specificity of 75%. In contrast, the AUC of cardiac index was only 0.73 (95% CI: 0.60-0.86, P<0.01). The combination of LVSWI and mean PCWP had greater ability for predicting the need for inotropic support compared with the use of the Forrester hemodynamic subsets (Figure).

Conclusions: The novel hemodynamic subsets based on combined RHC-derived LVSWI and mean PCWP has great utility in predicting the need for inotropic support and can guide an individualized therapeutic strategy in CHF.

P5583 | BENCH
High-fat diet ameliorates left ventricular remodelling and dysfunction
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Aims: Interleukin 13 receptor α1 (IL-13 Rα1) deficiency leads to the development of dilated cardiomyopathy (DCM) and left ventricular (LV) dysfunction in mice. We aimed to determine the role of a high-fat diet on LV remodelling and dysfunction in IL-13 Rα1-deficient mice.

Methods and results: We compared the outcome of 6-week old Il13ra1−/− (prone to DCM) with wild-type normal mice placed on an 18-week high-fat diet. Il13ra1−/− mice gained more weight than controls during the study period. Body composition was analyzed in-vivo using nuclear magnetic resonance. Fat-to-lean mass ratio was higher in Il13ra1−/− mice compared with controls (0.79±0.03 and 0.63±0.02, respectively, P<0.01). An echocardiography study was performed at the age of 24 weeks to evaluate the possible effect on cardiac dysfunction in pre-disease characterized Il13ra1−/− mice. Surprisingly, the high-fat diet normalized and prevented the development of DCM in the Il13ra1−/− mice. Cardiac indices such as LV ejection fraction (53.66±6.7 vs. 50.29±4.23%, P<0.06) posterior wall diastolic thickness (0.81±0.03 vs. 0.83±0.02 mm) and LV diastolic dimension...
(4.00±0.12 vs. 3.8±0.09 mm, p=0.21; n=6-9 per group), were similar in the DCM and normal mice, respectively, after 18 weeks of the high fat diet.

Conclusion: A high-fat diet prevents the development of adverse cardiac remodeling and dysfunction in mice prone to cardiomyopathy. Clinical studies are needed to confirm our provocative findings and determine the optimal diet composition in vulnerable patients with cardiomyopathy and heart failure.

P5584 | BEDSIDE
Impact of infiltrated immune-mediated cells in myocardium on long-term prognosis in patients with dilated cardiomyopathy

Background: The causes of dilated cardiomyopathy (DCM) have yet undetermined, but there is growing evidence that persistent inflammation in myocardium plays a pathophysiological role in DCM. Macrophages, along with dendritic cells (DCs), are characterized as antigen-presenting cells to the immune system and vitally important to regulate its consequential inflammatory response. A recent study showed macrophages and DCs are found in endomycocardial biopsy specimens from patients with DCM. However, the relationship between infiltration of immune-mediated cells and the prognosis of DCM has not well understood.

Method: A total of 110 consecutive patients with heart failure, who underwent right ventricular endomycocardial biopsy as diagnostic procedure in 2005 at our institution were reviewed. Of them, by excluding ischemic cardiomyopathy, hyper-tension-related cardiomyopathy, and secondary cardiomyopathy such as sarcoidosis and amyloidosis, 39 patients who were consequently diagnosed as DCM were enrolled in the study. We stained stored biopsy samples with antibodies specific for CD3 (T lymphocytes), CD68 (macrophages), CD163 (M2 macrophages), and CD209 (DCs) to count the infiltrated cells. We also obtained each patient's clinical data in medical records from diagnosis for up to 8 years.

Results: During the observation period, 6 patients (15%) died (1.8-7.7 years from diagnosis, Group D). Those patients showed no different baseline characteristics at diagnosis, e.g., age, LVEF, ejection fraction, LV end-diastolic dimension, serum Na, creatinine, total protein, total bilirubin and plasma BNP levels, from those who survived (Group S). The number of infiltrated CD68 and CD163 was larger in Group D compared to Group S (31±5 vs. 17±2/mm², p=0.01, and 15±3 vs. 8±1/mm², p=0.05). On the other hand, infiltrated CD3 did not differ between the groups (16±4 vs. 9±2/mm², p=N.S.).The number of CD209 are positively correlated with those of CD68 (R=0.42, p=0.009) and CD163 (R=0.64, p=0.0001).

Conclusions: Despite similar clinical background, patients with worse long-term prognosis showed more infiltrated macrophages in endomycocardial biopsy specimens at diagnosis of DCM. In addition, infiltration of DCs was associated with that of macrophages into myocardium, suggesting the possible role of immune-mediated cells in the pathophysiology of DCM.

P5585 | BEDSIDE
Models for management of acute heart failure: a comparison of acute heart failure referral pathways at two UK Tertiary Centres
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Purpose: The management of acute heart failure (AHF) patients is a complex syndrome with prognostic, evidence based therapy. In order to best manage the disease and improve short and long term outcomes, identification of patients is key.

Two linked, tertiary centre hospitals with established Heart Failure (HF) teams comprising consultants, dedicated specialist registrars and specialist nurses, developed different pathways for identification and referral of such patients. This abstract presents a comparison of their activity using these pathways to model different working practices.

Methods: At site 1, an NT-proBNP pathway was developed such that anyone with signs and symptoms of HF with an NT-proBNP ≥400 or NT-proBNP ≥400 ng/L was referred. At site 2 those admitted with signs and symptoms of HF underwent a transthoracic echocardiogram (TTE) prior to referral. Data on both sites was collected over a 4 month period and was made with 4 months of the previous year when neither pathway was in use.

Results: Site 1 saw 212 patients of whom 97 (46%) were male; mean age 75 years. Median time to review was 1 day from referral (0-1) but 4 days from admission (2-9), 33% had reduced EF. Median length of stay (LOS) did not change (15 days) however 30-day readmission rate was significantly decreased using the new pathway (20% vs 13%; p=0.03).

Site 2 reviewed 228 patients of whom 124 (54%) were male; mean age 70 years. Median time to review was 1 day from referral (0-1) and 4 days from admission (1-7), 87% had reduced EF. Median LOS did not change (14 vs 12 days; p=0.23). 30-day readmission rate was reduced but not significantly different (7.6% vs 1.0%; p=0.13).

Conclusions: This study shows that both an NT-proBNP/BNP and echo driven pathway for identification and referral of patients with acute decompensated HF is feasible. Site 2’s TTE driven pathway is associated with an increased specificity for those with HF and reduced EF.

Both pathways lead to reduced readmission rates at 1 month; however there is no significant difference in LOS.

P5586 | BEDSIDE
How accurate is clinical assessment in the estimation of central venous pressure in acute heart failure? Insights from a prospective study
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1 University Hospital Basel, Cardiovascular Research Institute of Basel (CRIB), Basel; 2 University Hospital Basel, Dept. of Angiology, Basel, 2 University Hospital Basel, Dept. of Cardiology, Basel, Switzerland

Background: Clinical assessment of signs of volume overload including elevated neck veins is important in the early diagnosis of acute heart failure (AHF). However, it is largely unknown how accurate is routine clinical assessment in the estimation of central venous pressure (CVP) in patients with AHF.

Methods: In 216 unselected AHF patients presenting to the Emergency Department (ED) neck veins were examined by the treating ED physician in an observational prospective study. CVP was measured using peripheral venous compression sonography at the forearm, a novel non-invasive method shown to be close correlated with invasive measurements, in a blinded fashion. The measures were done before the administration of vasodilators or diuretics. CVP determinations were registered as continuous data, and CVP >12mmHg was considered as elevated.

Results: In the study cohort [58% men, median age 80 years, left ventricular ejection fraction 40%, B-type natriuretic peptide 1372 pg/mL body mass index 26.4, neck veins were rated as normal in 32.4%, a positive hepatojugular reflex (neck veins normal at rest but distended during increased reflux) in 11.6% and distended AHF patients in 55% of AHF patients. Interestingly, the median CVP values were 8.5mmHg (IQR: 5.2-12.6mmHg), 8.1mmHg (IQR: 5.5-14.4mmHg), and 9.6mmHg (IQR: 5.5-12.6mmHg), respectively. A Kruskal-Wallis test showed no significant difference (p=0.72).

Physical examination had a sensitivity of 54% to detect an elevated CVP defined as CVP>12mmHg. Findings were similar in predefined subgroups including the obese, the elderly, and women.

Conclusion: Clinical estimation of CVP by physical examination of the neck veins in AHF is highly inaccurate. Reasons may include poor training of ED physicians in the pitfalls of examining neck veins (e.g. the critical distinction between normal and not assessable neck veins) and cheating/extrapolation (AHF has been diagnosed independent of this variable and findings are rated to match the presumed diagnosis).

P5587 | BEDSIDE
A heart-failure led one-stop diagnostic service for breathlessness: initial experiences and diagnostic yield
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Purpose: Breathlessness is the most common presenting complaint in heart failure, a condition known to be under-diagnosed. Primary care physicians are calling for direct access symptom-based diagnostic services to optimise secondary care referral pathways. We established a heart failure clinic staffed by members of a tertiary centre heart failure team, and assessed its potential clinical utility for detecting heart failure (and other cardiorespiratory disorders) that require further investigation and/or treatment.

Methods: Primary care physicians were invited to refer patients for one-stop testing, including ECG, B-natriuretic peptide (BNP), spirometry, echocardiography, cardiopulmonary exercise testing (CPX) and clinical assessment.

Results: 191 patients were assessed over 2.6 years (90 male, median age 75 years). Median body mass index was 29.1 kg/m²; 80 patients met criteria for obesity. Breathlessness was the presenting symptom in 82%, oedema in 12% and cough in 4%. 64 patients were known to have pre-existing cardiac conditions (including 13 with heart failure) and 56 had pre-existing respiratory conditions.

Left ventricular systolic function was mildly, moderately and severely impaired in 7%, 2% and 3% of patients respectively, with impaired diastolic function in a further 17% and valvular disease of at least moderate severity in 10%. Natriuretic peptides were elevated (BNP >100 or NT-proBNP >400) in 30% of the subjects in whom samples were taken. 58% of 120 patients undergoing CPX had reduced exercise capacity (defined by a peak VO₂ -85% predicted).

A cause for the patient’s breathlessness was found in 80% with a new cardiac diagnosis made in 17% (HFREF 4%, HFP EF 6%, likely angina 3%, arrhythmia 2%, valvular disease 2% and new respiratory diagnosis in 10%. 38% of subjects were reassured with no requirement for further secondary-level investigations or review.

Conclusions: Although breathlessness is the most common presenting symptom in heart failure, only a small proportion of subjects with unselected referral to a community breathlessness service had heart failure with a reduced ejection fraction. Further exper’t investigation and management. This one-stop approach in breathless patients offers a streamlined assessment with the additional potential for fully reassuring patients of the absence of significant cardiac or respiratory pathology.
P5588 | BENCH Diagnosis and therapy monitoring of idiopathic giant cell myocarditis and cardiac sarcoidosis by myocardial gene expression profiling

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Objective: Improvement of clinical diagnostics of idiopathic giant cell myocarditis (ICGM) and cardiac sarcoidosis (CS), two frequently human myocardial diseases. Currently, ICGM and CS are diagnosed based on differential patterns of inflammatory cell infiltration and non-caseating granulomas in histological sections of endomyocardial biopsies (EMB), after heart explantation or postmortem. We report on a method for improved differential diagnosis by myocardial gene expression profiling in EMBs.

Methods: We examined gene expression profiles in EMBs from 10 patients with histopathologically proven ICGM, 10 with CS, 18 with active myocarditis (MCA), and 80 inflammation-free control subjects by quantitative RT-QPCR. We identified distinct differential profiles that allowed a clear discrimination of tissues harboring giant cells (ICGS, CS) from those with MCA or inflammation-free controls.

Results: The expression levels of genes coding for cytokines or chemokines (CCL20, ILNF1, IL6, IL-17D; p≤0.05), cellular receptors (ADIPOR2, CCR5, CR5, CCR7, CR8; p≤0.05) and proteins involved in the mitochondrial energy metabolism (CPT1, CYB, DHDODH; p≤0.05) were deregulated in 2 to 300 fold range, respectively. Bioinformatic analyses and correlation of the gene expression data with immunohistochemical findings provided novel information regarding the differential cellular and molecular pathomechanisms in ICGM, CS and MCA.

Conclusion: Myocardial gene expression profiling is a reliable method to predict the presence of multinuclear giant cells in the myocardium, even without a direct histological proof! in small single EMB sections, and thus to reduce the risk of sampling error. This profiling also facilitates the discrimination between ICGM and CS, as two different clinical entities that require immediate and tailored differential therapy.

P5589 | BEDSIDE Endovascular versus epicardial lead placement for resynchronization therapy?

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Objective: To study the clinical outcome in Cardiac Resynchronization Therapy (CRT)-eligible patients of transvenous versus epicardial left ventricular (LV) lead implantation.

Methods: A total of 290 consecutive CRT recipients from an ongoing, single center registry were included in the present analysis. The follow-up was 7.76±2.33 years. Patients were selected for CRT according to the presence of LV ejection fraction (LVEF) <35%, heart failure (HF) symptoms despite optimal medical therapy, and a QRS duration ≥120ms. The LV lead placement was guided by an intraoperative coronary sinus (CS) occlusive venogram. LV leads were placed in the lateral (54.1%, n=157), posterolateral (19%, n=55), anterolateral (15.9%, n=46), interventricular anterior (1.7%, n=5) coronary veins and epicardial placement (9.3%, n=27).

Results: Both groups demonstrated improvement in the ejection fraction (EF) at 6 months. The baseline EF, LVEF, LVEDD was similar for the transvenous and epicardial groups, with no difference in the change over 6 months (Table 1). The baseline NYHA class was a median of II and improved to II in both groups at 6 months. A total of 93 deaths: 19 (38.8%) HF in lateral vein, 10 (50.0%) HF in intercostal vein, 10 (50.0%) HF in intracardial vein and 1 (50.0%) HF in epicardial LV. The second cause was infectious (11.8%, n=27). The third cause was ventricular fibrillation (10.8%, n=27). In the transvenous group 102p (40.2%) needed new hospitalizations, in the epicardic group 6 (23.1%, p=0.089). The overall survival was worse in epicardic group versus endovascular group (γ=0.28; df=1; p=0.002).

P5590 | BENCH Modification of cardiac disease by histone deacetylation 6 in pressure-overloaded hypertrophy

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Background: Alpha-tubulin, a component of microtubules, is acetylated at the amino acid lysine at position 14, and its deacetylation is regulated by histone deacetylase 6 (HDAC6). Although this acetylation of tubulin may be associated with cell cycle, cellular and functional changes in the cardiomyocytes, the functional role of acetylated tubulin in disease conditions such as a pressure-overloaded hypertrophy and disease progression to heart failure remains uncertain.

Methods and results: Modification of cardiac HDAC6 was performed by transgenic (TG) overexpression of the active HDAC6 and dominant negative HDAC6 (H216A, H611A) proteins specifically in the cardiomyocytes. Overexpression of active HDAC6 significantly reduced acetylated tubulin levels and overexpression of dominant negative HDAC6 significantly increased it in the mouse heart, suggesting that HDAC6 can regulate cardiac tubulin deacetylation. Neither histological alteration nor alteration of cardiac function determined by echocardiography was seen in the active and dominant negative TG mouse hearts from mice one year of age or older. These results suggest that HDAC6 activity has no critical role in mouse cardiomyocytes. To analyze the role of HDAC6 and acetylated tubulin in the disease conditions, we studied the pressure over-loaded stress responses in TG mice hearts. Pressure-overloaded hypertrophy was generated by surgical thoracic aortic banding (TAC). Cardiac hypertrophy was observed in nontransgenic (NTG) TAC mouse hearts within injection in shortening fraction by echocardiography two weeks after surgery. Cardiac acetylated tubulin was decreased in the hypertrophic NTG mouse hearts compared with that in the NTG mouse hearts. A marked reduction in the shortening fraction and dilated chamber dilatation was detected in the active HDAC6 TG mice hearts two weeks after surgery. Sustained low level of acetylated tubulin was observed in the TAC HDAC6 active TG mouse hearts, suggesting that activation of HADCD6 with concomitant reduction in acetylated tubulin can worsen cardiac disease in pressure-overloaded hypertrophy.

Conclusion: Cardiac HDAC6 activity and the cardiac acetylated tubulin level may be critical factors involved in cardiac disease in pressure-overloaded hypertrophy.

HEART FAILURE, PATHOPHYSIOLOGY AND PROGNOSIS

P5592 | SPOTLIGHT Parameters predicting the preserved ICD indication for primary prevention after optimal medical treatment in patients with chronic systolic heart failure

Z. Majro1, M. Dekany1, B. Muk1, B. Szabo1, T. Borsányi1, P. Bogyi1, M. Szabo2, D. Vagány1, R.G. Kiss1, N. Nyolczi1, 1Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary; 2Semmelweis University, Budapest, Hungary

Background: Optimization of medical treatment (OMT) before initiation of device therapy (DT) is recommended by guidelines (Class I) for chronic systolic heart failure (HF/EF) patients (pts). Until present, however, we have limited information about the extent to which OMT can reduce the proportion of pts with ICD indication that may predict the therapeutic answer.

Methods: Parameters of 693 pts managed at our Heart Failure Clinic (mean age: 62.5±24.0 years, ischemic etiology: 49.1%, NYHA class: 2.95±0.94, left ventricular ejection fraction: 30.9±8.3%) were evaluated. We assessed clinical and echocardiographic parameters of the pts before OMT and 6 months later (after drug-titration and 3 months use of OMT). Prognostic value of several clinical, echocardiographic, ECG and laboratory parameters was investigated by logistic regression analysis.

Results: From 693 pts with HF/EF 253 (36.5%) met the indication criteria of PP ICD at the first examination, before OMT. During the 6 months follow up of 4 of 253 pts died. From the remaining 249 pts 157 (63%) improved on OMT and to assess the potential prognostic factors that may predict the therapeutic answer.

Parameters predicting the preserved ICD indication for primary prevention after optimal medical treatment in patients with chronic systolic heart failure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF &lt;40%</td>
<td>3.41 (1.91 - 6.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>3.41 (1.91 - 6.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESD &gt;35 mm</td>
<td>3.41 (1.91 - 6.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LPW &gt;40 mm</td>
<td>3.41 (1.91 - 6.05)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The expression levels of genes coding for cytokines or chemokines (CCL20, ILNF1, IL6, IL-17D; p≤0.05), cellular receptors (ADIPOR2, CCR5, CR5, CCR7, CR8; p≤0.05) and proteins involved in the mitochondrial energy metabolism (CPT1, CYB, DHDODH; p≤0.05) were deregulated in 2 to 300 fold range, respectively. Bioinformatic analyses and correlation of the gene expression data with immunohistochemical findings provided novel information regarding the differential cellular and molecular pathomechanisms in ICGM, CS and MCA.

Conclusion: Myocardial gene expression profiling is a reliable method to predict the presence of multinuclear giant cells in the myocardium, even without a direct histological proof! in small single EMB sections, and thus to reduce the risk of sampling error. This profiling also facilitates the discrimination between ICGM and CS, as two different clinical entities that require immediate and tailored differential therapy.
ICD indication. Significantly impaired left ventricular ejection fraction, left ventricular dilatation and low systolic blood pressure could predict the preservance of PP ICD indication on OMT.

P5593 | BEDSIDE
Liver stiffness measured by transient elastography predicts clinical events in patients with heart failure
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Background: Passive liver congestion due to elevated right-sided filling pressure is a common finding in patients with heart failure (HF). However, the clinical impact of liver congestion on HF outcomes has been poorly described. Transient elastography is a new non-invasive method to evaluate liver stiffness (LS). We investigated the clinical impact of LS on clinical outcomes in HF patients.

Methods: LS values in 157 consecutive HF patients (age 64±15 years, male 69%, LVEF 44±18%) were determined before discharge using a (...) device. Patients with invalid liver stiffness measurements due to severe obesity, narrow intercostal space and substantial ascites were excluded. Patients were followed for cardiac death or rehospitalization due to HF. ROC curve analysis was used to derive optimal cutoff value for predicting outcomes. Cox proportional-hazards regression was used to adjust for the effect of differences in pertinent covariates on the clinical event rate.

Results: The median of LS in our study patients was 6.5 kPa (range 2.3 - 39.7). Twenty patients (13%) died or were hospitalized for decompensated HF after a mean follow-up of 75±28 days. ROC curve analysis of LS for predicting events revealed an optimal cutoff value of 10.1 kPa. The cardiac event rate was higher in patients with high LS (≥10.1 kPa) than in those with low LS (<10.1 kPa) (37% vs. 4%, p<0.0001). In univariate analysis, LS was related to higher risk of clinical events (crude HR: 1.11, 95% CI: 1.07 - 1.15, p<0.0001). Even after adjusting for age, sex, total bilirubin, LVEF, and BNP, LS was still associated with a higher event rate (adjusted HR: 1.10, 95% CI: 1.05 - 1.15, p<0.0001).

Conclusion: LS offers a rapid and noninvasive diagnostic method to identify patients at a risk of cardiac death or rehospitalization for HF.

P5594 | BEDSIDE
Antigen carbohydrate 125 predicts 30-day readmission in acute heart failure
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Background: Early readmission after a hospitalization for acute heart failure (AHF) remains prohibitively high and there are not well established markers for risk stratification. Plasma antigen carbohydrate 125 (CA125) has emerged as a biomarker related to fluid overload severity of the disease and adverse outcomes. We aimed to evaluate the performance of CA125 to predict 30-day readmission risk in an unelected cohort of patients admitted for AHF.

Methods: We included 1869 consecutive patients discharged alive with AHF diagnosis in a third level hospital (2004-2013). CA125 was measured before discharge and categorized in quartiles (Q). Cox regression analysis adapted for competing events (death) was used to evaluate the independent association between CA125 and the risk of unplanned 30-day readmission. More than 40 variables were evaluated in the multivariate analysis.

Results: At 30 days after discharge, 11 (0.6%) and 236 (12.6%) patients died and were readmitted, respectively. Cumulative incidence for readmission was lower for Q1 (CA125 ≤25U/mL) compared to upper quartiles (fig-1). In the multivariate analysis, patients in the lower quartiles of CA125 exhibited a 30% of risk reduction compared to those in the upper quartiles (HR: 0.70, CI 95%=0.51-0.99, p=0.046). Natriuretic peptides did not predict the risk of readmission.

Conclusion: Low CA125 identified a subset of patients with lower risk of unplanned 30-day readmission after an episode of AHF.

P5595 | BENCH
Archaeaosomal microparticles ridding metalloproteases from the serum may explain protection against heart failure in chagasic patients with asymptomatic indeterminate form
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Background: Microparticles (MPs) in the serum have been related with presence of Heart Failure (HF). HF occurs in 30% of Trypanosoma cruzi infected chagasic individuals, being a useful model to study of MPs. In previous work we found in chagasic endomyocardial biopsies that archaeal gene encoded electron donating MPs (ED) organelles are possibly archaeosomes that entrap extracellular proteins having the function of ridding abnormal proteins, and are increased in asymptomatic indeterminate form (IF) patients. Electron lucent pathogenic archaemia were increased in HF patients, possibly releasing metalloprotease.

Objective: In this work we searched if ED MPs (archaeosomes) are increased in the serum of IF, entrapping Archaeaetrichin-1 (AMZ1), a metalloprotease widely seen in archaea, compared with serum of HF patients.

Material and methods: Sera from 8 HF and 7 from IF chagasic patients were submitted to a technique of MP separation, in a mannitol/sucrose rich solution. After centrifugation, MPs in the pellet and in the supernatant were studied at immunoelectron microscopy, using anti-AMZ1 monoclonal antibody (Novus Biologicals). The mean number ±m2 of ED MPs <100nm and of AMZ1 positive dots intra or extra ED MPs were obtained from 10 photos/case in 50K magnification.

Results: In the supernatant, ED MPs were present in higher numbers in IF (33±4.5±0.9) than in HF (0.2±1.1), P<0.001; if the ED MPs contained AMZ1 positive dots (1.6±3.7), in positive correlation with numbers of ED MPs (r=0.47, P<0.0001) and in HF, ED MPs were almost absent and did not contain AMZ1 dots. In the pellet, the amount of ED MPs did not differ between HF versus IF groups (3.6±5.9 vs 2.5±4.9, P=0.74), but AMZ1 positive dots extra ED MPs were significantly increased in HF (80±132.2) compared to IF (15±19.2), P<0.001. The numbers of ED MPs correlated negatively with AMZ1 extra ED MPs in HF (r=-0.63, P<0.001), but not in IF (r=0.13, P=0.34).

Conclusion: ED MPs <100nm in the serum of IF chagasic patients seem to be archaeosomes, which remove free metalloprotease particles, preventing development of HF whereas the absence of the ED MPs is associated with increased free metalloprotease in serum of HF patients. This is a first human documentation of removal of free abnormal protein from the serum by archaeosomes.

P5596 | BENCH
Myocardial strain but not ejection fraction adds incremental value to clinical predictors of readmission for heart failure
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Background: Risk stratification for heart failure (HF) readmission might enable targeting resources to prevent readmission in the higher risk pts. Unfortunately, clinical risk scores have limited predictive value, and the contribution of EF is variable, based on prevalence of HF and preserved EF. Strain has been shown to improve prognostic assessment over traditional parameters. We hypothesized that adjustment of risk score with strain would enable a more accurate appreciation of risk.

Methods: 468 pts who underwent echo at the time of the first admission for HF were followed for 30-day hospital readmission or death. Three validated risk scores of HF whereas the absence of the ED MPs is associated with increased free metalloprotease in serum of HF patients. This is a first human documentation of removal of free abnormal protein from the serum by archaeosomes.

Conclusion: Low CA125 identified a subset of patients with lower risk of unplanned 30-day readmission after an episode of AHF.

Results: Outcome was reported in 92 pts. Only the Yale score was associated with outcome. Global longitudinal strain (GLS; cutoff -12%), global circumferential strain (cutoff -10.7%), and e' (cutoff 5.9 cm/s) were associated with outcome after adjusted by Yale score (all p<0.10). In sequential Cox models, although the Yale score model was not improved by adding e', the model based on Yale score and e' was significantly improved by adding GLS (Figure) Adding e' or GLS to Yale

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score led to a significant reclassification improvement (Yale+e’e: NRI=0.23, p=0.05, Yale+GLS: NRI=0.45, p<0.01).

Conclusion: Imaging parameters provide incremental value over the validated risk score for predicting 30-day readmission in pts with HF.

P5597 | BEDSIDE
Relationship between LV contractility and coronary flow reserve in non-ischemic dilated cardiomyopathy: a noninvasive stress-echo study
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Background: LV contractility plays an important diagnostic and prognostic role in non-ischemic dilated cardiomyopathy (IDC). Systolic pressure/end-systolic volume relationship (SP/ESVi) was a useful method for evaluating LV myocardial contractility during stress echocardiography (SE). Coronary flow reserve (CFR) on left anterior descending (LAD) can be reduced in IDC.

Aim: To assess the relationship between SP/ESVi and CFR on LAD in IDC patients.

Methods: We enrolled 134 IDC patients (98 men; 62±12 years, mean value of ejection fraction: 34±8%) and 38 age-sex matched normal subjects as controls.

Results: SP/ESVi was defined as systolic cuff pressure/end-systolic volume index difference between rest-peak dip-SE. CFR was defined as the ratio between maximal vasodilation and rest peak diastolic flow velocity in LAD. SP/ESVi was not related to ejection fraction at rest, while it was directly related to ejection fraction at peak dip-SE (r=0.448, p<0.001). CFR on LAD was abnormal (-2) in 66 (49%) IDC patients. SP/ESVi was directly related to CFR on LAD (r=-0.369, p=0.001, Figure, red points) in IDC patients: LV contractile and rest-stress difference in ejection fraction (r=0.435, p<0.001) (Figure, red points) in IDC patients: LV contractile and rest-stress difference in ejection fraction (r=0.435, p<0.001).

Conclusions: In IDC with impaired LV systolic function CFR was directly related to LV myocardial contractility, while this relationship disappeared in normal subjects.

P5598 | BEDSIDE
Exercise ventilatory power in heart failure patients: functional phenotypes definition by combining cardiopulmonary exercise testing with stress echocardiography
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Exercise Ventilatory Power (EVP; peak systolic blood pressure/exercise ventilatory lactate threshold on CO2 production slope) is a powerful prognostic marker that combines ventilator abnormalities with systemic hemodynamic during exercise. The phenotype and clinical relevance of patients with a worse EVP is broadly undefined and we aimed at this definition across a population of heart failure reduced ejection fraction (HFrEF) of different severity.

Methods: 77 HFrEF patients (mean age 65±11; male 70%; ischemic etiology 59%; NYHA class I, II, III and IV 23%, 33%, 31% and 13%, respectively; mean LVEF 34±9%) underwent cardipulmonary exercise test (CPET) evaluation (ramp protocol on performed on a tilt-table cycleergometer) combined with simultaneous echocardiographic assessment.

Results: Patients were divided in 2 EVP classes (cutoff 3.5 mmHg) focusing on peak exercise echocardiographic variables.

Exercise ventilatory power in HF
<table>
<thead>
<tr>
<th>EVP ≥ 3.5 mmHg (n=61)</th>
<th>EVP &lt; 3.5 mmHg (n=16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak oxygen consumption (VO2), ml/kg/min</td>
<td>13.8±3.5</td>
<td>9.9±2.6</td>
</tr>
<tr>
<td>Rest LV EF (%)</td>
<td>33±8</td>
<td>28±10</td>
</tr>
<tr>
<td>Peak LV EF (%)</td>
<td>35±9</td>
<td>31±13</td>
</tr>
<tr>
<td>Rest cardiac output, (CO) l/min</td>
<td>3.85±1.18</td>
<td>3.20±1.50</td>
</tr>
<tr>
<td>Peak cardiac output, (CO) l/min</td>
<td>7.34±2.46</td>
<td>4.59±1.86</td>
</tr>
<tr>
<td>Rest troponin annular systolic excursion (TAPSE), mm</td>
<td>18.5±4.06</td>
<td>13.6±3.18</td>
</tr>
<tr>
<td>Peak troponin annular systolic excursion (TAPSE), mm</td>
<td>20.8±4.03</td>
<td>15.5±4.32</td>
</tr>
<tr>
<td>Rest pulmonary artery systolic pressure (PASP), mmHg</td>
<td>31.6±9.20</td>
<td>56.5±19.43</td>
</tr>
<tr>
<td>Peak pulmonary artery systolic pressure (PASP), mmHg</td>
<td>54.3±14.36</td>
<td>74.5±23.47</td>
</tr>
</tbody>
</table>

Conclusions: A low EVP translates in a very unfavorable phenotype characterized by lower peak VO2 and CO response at peak exercise. Remarkable impairment in right heart function and pulmonary hemodynamics were also peculiar of a low EVP. All the LV-pulmonary circulation- RV apparatus is abnormally involved in the exercise response of the EVP HFrEF phenotype.

P5599 | BENCH
Left ventricular diastolic dysfunction is associated with myocardial fibro-inflammation and elevated serum B-type natriuretic peptide
C.J. Watson1, P. Collier1, N. Glezeva1, V. Voon2, J. Gallagher2, R. Ohanlon2, J. Bagnall1, K. Mcdonald1, M. Ledwidge2. 1 University College Dublin, Dublin, Ireland; 2 Heart Failure Unit, St Vincent’s University Hospital, Dublin, Ireland

Aims: To compare serum biomarkers of inflammation, collagen turnover, extracellular matrix turnover, myocardial tissue evidence of fibrosis, macrophage activity and expression of associated genes in patients with and without ALVDD.

Methods: Myocardial tissue and peripheral serum samples were procured from 35 consecutive, consenting stable patients undergoing elective coronary artery bypass grafting surgery. All patients were screened with echocardiography before and had a normal ejection fraction. They were further classified as having right ventricular dysfunction to CO2 production slope) is a new powerful prognostic marker that combines having evidence of ALVDD or not based on elevated E/E’ (>15) or E/E’ ≤8·5 with at least one of E/a<0·5, DCT>280 ms, LVM>122 g/m2 in women, >149 g/m2 men, LAVI>40 mm2/m3 and the presence of atrial fibrillation. Myocardial specimens were obtained adjacent to the venous cannulation site in the right atrial appendage. All subjects gave written informed consent to participate in the study.

Results: Patients were aged 67±14±8.8 years, 25 (69%) were male, all had symptomatic angina and 18 (53%) had hypertension, 5 (14%) had diabetes. ALVDD patients (n=10) had greater E/E’ (12.5±3.6 vs. 8.4±2.0), greater LAVI (30.6±4.2 vs. 27.8±3.4), and more atrial fibrillation (70% vs. 8%) than controls, all p<0.05. BNP levels were significantly higher in ALVDD patients (163±147 vs. 57±85, p<0.01) but no other blood biomarkers of inflammation, collagen turnover or extracellular matrix turnover differed between the groups. Tissue collagen volume fraction was significantly higher in the ALVDD group (55±7% vs. 47±8%) as was myocardial gene expression of collagen 1, collagen 3, MMP2, TNF alpha, Thy1, LOX and RPCP.

Conclusion: ALVDD is associated with elevated serum BNP, myocardial fibrosis and elevated expression of fibro-inflammatory genes in the myocardium in stable patients undergoing elective coronary artery bypass grafting surgery. Therapeutic strategies directed at modulating of fibrosis and inflammation in the heart may attenuate the progression of ALVDD to HFrEF.
**P5600 | BEDSIDE**

Effective symptomatic improvement by ivabradine treatment in chronic systolic heart failure patients in daily clinical practice is independent of beta blocker dose

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Objectives: The open-label, observational multicenter INTENSIFY study evaluated the effectiveness, tolerability, and effect on quality of life (QoL) of ivabradine treatment over a 4-month period in patients with chronic systolic heart failure (CHF).

Methods: Resting heart rate (HR), heart failure symptoms (NYHA class, signs of decompensation), BNP values and concomitant medication were documented in ambulatory CHF patients. Treatment with ivabradine twice daily was initiated for 4 months. QoL was evaluated by the EQ-SD patient questionnaire. A descriptive statistical analysis of the results was performed for three subgroups defined by beta blocker background dose (<100%, 50% to 99%, and ≤50% of recommended target dose).

Results: In total 1956 patients (mean age 67±11.7 years) with CHF were analyzed. Etiology was ischemic for 62% of the cohort and the diagnosis had been known for more than 6 months for 85% of all patients. 78% received beta blockers. Other concomitant medication consisted e.g. of ACEI/ARB 83%, diuretics 61%, aldosterone antagonists 18%, cardiac glycosides 8%, aspirin 58% and sildenﬁx 56%.

After 4 months of ivabradine treatment (mean dose 12.44 mg per day), the proportion of patients presenting with signs of decompensation and BNP >400 pg/ml decreased from 23% to 5% and from 54% to 27%, respectively. EQ-SF index also improved from 0.64±0.26 to 0.79±0.23, accompanied by a shift in NYHA classiﬁcation towards lower grades. HR reduction by ivabradine was 18.1±11 bpm in the total study cohort. Overall response rate to treatment, defined as patient proportion with HR <70 bpm or HR reduction of ≥10 bpm at study end, was 89%. Treatment effects were similar in all three subgroups defined by beta blocker background dose (<100%, 50% to 99%, and ≤50% of recommended target dose).

Conclusion: Over 4 months of treatment, ivabradine was effective in improving heart failure symptoms in CHF patients in daily clinical practice. Ivabradine also reduced BNP and improved QoL in these patients, accompanied by high treatment response rates. Treatment effects were independent of beta blocker background dose.

**Table 1**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>&lt;50% of beta-blocker</th>
<th>50–99% of beta-blocker</th>
<th>≥100% of beta-blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>Baseline-4 months</td>
<td>Heart rate</td>
<td>Baseline-4 months</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>-18±13 bpm (n=305)</td>
<td>-20±11 bpm (n=702)</td>
<td>-19.0±12 bpm (n=257)</td>
</tr>
<tr>
<td>Treatment responders</td>
<td>-23% (n=75)</td>
<td>-27% (n=200)</td>
<td>-24% (n=63)</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>93% (n=649)</td>
<td>91% (n=233)</td>
<td></td>
</tr>
</tbody>
</table>

**P5602 | BEDSIDE**

Performance of an integrated device diagnostic algorithm to predict the risk of worsening heart failure

R. Dierckx1, V. Sharma2, J. Koehler2, R. Houwen3, M. Goethals4, J. Bartunek5, S. Verstreken5, M. Vanderheyden5, 1OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium; 2Medtronic Inc, Mounds View, MN, United States of America; 3Applied Biomedical Systems BV (ABS), Maastricht, Netherlands

Background: Heart failure (HF) is a prevalent disease characterized by frequent hospital admissions and poor prognosis. The inability to adequately predict HF exacerbations remains the Achilles heel of HF management.

Aim: To test the performance of a novel HF risk stratification model, derived from real-world measurements of multiple device diagnostic variables, to identify patients at risk for worsening HF.

Methods and results: Between Dec 2010 and May 2012 we recruited 63 HF pts (49 men) with reduced ejection fraction (EF). All pts were implanted with an Optim atrioventricular Medtronic CRT-D® or CRT-D device at least 30 days prior to enrollment (mean time from implant to enrollment: 506±477 days). Study participants were prospectively followed for a minimum of 6 months. Demographic, clinical, device and outcome data were collected.

Mean age was 63±12 years, mean EF 29±11%, median NT-proBNP 2154 ng/L (IQ: 814 to 4311 ng/L). At the time of inclusion, most pts had mild to moderate HF (52.5% NYHA II and 21.3% NYHA III) and suffered from ischemic cardiomyopathy (52.4%). Permanent AF was present in 14.3% pts.

HF events were classiﬁed as major or minor, depending on the need for hospitalization vs. presence of signs and/or symptoms of HF requiring ambulatory treatment. After a mean follow-up of 624±152 days, 88 episodes of HF were identiﬁed, with 41 major and 47 minor events. By combining device diagnostic data on in- trathoracic impedance, AF burden, % CRT pacing, ventricular arrhythmia, night heart rate, heart rate variability and patient activity, the algorithm computed a daily HF risk score and categorized pts as being at low (L), medium (M) or high (H) risk for an event in the following 30 days (L: 0 < score ≤5; M: 5 < score ≤20; H: score > 20). Compared to pts in the L group, pts in the M and H group had a relative risk (RR) of respectively 1.0 and 3.3 (95% CI: 0.6-1.9; 1.7-6.6) for worsening HF (mi- nor+major events). Risk stratification was even better when only major HF events were considered, with a RR of 1.6 (95% CI: 0.6-4.4) and 4.3 (CI: 1.2-15.5) for pts in the M and H group, compared to the L group.

Conclusion: A HF risk model based on device diagnostic variables can identify pts at risk for worsening HF, especially those at risk for HF hospitalization.
HEART FAILURE BASICS

P5655 | BENCH
Chronic treatment with dihydroartemisinin, a Transiently Controlled Tumor Protein (TCTP) down-regulating agent, results in cardiac dysfunction and shrunken cells

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Objectives: Dihydroartemisinin (DHA), isolated from the traditional Chinese herb Artemisia annua, is an established agent for the treatment of malaria. In addition, recent studies both in vivo and in vitro have demonstrated the antitumor activity of DHA. DHA is reported to bind to transiently controlled tumor protein (TCTP), a hyperplastic apoptotic protein that is up-regulated in various cancers. Thus, TCTP is indicated to be involved in DHA-induced cell death. On the other hand, our recent results indicated that TCTP plays an important role in the prevention of cardiac apoptosis. Based on these findings, we hypothesize that chronic DHA treatment may induce cardiac dysfunction through down-regulation of TCTP expression in the heart.

Methods and results: In neonatal rat ventricular cardiomyocytes, DHA treatment (50 μM, 60 hours) induced apoptosis of cardiomyocytes (~3.25 fold higher than vehicle-treated control cells, p < 0.01, N=4–5). Apoptosis was measured by fluorescence Activated Cell Sorter (FACS) analysis with Annexin V and 7-AAD staining. The expression of TCTP was decreased (~33% lower than vehicle-treated control cells, p < 0.001, N=4–8) after 48 hours treatment of DHA (50 μM). Moreover, down-regulation of TCTP by siRNA enhanced apoptosis of cardiomyocytes (~1.38 fold higher than control siRNA-treated cells, P < 0.05, N=4–5). To examine the effects of DHA on cardiac function in vivo, we performed echocardiography and cardiac catheterization after chronic DHA treatment (30 mg/kg/day, via intraperitoneal injection for 4 weeks) in wild type (WT) mice. Left ventricular systolic pressure (LV dp/dt max) was significantly decreased in DHA-treated mice compared with vehicle-treated control mice (CTRL) (LV EF: CTRL vs. DHA: 71.8 ± 1.8%, P < 0.01, N=4–6, LV dp/dt max: CTRL vs. DHA: 1135.8 ± 205.6 mmHg/sec vs. 710.9 ± 480.6 mmHg/sec, P < 0.01, N=4–5). Consistently, the LV-A-induced cardiac dysfunction was significantly rescued by cardiac specific over-expression of TCTP (TCTP transgenic mice: TG). (LVEF: CTRL vs. TG: 56.0 ± 1.8% vs. 66.3 ± 1.0%, P < 0.01, N=5, LV dp/dt max: WT vs. TG: 710.9 ± 460.6 mmHg/sec vs. 9286 ± 646.8 mmHg/sec, P < 0.05, N=5).

Conclusions: These results indicate that chronic DHA treatment results in cardiac dysfunction in mice. DHA-induced TCTP down-regulation of TCTP may be involved in the mechanism.

P5656 | BENCH
Simultaneous assessment of the impact of heart failure on protein and lipid synthesis using a new 2H2O-metabolic labeling method in a preclinical animal model

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Heart failure (HF) alters protein and lipid concentrations in plasma and tissues, however in vivo measurements of their rate of synthesis have been thus far hindered by the lack of adequate methodologies. We tested in dogs a new method to simultaneously measure rates of protein and lipid turnover using 2H2O (deuterated water) and subsequent endogenous labeling of 2H to amino acids and lipids. A loading dose of 2H2O was infused intravenously (15 mkg), followed by 72 hours of oral administration in the drinking water (5%) to dogs with advanced pacing-induced congestive HF (left ventricular end-diastolic pressure ≥25mmHg) and to normal controls (n=7/group). Blood samples were periodically drawn and left ventricular tissue was harvested at the end of the protocol. We initially focused on three cardiac and ten plasma major proteins, which were trypsinized after albumin depletion or gel electrophoresis, and peptide fragments analyzed by gas chromatography–MS. Data are expressed as percent of newly synthesized molecules/hour over their respective total pools. Compared to control, in plasma after albumin depletion or gel electrophoresis, and peptide fragments analyzed by gas chromatography–MS. Data are expressed as percent of newly synthesized molecules/hour over their respective total pools. Compared to control, in ox-LDL treated mice compared with vehicle-treated control mice (CTRL) (LVEF: CTRL vs. DHA: 71.8 ± 0.95% vs. 65.0 ± 1.8%, P < 0.01, N=4–6, LV dp/dt max: CTRL vs. DHA: 1135.8 ± 205.6 mmHg/sec vs. 710.9 ± 480.6 mmHg/sec, P < 0.01, N=4–5). Consistently, the LV-A-induced cardiac dysfunction was significantly rescued by cardiac specific over-expression of TCTP (TCTP transgenic mice: TG). (LVEF: CTRL vs. TG: 56.0 ± 1.8% vs. 66.3 ± 1.0%, P < 0.01, N=5, LV dp/dt max: WT vs. TG: 710.9 ± 460.6 mmHg/sec vs. 9286 ± 646.8 mmHg/sec, P < 0.05, N=5).

Conclusions: These results indicate that chronic DHA treatment results in cardiac dysfunction in mice. DHA-induced TCTP down-regulation of TCTP may be involved in the mechanism.

P5657 | SPOTLIGHT
Ox-LDL contributes to cardiomyocyte apoptosis and heart failure via lectin-like oxidized low-density lipoprotein receptor-1

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Purpose: Ox-LDL plasma level is a useful predictor of mortality in HF patients, however the precise mechanisms of ox-LDL on HF is poorly understood. This study investigates whether ox-LDL is involved in the development of HF and its mechanisms.

Methods: ox-LDL (200mg/kg, min) infused into mouse results in heart failure which was evaluated by echocardiography and BNP. To explore the mechanisms we find that Ox-LDL increases LOX-1 expression, leads to apoptosis of mouse heart and cultured cardiomyocytes, the signal pathways were determined by TUNEL assay, qPCR and western blot.

Results: 4 weeks after infusion of ox-LDL, the ratio of heart weight to body weight in ox-LDL group (1.38 fold higher than control siRNA-treated cells, P < 0.01, N=5, LV dp/dt max: CTRL vs. ox-LDL: 460 mmHg/sec, P < 0.01, N=4-6, L V dP/dt max: CTRL vs. ox-LDL: 25mmHg) induced apoptosis of cardiomyocytes (1.38 fold higher than control siRNA-treated cells, P < 0.05, N=4–5). To examine the effects of DHA on cardiac function in vivo, we performed echocardiography and cardiac catheterization after chronic DHA treatment (30 mg/kg/day, via intraperitoneal injection for 4 weeks) in wild type (WT) mice. Left ventricular systolic pressure (LV dp/dt max) was significantly decreased in DHA-treated mice compared with vehicle-treated control mice (CTRL) (LV EF: CTRL vs. DHA: 71.8 ± 1.8%, P < 0.01, N=4–6, LV dp/dt max: CTRL vs. DHA: 1135.8 ± 205.6 mmHg/sec vs. 710.9 ± 480.6 mmHg/sec, P < 0.01, N=4–5). Consistently, the LV-A-induced cardiac dysfunction was significantly rescued by cardiac specific over-expression of TCTP (TCTP transgenic mice: TG). (LVEF: CTRL vs. TG: 56.0 ± 1.8% vs. 66.3 ± 1.0%, P < 0.01, N=5, LV dp/dt max: WT vs. TG: 710.9 ± 460.6 mmHg/sec vs. 9286 ± 646.8 mmHg/sec, P < 0.05, N=5).

Conclusions: Our results indicate that ox-LDL increases LOX-1 expression, Bax/Bcl-2 ratio of cardiomyocyte which may contribute to apoptosis of cardiomyocyte and mouse heart, eventually lead to heart failure of the mice.

P5658 | BENCH
NOD1 expression and eNOS mediate Ang II up-regulation of nNOS protein expression

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Endothelial and neuronal nitric oxide synthases (eNOS & nNOS) are constitutively expressed in distinct subcellular locations within cardiomyocytes and exert diverse functions. In particular, nNOS protein expression and activity are significantly increased whereas eNOS protein expression is reduced in diseased heart and the myocardium was 6.08% ± 0.95% vs. 66.3 ± 1.0%, P < 0.01, N=4–6, L V dP/dt max: CTRL vs. ox-LDL: 460 mmHg/sec, P < 0.01, N=4-6, L V dP/dt max: CTRL vs. ox-LDL: 25mmHg) induced apoptosis of cardiomyocytes (1.38 fold higher than control siRNA-treated cells, P < 0.05, N=4–5). In conclusion, HF slowed the turnover rate of cardiac proteins changed as follows (all p < 0.05): heavy chain beta-myosin increased from 0.13±0.02 to 0.24±0.02%, adenine nucleotide translocase-1, a key enzyme involved in mitochondrial ATP production, decreased from 0.23±0.08 to 0.14±0.04%. The plasma albumin decreased from 0.29±0.03 to 0.16±0.01% and serotransferrin from 2.09±0.05 to 0.76±0.01%. Among the circulating lipids, palmitate displayed a reduced synthesis rate from 0.16±0.01 to 0.05±0.01% (p < 0.05) in HF, while the reduction in cholesterol was at the limit of significance (p = 0.041). The results show that ox-LDL contributes to cardiomyocyte and metabolic proteins. These initial results are the first to show the potential of 2H2O-metabolic labeling for quantitative assessment of protein turnover in different stages of heart failure in a larger animal model and may help to develop additional molecular monitoring methodologies.
P5609 | BEDSIDE
Role of sarcomeric gene polymorphisms on left ventricular dysfunction in coronary artery disease patients
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Purpose: In patients of coronary artery disease (CAD), left ventricular function is the most important determinant of prognosis. Many CAD patients develop left ventricle dysfunction (LVD), leading to congestive heart failure. Mutations in several genes including those encoding sarcomeric proteins such as MYBP3, TNNT2, and TTN are common genetic causes of hereditary cardiomyopathies. An intronic 25-bp deletion in MYBP3 at 3’ region is associated with dilated (DCM) and hypertrophic (HCM) cardiomyopathies in Southeast Asia. Their role in genesis of LVD in CAD patients is not known. We sought to determine the role of MYBP3 25bp, TNNT2 5bp and TTN 18bp insertion/deletion polymorphisms on LVD in CAD patients.

Methods: This case control study included a total of 1188 subjects including 988 angiographically confirmed CAD patients and 200 population matched controls. All patients had angiographically significant CAD and had coronary revascularization (coronary angioplasty or coronary bypass surgery) in the past. Left ventricular ejection fraction (LVEF) was analyzed by echocardiography. Patients with LVEF <45% were categorized as advanced LVD. MYBP3C 25bp, TNNT2 5bp and TTN 18bp insertion/deletion polymorphisms were determined by polymerase chain reaction amplification of quiescent fibroblasts to active myofibroblasts. Although it is well known that cyclic AMP signaling attenuated cardiac fibrosis through inhibiting transformation of quiescent fibroblasts to active myofibroblasts. It was also well known that prostaglandin E2 (PGE2) receptor EP4 acts via cyclic AMP and is abundantly expressed in the heart. Therefore, we aimed to determine how EP4 in cardiac fibrosis is not fully understood.

Results: Our results showed that MYBP3C 25bp deletion was significantly associated with CAD (p value = 0.003, OR = 4.08) as well as with LVD (p value = 0.011, OR=1.67). The TNNT2 5bp and TTN 18bp polymorphisms were not found to be associated with CAD (p value = 0.580, OR = 0.88; p value = 0.795, OR = 0.91 respectively) or LVD (p value = 0.146, OR = 1.35; p value = 0.935, OR=0.97 respectively) when compared to controls.

Conclusion: The frequency of MYBP3C 25bp genotype and D allele was associated with LVD implying that genetic variants of MYBP3C encoding mutant structural sarcomere protein could increase susceptibility to left ventricular dysfunction. Therefore, 25bp deletion in MYBP3C may represent a genetic marker for cardiac failure in CAD patients.

P5610 | BENCH
Prostaglandin E2-EP4 plays a protective role against cardiac fibrosis
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Purpose: Cardiac fibrosis, which is not curable in current therapies, leads to heart failure and is associated with high morbidity. Previously, we have shown that cyclic AMP signaling attenuated cardiac fibrosis through inhibiting transformation of quiescent fibroblasts to active myofibroblasts. Although it is well known that prostaglandin E2 (PGE2) receptor EP4 acts via cyclic AMP and is abundently expressed in the heart. Therefore, we aimed to determine how EP4 in cardiac fibrosis is not fully understood.

Methods: This study was designed to investigate the variations in mitochondrial protein expression. We found that baroreflex failure plays a crucial role in the pathogenesis of pulmonary edema in patients with HFpEF.

Results: We allocated 14 weeks old spontaneously hypertensive rats (SHR) into 2 groups. We conduct sinoatrial denervation (SAD, n=10) to abolish baroreflex or sham operation (Sham, n=10). In the following week, we implanted a telemetry system to measure arterial pressure (AP) and LAV 1 week after the 2nd surgery. Results: H-salt increased AP in both in Sham (167.9±3.6 vs. 150.5±6.2 mmHg, p<0.05) and in H-Salt (215.1±5.3 vs. 130.0±1.4 mmHg, p<0.05). In contrast, only SAD/H-salt increased mean LAP (SAD/H-salt 14.4±2.3 vs. Sham/H-salt 10.9±0.8 mmHg, p<0.05, Fig. 1) with increased increases in their SDs (Fig. 2). Furthermore, SAD/H-salt strikingly prolonged the high LAP period (≥20 mmHg, Fig. 3) that accounted for more than 20% of hours. Conclusion: Baroreflex failure markedly increases daily fluctuations of LAP and prolongs the period of high LAP indicating that baroreflex failure would play a crucial role in the pathogenesis of pulmonary edema in patients with HFpEF.

P5611 | BENCH
Baroreflex failure induces volume supersensitivity and predisposes to pulmonary edema
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Purpose: With heart failure with preserved ejection fraction (HFpEF) frequently suffer from pulmonary edema with little weight gain indicating underlying a volume supersensitive mechanism. These patients often have baroreflex dys- function and salt-sensitive hypertension. We recently demonstrated that barore- flex failure resulted in striking volume intolerance (J Cardiac Failure, 2014). In this study, we examined how baroreflex failure impacts on daily fluctuations of left atrial pressure (LAP) in hypertensive rats with high salt diet.

Methods: We allocated 14 weeks old spontaneously hypertensive rats (SHR) into 2 groups. We conduct sinoatrial denervation (SAD, n=10) to abolish baroreflex or sham operation (Sham, n=10). In the following week, we implanted a telemetry system to measure arterial pressure (AP) and LAV 1 week after the 2nd surgery. Results: H-salt increased AP in both in Sham (167.9±3.6 vs. 150.5±6.2 mmHg, p<0.05) and in H-Salt (215.1±5.3 vs. 130.0±1.4 mmHg, p<0.05). In contrast, only SAD/H-salt increased mean LAP (SAD/H-salt 14.4±2.3 vs. Sham/H-salt 10.9±0.8 mmHg, p<0.05, Fig. 1) with increased increases in their SDs (Fig. 2). Furthermore, SAD/H-salt strikingly prolonged the high LAP period (≥20 mmHg, Fig. 3) that accounted for more than 20% of hours. Conclusion: Baroreflex failure markedly increases daily fluctuations of LAP and prolongs the period of high LAP indicating that baroreflex failure would play a crucial role in the pathogenesis of pulmonary edema in patients with HFpEF.
Aging impairs adaptive cardiac hypertrophy to exercise via Akt/mTOR-dependent autophagy

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Purpose: Aging causes left-ventricular (LV) remodeling and susceptibility to heart failure (HF). Sustained exercise (EX) ameliorates HF, however, it is unclear EX may be beneficial for the aging-related HF. Because of the pivotal role of protein kinase Akt in aging, we hypothesized whether EX may modulate HF in aging via Akt axis.

Methods: Male 6-month-old genetic senescence -Prone (genP) & -Resistant (genR) SAM strain mice were subjected to EX 60-min treadmill for 6 months. The same protocol was tested on the acquired aging (12 m/o) mice [wild (agedC57) and Akt knock out (agedAktKO)] and young (14 w/o, youngC57) counterparts.

Results: At baseline, cardiac geometry of genP exhibited LV wall thinning. Sys- tolic function of both strains was preserved. After EX, body and heart weight of genR were increased, but EX had no influence on those genP. EX promoted cardiac hypertrophy and increased capillary density in genR, but absent in genP suggesting genP lacks physiological LV remodeling. EX impaired systolic function of genP [%EF (±1.5 vs. 74.3 ±1.2 at baseline]. Cardiac Akt/mTOR/S6K activity was enhanced by EX in genR. Unexpectedly, genP-CON exhibited basal increase vs. LIG 12 m/o animals.

Conclusion: Dissociation of time courses in the activation of BNP and CGB suggests sequential or separate signaling mechanisms in aHF and cHF after MI. It indicates that CGB may be a signal of myocardial remodeling in cHF. Of note, CGB seems not to be regulated in ischemic aHF nor cHF. Further studies are warranted to completely understand the role CGB plays in myocardial remodeling mechanisms with the ultimate goal to aid in diagnosis and treatment of HF patients.

Conclusions: EX-induced adaptive LV hypertrophy requires Akt activation. Aging promotes chronic and pathological Akt activation in heart, which promotes autophagic impairments. EX triggers to reverse Akt/mTOR/S6K-dependent autophagy.

Chromogranin B: A signal of myocardial remodeling in chronic ischemic heart failure

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Purpose: Cardiac myocyte apoptosis and hyperthrophy are important mecha- nisms of ventricular remodeling which may lead to heart failure (HF) in general. We studied rat ventricular CGB, CGA and BNP expression in LIG vs. CO animals.

Methods: Twenty-five patients with CS (8 men, 17 women; mean age, 60±9 years) diagnosed according to consensus criteria were enrolled in this study. We divided CS patients into two groups, known CS receiving corticosteroid therapy (Rx (+); n=13) and new onset CS (Rx (-); n=12), and analyzed 3 distinct monocyte subsets (CD14++CD16+, CD14++CD16−, and CD14−CD16+). Monocyte subsets were also analyzed in 7 Rx (-) patients before and 12 weeks after starting corticosteroid therapy. Inflammatory activity was quantified by 18F-FDG PET using the coefficient of variation (COV) of the standardized uptake value (SUV). The proportion of CD14++CD16+ monocytes in Rx (+) patients (10.8 ±2.35 %) was significantly lower than those in Rx (-) patients (25.2 ±17.7 to 38.4 %, P=0.001). After corticosteroid therapy, the COV of the SUV was significa-

Conclusion: In the PREVEND study cohort, healthy individuals who developed new onset heart failure during follow-up are characterized by shorter leukocyte telomeres, albeit not independent of date of birth, compared to heart failure-free subjects.

Conclusions: EX-induced adaptive LV hypertrophy requires Akt activation. Aging promotes chronic and pathological Akt activation in heart, which promotes autophagic impairments. EX triggers to reverse Akt/mTOR/S6K-dependent autophagy.
in healthy individuals is associated with adverse cardiovascular outcomes but whether the risk is further elevated in patients with existent heart disease is unknown. We aimed to investigate whether calcium supplements are associated with adverse outcomes in patients with chronic heart failure (CHF).

Methods: Data were analysed from 1053 patients with CHF (LVEF ≤45%) who were enrolled in a prospective observational study for the occurrence of hospitalisation and mortality. Using pseudonymized electronic general practice patient records, outcomes were compared between patients who were and were not prescribed calcium supplementation. CHF patients with diabetes mellitus (DM) are at highest overall risk, so we prespecified a subgroup analysis of patients with DM.

Results: During a mean follow-up of 3.2 years, there were 296 all-cause deaths and 181 cardiovascular deaths. Calcium supplement users (n=170 (16.1%)) were older, and were more likely to be women, diabetic, and more symptomatic (NYHA class). They had lower haemoglobin and worse renal function. They were less frequently prescribed ACE inhibitors, angiotensin receptor blockers and Beta-blockers. Calcium supplementation was associated with all-cause hospitalisation (odds ratio (OR) 1.60 (95% CI 1.12-2.30)), cardiovascular hospitalisation (OR 1.65 (95% CI 1.06-2.58)) and heart failure hospitalisation (OR 1.90 (95% CI 1.05-3.35)) but these associations were not statistically significant after adjustment for confounders.

In CHF patients with DM (n=275 (26.1%)), calcium users (n=55 (20%)) were more likely to be female, have lower haemoglobin and albumin, higher blood pressure and worse renal function compared to nonusers with DM. Calcium supplementation in diabetics was associated with an even greater trend to increased risk of all-cause (OR 2.03 (95% CI 1.11-3.72)), cardiovascular (OR 2.33 (95% CI 1.17-4.66)) and heart failure (OR 2.95 (95% CI 1.04-8.09)) hospitalisation, and after adjustment, this remained significant for all-cause hospitalisation (OR 2.13 (95% CI 1.04-4.38)).

Conclusions: Patients with CHF are frequently prescribed calcium supplementations, despite no evidence from randomised, placebo-controlled trials. Our study reveals a 50% higher hospitalisation rate, and in those at highest risk (those with DM), the risk of hospitalisation is more than doubled, and is statistically significant after correction for other factors. A larger cohort is needed to confirm the preliminary findings in this population.

HEART FAILURE RISK

P5618 | BEDSIDE

Acute Heart Failure (KorAHF) registry

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Purpose: Readmission after hospitalization for HF is common. However, there are limited data describing patterns of follow-up after HF hospitalization and its association with readmission rates.

Methods: The patients hospitalized for acute HF syndrome in ten regionally-representative tertiary university hospitals have been consecutively enrolled 4183 patients between March, 2011 and July, 2013. The study is expected to complete the enrollment of 4,500 patients in 2013 and to follow-up until 2016. The aim of the present study was to describe the clinical characteristics and outcomes of <90-day readmitted patients in this Korean Acute Heart Failure (KorAHF) registry.

Results: A total -90-day readmitted 955 patients among 4183 patients were enrolled in this analysis. At the hospital level, the mean age was 69.9±13.7 years; 52.8% were male; 42.3% were de novo HF; 63.8% had hypertension; 32% had ischemic heart disease. 88.6% of patients presented with NYHA III-IV dyspnea and the mean LVEF was 39.0±15.6%. Ischemia was both the leading cause (37.7%) and the most frequent aggravating factor (15.3%). Serum creatine level was 1.6±1.8mg/dL; Hemoglobin was 11.9±2.3g/dL; BNP and NT-proBNP level was 1457.6±1385.6 and 10458.2±13486.5 pg/ml. Angiotensin converting enzyme inhibitors/angiotensin receptor blockers and beta-blockers were prescribed in 97.8% and 94.2% of patients, respectively.

Conclusions: Clinical characteristics at hospital level and 90-day outcomes of readmitted patients from KorAHF registry were described. Readmitted patients group had a worse clinical characteristics and outcome compared to non-readmitted patients group.

P5619 | BEDSIDE

Calcium supplementation in patients with chronic heart failure: Is it safe?


Purpose: Recent observational studies suggest that calcium supplementation...
P5621 | BEDSIDE
A role of serum sodium to urea nitrogen ratio as a brief prognostic bio-marker in patients with diuretic-resistant congestive heart failure

Background: Pathophysiology is complex and long-term prognosis is hard to predict in diuretic-resistant congestive heart failure (DR-CHF). Recently, both an increase in serum Na (≥ 139 mmol/L) and a decrease in serum Na (< 136 mmol/L) were independently reported to be a risk factor for heart failure hospitalization. In this prospective study, we attempted to examine if serum Na level could be a marker of long-term prognosis. In this prospective study, we attempted to examine if serum Na level could be a marker of long-term prognosis.

Purpose and method: To examine the role of Na (139±5 mmol/L), BUN (30±20 mmol/L) and Na/BUN ratio (5.8±1.28) at hospitalization on long-term prognosis, consecutively 287 CHF pts (78±13 years old; 162 male aged 74±14, 125 female aged 83±18.4) requiring intravenous administration of various diuretic and vasoactive agents at intensive care unit were examined and followed retrospectively. Based on the average values and previous reports, cutoff point was estimated on each parameter, and cumulative survival rate was examined by log-rank test.

Results and conclusion: Prognostic impact was observed in pts with low Na (<139 mmol/L; p=0.03; chi-square test), sensitivity 0.63; specificity 0.41; positive predictive value 0.14; negative predictive value 0.94), with high BUN (>30 mg/dL; p=0.0005; 0.63; 0.70; 0.18; 0.05) and with low Na/BUN (<3.3; p=0.03; chi-square test, BUN levels: 0.64; 0.77; 0.21; 0.36), respectively. The low Na/BUN ratio of less than 3.93 was found to be a most predictive marker for long-term survival (Figure, p<0.01). Therefore, the combination of fluid volume (Na) and neurohormonal (BUN) factors (Na/BUN ratio) may be a candidate for additional brief prognostic marker in diuretic-resistant CHF.

Cumulative survival curve.

P5622 | BEDSIDE
Ultrasound assessment of jugular vein distensibility in patients with heart failure: prognostic significance. A report from the SICA-HF study
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Aims: Jugular venous distension reflects increased right atrial pressure and is a classical sign of heart failure (HF). However, its clinical assessment may be difficult.

Methods: Ambulatory patients with HF and control subjects enrolled in the SICA-HF study. Internal jugular vein diameter (JVD) was measured using a linear high-frequency ultrasound probe (10 MHz) at rest, during a Valsalva manoeuvre and during deep inspiration. JVD ratio was calculated as the diameter during Valsalva to that at rest.

Results: 311 patients (median inter-quartile range [IQR] age 71 (64-77) years, mean left ventricular ejection fraction 42±12%, median NT-proBNP 979 [IQR: 441-2007] ng/l) and 66 controls were included. JVD (median and IQR range) at rest was smaller in controls (0.16 (0.14-0.20) cm) than in patients with HF (0.23 (0.17-0.33) cm; p<0.001) but similar during Valsalva (1.03 (0.90-1.16) cm vs 1.08 (0.90-1.25) cm; p=0.28). Consequently, JVD ratio was greater in controls (6.3 (4.9-7.6)) than in patients (4.5 (2.9-6.1); p<0.001). During a median FU of 516 (IQR: 335-622) days, 48 patients with HF died or were hospitalized for heart failure. Different multivariable models were tested. Amongst clinical, echocardiographic or biochemical variables, only NTproBNP and ultrasound assessment of internal jugular vein (either at rest, JVD ratio or deep inspiration) was found to be a most predictive marker for long-term survival (HR: 10.05; 95% CI: 3.07-32.93).

Conclusions: Echocardiographic assessment of internal jugular vein identifies ambulatory patients with heart failure who have a high risk of an adverse outcome. Greater JVD diameter at rest or during deep inspiration or smaller JVD ratio provide similar prognostic information.

P5623 | BEDSIDE
Cardio-liver syndrome in acute decompensated heart failure hospitalizations: definition and prognostic evaluation
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Liver dysfunction (LD) may develop in patients (p) hospitalized for acute decompensated heart failure (ADHF). There is no consensus on LD diagnostic criteria in this setting.

Aims: To characterize LD in ADHF, propose a Cardio-Liver syndrome (CLS) definition and describe outcome.

Methods: Demographic, clinical and biochemical data were recorded at admission. LD was defined as an admission liver function test impairment characterized by aspartate aminotransferase > 60 IU/L, alanine aminotransferase > 75 IU/L; alkaline phosphatase > 225 IU/L; total Bilirubin > 1.5 mg/dl or gamma-glutamyl transferase >100 IU/L. Length of stay (LOS), mortality and readmission rates at 30, 60 and 90 days were compared.

Results: 454 consecutive p were admitted between July 2011 and December 2013. CLS was identified in 51%. Systolic pressure at admission (124 vs 139 mmHg; p<0.001) and left ventricular ejection fraction were lower in CLS (36 vs 42%, p<0.001). Considering clinical presentation, right-sided heart failure (RF) (35 vs 22%; p=0.002) and hypoperfusion were more frequent in CLS (24 vs 5.6%; p<0.001), as introtropic use and WFH (31 vs 9%; p<0.001) and 27 vs 11%; p<0.001). Right ventricular systolic pressure (53 vs 46 mmHg; p<0.001) and central venous pressure (14 vs 9 mmHg; p<0.001) were higher in CLS. There was a relationship among RD, thyroid dysfunction (THYR) and CLS (50 vs 41%; p=0.04 for RD; and 75 vs 62%; p<0.01 for THYR). Diuretic resistance (13 vs 5.4%; p<0.01) and previous Furosemide doses were higher in CLS (35 vs 16 mg; p<0.001). LOS was longer in CLS (7 vs 5 d; p<0.001). Previous admissions were more frequent in CLS (56 vs 33%; p<0.001). Time to readmission tended to be shorter in CLS (48 vs 82 d; p=NS).

In multivariate analysis hypoperfusion (OR 3.1; 95%CI 1.2-8.7; p=0.01), RF (OR 2.8; 95%CI 1.6-4.8; p<0.001), intropuc drug use (OR 2.1; 95%CI 1.0-4.6; p=0.04) and low T3 levels (OR 2; 95%CI 1.2-3.5; p=0.01) predicted CLS development.

In-hospital (12.6 vs 5.4%; OR 2.5; 95% CI 1.2-5.4; p<0.001) and 90 d follow-up mortality were higher for CLS (16.2 vs 5.9%; OR 3; 95%CI 1-6; p<0.001). Although CLS was not independently related to in-hospital mortality, it was strongly associated with 90 d follow-up mortality (OR 3.1; 95%CI 1.3-7.5; p<0.01).

Conclusions: CLS was prevalent in ADHF. It was associated with thyroid disorders, biventricular dysfunction, hemodynamic derangement, longer hospitalization days and higher mortality, particularly mid-term. Early organ dysfunction in ADHF should be emphasized for outcome prediction. Since CLS may occur with different patterns, it is important to further characterize this clinical syndrome.

P5624 | BEDSIDE
High-sensitivity cardiac troponin T predicts non-cardiac mortality in Heart Failure
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Background: Cardiac troponins are independent predictors of cardiac mortality in patients with heart failure (HF). Recently, elevation of troponins has been described in non-cardiac diseases such as stroke and infection, among others. However, it still remains unclear whether high-sensitive troponin T (hs-TnT) predicts non-cardiac mortality in HF patients.

Methods and results: Consecutive 444 HF patients admitted to our hospital for the treatment of decompensated HF were divided into 2 groups based on median hs-TnT: Group L (≤0.028 ng/ml, n=220) and Group H (>0.028 ng/ml, n=224). We compared all-cause mortality and echocardiographic findings between the two groups. In the follow-up period (mean 472 days), 77 deaths (49 cardiac deaths and 28 non-cardiac deaths (cancer, n=6; infection/sepsis, n=6; respiratory failure and/or pneumonia, n=5; stroke, n=4; digestive hemorrhage, n=3; renal failure, n=3; and aortic aneurysm, n=1)) were observed. The event-free survival (cardiac death, non-cardiac death and all-cause death) was significantly higher in Group L than in Group H (Figure). In the multivariate Cox proportional hazard analysis, a high hs-TnT was found to be an independent predictor of cardiac death (P<0.001), non-cardiac death (P=0.042) and all-cause mortality (P<0.001) in HF patients after adjusting for other known risk factors. Regarding echocardiographic parameters, left ventricular wall thickness was higher (P<0.001) and left ventricular ejection fraction was lower (P=0.011) in Group H than in Group L.

Conclusions: Hs-TnT is an independent predictor not only of cardiac mortality, but also non-cardiac mortality in HF patients.
Left ventricular ejection fraction during acute coronary syndrome has different association with mortality in men and women (From the ABC-3 Study on Acute Coronary Syndrome)*

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1University of Udine, Internal Medicine Clinic, Udine, Italy; 2Bassano General Hospital, Bassano, Italy; 3University Hospital of Padova, Internal Medicine Clinic IV, Padua, Italy

Purpose: To investigate sex-based differences in the association between left ventricular ejection fraction (LVEF) and 15-year mortality after acute coronary syndrome (ACS).

Methods: The ABC-3 Study on Acute Coronary Syndrome is an ongoing, prospective investigation designed to reflect, as closely as possible, an unbiased population of patients with ACS. The present analysis includes 504 patients. Baseline, clinical and laboratory data were obtained within the first 3 days of hospitalization. Measured variables were analyzed as quartiles of increasing values. Interaction between gender and LVEF was studied first by means of relative risks (RR) and Mantel-Haenszel test of homogeneity (with p < 0.05 indicating dis-homogeneity of the RR), then using Cox surviving regressions including an interaction term and adjusting for age. All analysis were made both for early mortality (3rd to 66th day after admission) and long-term cardiovascular (CV) mortality (67th day to 15th year).

Results: Median age was 66 (IC 58-73) years, female were 28%, LVEF was 52 (IC 45-60)%; NSTEMI were 37%. All the patients were followed up to observation or time of death. Of them, 48 had died in the early- and 162 in the long-term for CV cause. The RR by quartiles of LVEF was 0.95 (95%CI 0.1-0.3) and 0.95 (95%CI 0.2-1.1), in male and females respectively, for early mortality, p for dis-homogeneity =0.02, and 0.4 (95%CI 0.3-0.6) and 0.6 (95%CI 0.4-0.8), in male and females respectively, for long-term-CV-mortality, p for dis-homogeneity =0.10. Age adjusted gender-LVEF interaction was 2.1 (95%CI 1.1-4.0) p<0.01, for early mortality, and 1.1 (95% CI 0.8-1.5) p=0.55, for long-term-CV-mortality. Full adjusted (age, previous myocardial infarction, NSTEMI, CK-MB peak, p blockers, ACE-inhibitor/anti angiotensin II receptor blockers, lipid lowering treat- ment, thrombolysis) early mortality interaction was 2.1 (95%CI 1.1-4.1:1) p=0.02. Full adjusted long-term-CV-mortality interaction was not significant, p=0.29.

Conclusions: A gender based different association of LVEF with early mortality after ACS, being women with higher LVEF values at higher risk than men for early mortality.

P5652 | BEDSIDE

G-protein-coupled receptor kinase 5 polymorphism and Takotsubo cardiomyopathy

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Purpose: Takotsubo cardiomyopathy (TTC) is an increasingly reported clinical syndrome that mimics acute myocardial infarction with no obstructive coronary artery disease. The recent systolic dysfunction of the apical and/or midseg- ments of the left ventricle. The syndrome occurs mainly in postmenopausal women with high adrenergic state conditions. Nowadays, the pathophysiology of TTC is not yet known and the possibility of a genetic predisposition is controver-

Methods and results: A case-control study showed a gender based different association of LVEF with early mortality after ACS, being women with higher LVEF values at higher risk than men for early mortality.

Conclusions: A gender based different association of LVEF with early mortality after ACS, being women with higher LVEF values at higher risk than men for early mortality.

Materials and methods: A total of 1,180 nondiabetic patients attending 17 hos- pital centers were included. Genotyping of CYP1A2 SNP was performed by real time PCR in 639 subjects. Prediabetes was defined as fasting plasma glucose measurement, at the final available visit between 100 and 125 mg/dL.

Results: Seventy-four percent of our subjects drank coffee. Among the coffee drinkers, 87% drank 1–3 cups/day (moderate), and 13% drank over 3 cups/day (heavy). CYP1A2 genotype frequencies were: *1A*1A=41.9%, *1A*1F=43.7%, *1F*1F=14.4%. At the end of a median follow-up of 6.1 years, prediabetes was di-agnosed in 24.0% of the subjects (27.1% in men and 15.9% in women, p < 0.001).

In a multivariable Cox regression coffee use was a predictor of incident prediabete-

Conclusions: These data show that coffee consumption increases the risk of prediabetes in hypertension patients among carriers of the slow CYP1A2 *1F allele and in individuals with overweight or obesity.

5706 | BEDSIDE

Association between mind-body practice and cardiometabolic risk factors: the Rotterdam study


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Purpose: In this study we aimed to determine the association between mind-body (MB) practice and cardiometabolic risk factors.

Methods: This study was embedded within the population-based Rotterdam Study (visit 2009-2013) and included 2579 participants free of cardiovascular dis-
ease. Participants were categorised according to their involvement in any form of MB practice (i.e. >1 hour per week of meditation, yoga, self-prayer) based on a structured home interview. Cardiometabolic risk factors (body mass index (BMI), blood pressure, and fasting blood levels of cholesterol, triglycerides, and glucose) were individually analysed with linear regression. Presence of the metabolic syndrome (according to the National Cholesterol Education Program (NCEP)) was analyzed with logistic regression. Analyses were adjusted for age, sex, educational level, smoking, alcohol consumption, (in)activities in daily living, grief, and stress.

**Results:** In our study population (57.5% women, mean age 66.2±7.6 years), 16.6% of the participants were involved in any form of MB practice. Those who were involved in MB practices had significantly lower BMI, total cholesterol levels, triglyceride levels, and glucose levels (Table 1). Additionally, the odds-ratio for the presence of metabolic syndrome was 0.68 (95% CI 0.52;0.90) for individuals performing mind-body practices.

**MB practice and cardiometabolic risk**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>β (95% confidence interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index, kg/m²</td>
<td>-0.82 (-1.26; -0.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>-1.47 (-3.52; 0.58)</td>
<td>0.160</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>-0.77 (-1.93; 0.39)</td>
<td>0.191</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>-4.45 (-8.56; -0.34)</td>
<td>0.034</td>
</tr>
<tr>
<td>High-density lipoprotein, mg/dL</td>
<td>0.001 (-0.01 ; 0.001)</td>
<td>0.927</td>
</tr>
<tr>
<td>Low-density lipoprotein, mg/dL</td>
<td>-3.32 (-7.17; 0.53)</td>
<td>0.091</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>-0.02 (-0.04; -0.002)</td>
<td>0.032</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>-0.01 (-0.02; -0.001)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, educational level, smoking, alcohol consumption, (in)activities in daily living, grief, and stress.*

**Conclusions:** Persons involved in mind-body practices have a favourable cardiometabolic risk profile compared to those who are not. However, our findings do not indicate a causal relation.

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**5708 | SPOTLIGHT**

**Growth differentiation factor-15 predicts diabetic cardiomyopathy in asymptomatic patients with type 2 diabetes**

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**Purpose:** Growth differentiation factor-15 (GDF-15) is a stress-responsive cytokine that is increased in established type 2 diabetes (T2D). Diabetic cardiomyopathy (DC) is defined as left ventricular diastolic dysfunction (LVDD) in patients with T2D in the absence of arterial hypertension, ischemic heart disease or other heart disease. We assessed whether GDF-15 can predict diabetic cardiomyopathy (DC).

**Methods:** We prospectively included 213 consecutive outpatient T2D patients, 65.7% males, aged 61.5±6.34 years. A complete history and clinical examination was performed, including 12-lead electrocardiogram, symptom-limited treadmill exercise and echocardiography. Plasma GDF-15 concentrations were measured with an automated electrochemiluminescent immunoassay at baseline. DC was defined as LVDD in patients with T2D in the absence of arterial hypertension, ischemic heart disease or other heart disease.

**Results:** The prevalence of DC was 21.1% (45 patients), while 78.9% (168 patients) did not fulfill the criteria. There were no statistical differences in baseline characteristics (age, gender, dyslipidemia and smoking) between both groups. GDF-15 levels were higher in patients with DC compared to those with T2D in the absence of arterial hypertension, ischemic heart disease or other heart disease.

**Conclusions:** Our study indicates that GDF-15 levels represent a useful and novel tool to screen DC in patients with T2D.
GLS remained different with microalbuminuria (p=0.036), and macroalbuminuria (p=0.001) compared to normoalbuminuria. Including duration of diabetes or renin-angiotensin-aldosterone medication did not change the association.

Conclusions: Systolic function assessed by GLS was impaired in T1DM patients with albuminuria and no known heart disease independently of LVEF and other clinical characteristics. These findings suggest early systolic impairment in T1DM and support the concept of a specific diabetic cardiomyopathy.

5710 | BEDSIDE
Impact of pioglitazone on cardiovascular events in patients with diabetes mellitus after drug-eluting stent implantation

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Background: Patients with diabetes mellitus (DM) after drug-eluting stent (DES) implantation is a clinical problem. This study indicated the predictive effect of pioglitazone (Pio) on clinical cardiovascular events via its anti-atherosclerotic effects, as well as a blood glucose-lowering effect in patients with DM.

Objective: This study aimed to evaluate the preventive effect of Pio on cardiovascular events in patients with DM after DES implantation based on 1-year follow-up results of the J-DESsERT trial.

Methods: In the J-DESsERT trial, a prospective multicenter randomized controlled trial, 3533 patients with coronary artery disease were randomized 1:1 to stenting with either a sirolimus-eluting stent or a paclitaxel-eluting stent, and 144 patients were in the study arm. The criteria of lesion length was ≥46 mm with vessel diameters from ≥2.5 to ≤3.75 mm. Definitions for DM in this trial were (1) previous diagnosis of DM; (2) currently on diabetic medication (oral hypoglycemic drugs or injection of insulin preparation); and (3) HbA1c≥6.9% within 30 days before the procedure.

Results: A total of 1705 (48%) participants were diagnosed as having DM. The rate of cardiovascular events (death/myocardial infarction/target vessel revascularization/cerebrovascular disorders) 1 year after DES implantation in patients with DM was significantly higher (11.0%) than that in patients without DM (7.7%) (P<0.01). Of the patients with DM, 357 patients (21%) had been medicated with Pio before percutaneous intervention. In patients with DM, the rate of cardiovascular events 1 year after DES implantation in the Pio-treated group was significantly lower (4.5%) than that with other therapies in the group without Pio (8.2%) (P=0.02). Multivariate analysis showed that treatment with Pio was associated with the prevention of cardiovascular events in patients with DM (OR=0.55, P=0.01).

Conclusion: Pioglitazone significantly decreased cardiovascular events of patients with DM 1 year after DES implantation. These results suggest that Pio may have a preventive effect on restenosis after DES implantation.

5711 | BEDSIDE
Efficacy of aspirin in people with diabetes: an individual participant data meta-analysis of 26 randomised trials


Purpose: Aspirin produced a 13% proportional reduction in SVE (RR 0.87, 95% CI 0.80-0.95) and mortality according to diabetes status and to predicted 5 year risk of coronary stenting with either a sirolimus-eluting stent or a paclitaxel-eluting stent, and 144 patients were in the study arm. The criteria of lesion length was ≥46 mm with vessel diameters from ≥2.5 to ≤3.75 mm. Definitions for DM in this trial were (1) previous diagnosis of DM; (2) currently on diabetic medication (oral hypoglycemic drugs or injection of insulin preparation); and (3) HbA1c≥6.9% within 30 days before the procedure.

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5712 | BEDSIDE
Relationship between diabetes management and coronary atherosclerotic change in non-culprit lesions after percutaneous coronary intervention - Serial integrated backscatter IVUS study


Purpose: Diabetic patients continue to have high cardiovascular events after percutaneous coronary intervention (PCI). However, serial changes in volume and tissue characteristics of coronary atherosclerotic plaques in non-culprit lesions and no evidence that this reduction differed in primary and secondary prevention (p=0.25). Among people with diabetes in primary prevention, the independent proportional reduction in SVE was not statistically significant (RR 0.92, 95% CI 0.83-1.02); there was no evidence that the proportional effects on serious vascular events differed among people with diabetes at low (<5%), medium (5-10%) and high (≥10%) 5-year risk of CHD (p=0.72), but these analyses lacked statistical power.

Conclusions: The proportional effects of aspirin on SVE, major extracranial (excluding stroke and mortality are almost similar among people with and without diabetes. Further information about the balance of benefit and hazard of aspirin for primary prevention among people with diabetes, and its relationship to estimated CHD risk, is needed from ongoing trials.
Patients.

Japanese AF patients. DM may not be a risk of stroke, at least in Japanese AF

The Fushimi AF registry represents the clinical profile of real-world

ous stroke were independent determinants of stroke, but DM was not an indepen-

CHADS2 score and anticoagulation prescription revealed that the age and previ-

Furthermore, Multiple logistic regression analysis including risk factors of

anticoagulants and those without them (with anticoagulants 2.49% vs. 2.58%,

5.16% vs. 3.97%; p=0.18, heart failure: 4.87% vs. 3.97%; p=0.24, death: 8.17%

p=0.57).

p=0.0040), but the rate of previous stroke was comparable (20.1% vs. 19.1%;

Complications dependent on hypoglycemia.

Conclusions: Hypo is frequent in intensified glucose control of T2D. It is associ-

ated with an increased micro- and macro-vascular complications. Considering in-

dividual patient characteristics and co-morbidity, careful selection of anti-diabetic

pharmacotherapy have the potential to avoid complicating hypo.

7514 | BEDSIDE

Diabetes mellitus may not be a risk of stroke in Japanese patients with

atrial fibrillation: From the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) is a common arrhythmic disorder among the el-

derly, and is increasing significantly as the population ages (reportedly 0.6% of
total population in Japan). Diabetes mellitus (DM) is considered a major risk fac-

tor of ischemic stroke in patients with atrial fibrillation (AF), and is one of the

components of CHADS2 score. The purpose of this study was to investigate the relationship between DM and incidence of stroke in Japanese AF patients.

Methods: The Fushimi AF Registry, a community-based prospective survey, was
designed to enroll all of the AF patients in Fushimi-ku, Kyoto. Fushimi-ku is densely populated with a total population of 283,000, and is assumed to rep-
resent a typical urban community in Japan. At present, we have enrolled 3,821
patients (1.4% of total population) from March 2011 to December 2013. One-year
follow-up was completed in 2,966 patients as of December 2013.

Results: 698 patients were diagnosed as DM (23.5% of total, the mean age 73.7
years (OR 2.09; 95%CI 1.10-3.98), male gender (OR 1.99; 95%CI 1.09-3.64),

heart failure (OR 2.40; 95%CI 2.07-16.70) and history of prior hypo (OR 5.88;

95%CI 2.07-16.70). The use of DPP-4 inhibitors was associated with a 31% rel-

ative risk reduction for hypo (OR 0.69; 95% CI 0.53-0.89). Macro-vascular events
(new MI, stroke and PAD) were more frequent in patients with severe hypo (OR
3.39 for macro-vascular events, 5.28 for new MI). Micro-vascular events (not pre-
viously known retinopathy, nephropathy, neuropathy, and amputation) were more frequent in those with non-severe hypo (OR 1.92; 95%CI 1.49-2.49).

Conclusions: Hypo is frequent in intensified glucose control of T2D. It is associ-
ated with an increased micro- and macro-vascular complications. Considering in-
dividual patient characteristics and co-morbidity, careful selection of anti-diabetic
pharmacotherapy have the potential to avoid complicating hypo.

7516 | BEDSIDE

Added value of 18F-FDG PET/CT-Angiography with myocardial suppression in the diagnosis of infective endocarditis in prosthetic valves and intracardiac devices

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Purpose: To evaluate the added value of 18F-FDG PET/CT-Angiography (PET/CTA) in the diagnosis of infective endocarditis (IE) in prosthetic valves (PV) and cardiac devices (CD), where modified Duke criteria (DC) and echocardiogra-
phy (ECO) have limitations.

Methods: A prospective study was conducted in a hospital with a multidisciplinary IE unit. PET/CT was performed and compared with ECHO in all consecutive pa-
tients with suspected prosthetic IE, with exclusion of unstable patients requiring emergent surgery. Initial diagnosis with DC, PET/CTA and DC+PET/CTA informa-
tion were compared with a final expert team diagnostic consensus performed with all clinical, microbiological and imaging information.

Results: 39 patients (32 men; median age 64 years) from Nov-12 to Feb-14 en-
tered the study. Patients had PV aortic tubes: 6; PV: 13; CD: 10; PV+CD: 6 and
treated the study. Patients had PV aortic tubes: 6; PV: 13; CD: 10; PV+CD: 6 and

In patients who had a PV+CD, PET/CT A could locate the site of infection in all
discordant cases, PET/CT A confirmed and accelerated the diagnosis of IE in 9
and doubtful in 8 cases. PET/CT A was positive in 24, negative in 14 and doubtful
in 1 case. PET/CTA and ECO were concordant in 59 (kappa 0.3) and among discordant cases, PET/CTA confirmed and accelerated the diagnosis of IE in 9
false negative/doubtful ECHO and ruled out IE in 4 false positive/doubtful ECHO.

In patients who had a PV+CD, PET/CTA could locate the site of infection in all

discases. Table shows IE classification. DC+PET/CTA allowed reclassification of 59%
of the IE initially classified as (P) confirming/ruling out diagnosis, and the expert team could give a more conclusive diagnosis (D/R) in 73% of (P) IE. Sensibility, specificity, PPV and NPV were 48.1%/100%/70.9% for DC,
81.5%/83.3%/91.7%/86.7% for PET/CTA and 85.2%/83.3%/92%/71.4% for

DC+PET/CTA. PET/CTA additionally provided an alternative diagnosis in 55% of

Conclusions: Epidemiologic and microbiologic profile has changed in the last two decades. Patients from the last periods were older, had more comorbidity and a more virulent microbiological profile than those from the first period. As a result, the incidence of in-hospital events was higher in this group. Nevertheless, in-
hospital mortality did not change over the study period.

7515 | BEDSIDE

Temporal trends in infective endocarditis. Insights from a multicenter 1100-patient cohort study

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Clinic Hospital, Valladolid, Spain

Aim: To evaluate epidemiological and microbiological changes in infective endo-

carditis (IE) in the last two decades, and to assess the impact of these changes on

patients’ outcome.

Methods: We analyzed 1120 consecutive episodes of IE who were recruited prospectively at 3 referral centers between 1996 and 2012. They were classi-
fied into 2 groups: Group I (N=497), episodes of IE from 1996 to 2004, and Group

II (N=623), episodes from 2005 to 2012.

Results: Patients from Group II were older (59 (±16) vs 65 (±14); p<0.001). The frequency of patients with comorbidities, including diabetes (15.7% vs 23.4%;
p<0.001), malignancies (6.9% vs 12.7%; p<0.001), chronic renal insufficiency
(8.1% vs 15.2%; p<0.001), and history of intravenous drug use (11% vs 2.4%;
p<0.001) increased significantly during the study period. Nosocomial episodes of
IE were more frequent (29.3% vs 34.4%; p=0.005) in the last period. Degener-
avative valvulopathy (8.7% vs 16.7%; p=0.001) was also more frequent in this group. Enterococcus infection significantly increased over time (6.5% vs 10.1%;
p=0.039). S. aureus remained the most common cause of IE in both periods of

19% of cases). Vegetation detection was more common in Group II (79.2% vs 86%; p=0.004). Perianural complications were similar in both groups. Clinical and in-hospital mortality appeared more frequently in the second period (Ta-

ble). However, the percentage of patients that underwent surgery and in-hospital mortality rate were similar in both groups.

In-hospital evolution

Table shows IE classification. DC+PET/CT A allowed reclassification of 59%
of the IE initially classified as (P) confirming/ruling out diagnosis, and the

expert team could give a more conclusive diagnosis (D/R) in 73% of (P) IE. Sensibility, specificity, PPV and NPV were 48.1%/100%/70.9% for DC,
81.5%/83.3%/91.7%/86.7% for PET/CTA and 85.2%/83.3%/92%/71.4% for

DC+PET/CTA. PET/CTA additionally provided an alternative diagnosis in 55% of
the (R) IE, detected peripheral embolisms in 10 cases and 4 unsuspected neo-
plastic lesions.

Conclusions: PET/CTA could be a useful diagnostic tool in the diagnosis of pro-
thetic IE with an added diagnostic value to modified DC, increasing its sensibility.

5717 | BESIDE

Responsive performances of FDG-PET and radiolabeled leukocyte
scintigraphy for the diagnosis of prosthetic valve endocarditis
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Purpose: Echocardiography plays a key role in the infective endocarditis (IE) diagnosis but can be inconclusive in patients with suspicion of prosthetic valve (PVE)-IE. The incremental diagnostic value of 18-fluorodeoxyglucose positron emission tomography (FDG-PET) and radiolabeled leukocyte scintigraphy (LS) has already been demonstrated in IE patients. The aim of this study was to com-
pare the respective performances of FDG-PET and LS for the diagnosis of PVE in 39 patients.

Methods: FDG-PET and LS were performed in 39 patients admitted for a clinical suspicion of PVE and inconclusive echocardiography. All patients underwent both FDG-PET and LS, which were analysed separately and retrospectively by ex-
perienced physicians blinded to the results of the other imaging technique and to patient outcome. Fina
d Duke-LI IE classification was performed after a 3-month follow-up period.

Results: Mean age and sex ratio were respectively 62±17 years and 56%. Pa-
tients were imaged on average 45 months (range: 14 days - 24 years) following cardiac surgery. Average time interval between FDG-PET and LS acquisitions was 7±7 days. Out of the 39 patients, 15 patients were classified with definitive IE, 3 possible IE and 21 excluded IE. Sensitivity, specificity, positive predictive value and negative predictive value were 93%, 71%, 70% and 94% for FDG-PET and 60%, 100%, 100%, and 78% for LS, respectively. Discrepancies between the results of FDG-PET and LS occurred in 12 patients (31%). In patients with definite IE, 5 were identified with true positive FDG-PET but false negative LS. Out of these 5 patients, 3 presented non-pyogenic microorganism IE (Coxella or Candida). In patients with excluded endocarditis, 6 patients were identified with true negative LS but false positive FDG-PET. These 6 patients had been imaged in the first two months following the last cardiac surgery. The last patient with a discrepancy between FDG-PET and LS was classified as a possible endocarditis and presented positive FDG-PET and negative LS.

Conclusions: FDG-PET offers a higher sensitivity for the detection of active infec-
tion in patients with a suspicion of PVE and inconclusive echocardiography. LS offers however a higher specificity than FDG-PET for IE diagnosis and should be considered in case of inconclusive FDG-PET findings or in the first two months after cardiac surgery.

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High mortality associated with sepsis or endocarditis after pacemaker and ICD implantation - a nationwide cohort study
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Purpose: To determine the cumulative incidence, predictors and risk of mortality after sepsis and overall infective endocarditis (IE) among first-time cardiac im-
plantable electronic device recipients in Denmark.

Methods: We identified all de novo pacemakers (PMs) and implantable car-
dioverter defibrillators, (ICDs) in the period 1997-2012 from nationwide admin-
istrative registers. Logistic and Cox regression models were used to determine
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Impact of an infective endocarditis multidisciplinary team on mortality in a tertiary university hospital
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Purpose: To evaluate for prevalence and clinical significance of tricuspid regurgitation (TR) in patients with left ventricular (LV) dysfunction.

Methods: A single center analysis for TR of all echocardiographic studies, per-
formed between 2000 and 2013 in patients with ejection fraction <35% was per-
formed. Patients with mechanical valves, mitral stenosis, moderate to severe aor-
tic stenosis or regression, were excluded. Associations of TR with baseline ex-
amined echocardiographic findings and mortality were performed using Chi-square test.

Results: The study included 4028 patients (25% female, age 69±12.5 years). Se-
venty percent had no or mild TR, 23.7% had moderate and 6.3% had severe TR. Fre-
quency of severe TR was significantly higher than patients with moderate or no TR (p<0.001). LV di-
mensions were not associated with TR severity, however, severity of TR signifi-
cantly correlated with mital regurgitation (r=0.448, p<0.001) irrespective of left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), age, gender or body mass index. Left atrial diameter and left atrial area associated with TR severity as well (p<0.001). Severity of TR was significantly (p<0.001) associated with pulmonary hypertension assessed by gradient over the tricuspid valve. Total mortality during follow-up was 63.6%. There was a sig-
nificant association between TR grade and mortality in the Cox hazard model. TR 73% in moderate and 82% mortality in patients with severe TR (p<0.001).

Conclusions: Significant TR occurs frequently (30%) in patients with LV dys-
function and has prognostic implications. Female gender, MR, LA size and pul-

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Prevalence and echocardiographic correlations of tricuspid regurgitation in patients with significant left ventricular dysfunction
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Purpose: To evaluate for prevalence and clinical significance of tricuspid regurgi-
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nificant association between TR grade and mortality in the Cox hazard model. TR 73% in moderate and 82% mortality in patients with severe TR (p<0.001).

Conclusions: Significant TR occurs frequently (30%) in patients with LV dys-
function and has prognostic implications. Female gender, MR, LA size and pul-
monary hypertension correlate with TR severity and may have possible mecha-
nistic and/or prognostic implications.

5721 | BEDSIDE
Right ventricular dysfunction but not tricuspid regurgitation is associated with outcome in patients after left-sided valve surgery
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Background: Significant tricuspid regurgitation (TR) after previous left-heart valve surgery is frequent and associated with increased morbidity. Mortality rates for re-operation are high, while the impact of TR on survival in these patients remains unclear.

Methods: 571 consecutive patients ≥29 months after left heart valve surgery were prospectively followed for 53±15 months. Significant TR was defined as TR ≥ moderate by echocardiography.

Results: Significant TR was present in 123 (21.5%) patients (64% female, p=0.002). Patients with significant TR more often had atrial fibrillation (46% vs. 20%, p<0.001), they were more symptomatic (NYHA II:56% vs. 31%, p<0.001), presented with larger left and right atria (68.6±12.5mm vs. 57.7±7.8mm and 64.9±12.4mm vs. 55.6±7.3mm; both p<0.001), lower glomerular filtration rates (66.1±22.3 vs. 82.5±18.4, p<0.001), worse left ventricular (LVEF:<50%: 19% vs. 3%, p<0.032) and RV systolic function (17% vs. 3%, p<0.001). 127 (22.2%) patients died during follow-up; 84 patients with significant TR vs. 43 without (p<0.001).

By Kaplan-Meier analysis, overall survival was worse in patients with significant TR (p<0.001). However, by multivariable Cox analysis, age (p<0.001), left atrial size (p<0.001) coronary artery disease (p<0.01), chronic obstructive pulmonary disease (p=0.047) and RV dysfunction (p=0.032) but not TR were signifi-
cantly associated with mortality.

Conclusions: Right heart dysfunction but not late after left-sided valve surgery is signifi-
cantly associated with survival. Thus isolated surgery of TR in this setting has to be scrutinized. Further studies are needed to define specific patient groups that would clearly benefit from such a procedure.

5722 | BEDSIDE
Long-term outcomes of surgery for severe tricuspid regurgitation in patients who underwent previous open heart surgery
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Purpose: Patients with severe tricuspid regurgitation who need surgical treat-
ment usually have any left valve dysfunction or any congenital heart disease that pro-
cures to tricuspid valve (TV) regurgitation. Our aim was to analyze clinical outcomes of surgery for severe tricuspid regurgitation in patients who underwent previous heart surgery.

Methods: In this retrospective study, we included all patients with severe tricuspid regurgitation who underwent surgery for tricuspid valve replacement or repair in our center between April 1996 and November 2012 and in addition to this had undergone previous open heart surgery. We analyzed perioperative and long-
term mortality, and we indentified predictive factors using multivariable analysis.

Results: 190 patients underwent surgery after severe tricuspid regurgitation, and 33.1% of them (63 patients) had undergone previous heart surgery. These 63 pa-
tients were included in this study. 83.7% of the patients were female. Mean age was 60.1±10.7 years, and mean logistic EuroSCORE was 15±7.3. Table shows data regarding previous heart surgery. Concerning the surgery for tricuspid re-
regurgitation, ringless annuloplasty was performed in 23.8% of the patients, ring
annuloplasty in 25.4%, 28.6% of patients received a bioprosthesis and 22.2% a
mitral prosthesis, 1.6% implanting a pulmonary prosthesis, and 3.2% involved
repair. Perioperative mortality was 19%, and it was related to age (OR 1.1
1.02-1.2 p=0.02) and to tricuspid mechanical prosthesis (OR 10.2 1.8-55.7 p=0.07).

After a follow-up (median 62 months) conducted in 100% of patients, mortality was 39.7%. It was related to age (HR 1.6 0.01-11 p=0.002) and to extracorpo-
real circulation time (HR 1.01 1.005-1.018 p=0.001).

Conclusions: Surgery for severe tricuspid regurgitation in patients who under-
went previous heart surgery showed a high mortality. Age and tricuspid mecha-
nical prosthesis were predictors of perioperative mortality. Age and extracorpo-
real circulation time were predictors of long-term mortality.

5723 | BEDSIDE
Functional tricuspid regurgitation in organic mitral regurgitation. New insights in right ventricular function
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Objective: To assess the determinants of functional tricuspid regurgitation (TR) and its relations to right ventricular (RV) function in chronic organic mitral regur-
gitation (MR).

Methods: Three-hundred twenty-five patients (63±12 years, 206 males) with or-
ganic MR (82% degenerative etiology) referred to surgery and who underwent a preoperative gradation of TR were included in this study. Radionuclide angio-
graphy was carried out in 237 patients.

Results: Fifty patients had a TR ≥ grade 2. Patients with TR ≥ 2 were older, had more AF (54 vs 24%, p<0.0001) and were more symptomatic. Mean LV EF and RV EF were lower, and LV sepal function and RV free wall function were impaired in those with TR ≥ 2. By echocardiography, LV-RV left and right atrial remodeling were worse, PASP was higher and inter ventricular systolic pressure was lower whereas the severity of MR was similar. RV S velocity was also signifi-
cantly decreased. Ventricular function was stratified in normal RV-LV (Normal), isolated RV dysfunction (RVdysf. RV EF<35%), isolated LV dysfunction (LVdysf, LV EF<60%), and biventricular impairment (BIV, LV EF<60% and RV EF<35%).

TR ≥2 was found mainly in either BIV (33%) or LVdysf (22%) but almost never in RVdysf (3%) or Normal (3%) groups. In BIV TR ≥2 was associated with overall (p<0.001), RVdysf volume overload was higher, RV S wave velocity was not reduced, and RV EF impairment after surgery was greater suggesting lim-
ited impairment of intrinsic myocardial function. These specific features probably explain the absence of TR in this subgroup of patients.

Conclusions: In patients with organic MR referred to surgery TR ≥2 is associ-
ated with the longstanding presence of chronic organic MR. Mortality TR ≥2 occurs mainly in patients with BIV or LVdysf but is almost absent in RVdysf or Nor-
mal groups. Finally RVdysf group exhibits features suggesting a direct reversible effect of volume overload on the RV.
LIPID SIGNALLING AND INFLAMMATION

5738 | BENCH
ApoA-I mimetic peptide FAMP induces neovascularization through activation of endothelial cell nitric oxide related pathway

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Purpose: We developed an apoA-I mimetic peptide FAMP which has high capacity of cholesterol efflux and enhances the function of HDL. The aim of this study is to show FAMP induces functionally important angiogenesis.

Methods: We examined the effect of FAMP on eNOS phosphorylation and tube formation of human aortic endothelial cells (HAoECs) in vitro and ischemia induced angiogenesis in zebrafish embryo model of hind limb ischemia. Before ischemia surgery we fed mice with high-cholesterol diet (HCD) for 7 weeks to cause the endothelial dysfunction and to impair the HDL function. Mice were also assed for functional recovery after hind limb ischemia by determining the body speed of a step cycle of a specific paw.

Results: FAMP significantly promoted the tube formation of HAoECs, and activated phospho-Akt at serine residue 473 and phospho-eNOS at serine residue 1177. The nitric oxide synthase inhibitor L-NAME inhibited the effect of FAMP on HAoECs. In hind limb ischemia model mice with high-cholesterol diet FAMP treatment showed significant improvement of blood perfusion recovery and increased CD-31 positive endothelial cells number compared with the control (figure). In addition, functional recovery of the FAMP group at 7 days after the induction of hind limb ischemia was greater than control. On the other hand, there was no beneficial effect of FAMP in eNOS-deficient mice.

Conclusions: Results of the present study indicate that FAMP treatment lead to angiogenesis and functional recovery in ischemic limbs of mice fed high-cholesterol diet through activation of nitric oxide (NO)-related pathway.

5739 | BENCH
TTC39B, a novel gene influencing HDL cholesterol levels - Ttc39b deficient enhanced intestinal abca1, increased HDL cholesterol levels and reduced atherosclerosis -

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TTC39B, encoding tetra/tricopeptide repeat domain 39B(T39), was identified in genome wide association studies (GWAS) as a novel gene influencing HDL-cholesterol (HDL-C) levels. Although GWAS was initially used for finding genetic differences in a case-control design for particular diseases, its use quickly spread to traits measured on a continuum such as serum lipid levels. In fact, several studies published in 2009 revealed newly identified loci associated with levels of HDL-C, LDL-C and/or triglycerides and allowed many researchers including us to challenge to explore for a novel regulatory pathway for lipoprotein metabolism and atherosclerosis. T39 had not been previously implicated in lipoprotein metabolism at all and anything were unknown well, we decided to convert these information into animal models. We have now verified increased HDL-C levels in T39−/− mice. When increases in LXR protein but not mRNA, increased expression of Abca1 mRNA into animal models. We have now verified increased HDL-C levels in T39−/− mice.

There are several studies showing that abca1 is expressed in intestines and its role in cholesterol absorption is not well understood. We postulated that abca1 is involved in intestine functions related to glycosylation, angiogenesis and cholestasis remodeling. Furthermore, the expression level of Ttc39b is regulated by Gluc and the inflammatory cytokine TNFα. While, stimulation with high Gluc concentrations (25mM) further enhanced Nf-κB activity by 2-fold. Ttc39b overexpression in VSMCs caused a strong enhancement of the monocyte chemoattractant protein-1 (MCP-1) expression in the presence of high Gluc (25mM) compared to EGFP control cells with the maximum detected after 4 h Gluc presencenc (Ttc39b: 202%±19% vs. EGFP: 50%±5.7%, p<0.05, n=4).

MAP-kinase Erk1/2 phosphorylation was increased in Ttc39b overexpressing cells compared to EGFP control cells in a Gluc-dependent manner (Gluc 0 min: +56%±45%, Gluc 90 min: +345%±56%, p<0.05, n=4). Furthermore, the expression of Ttc39b is regulated by Gluc and the inflammatory cytokine TNFα. Both stimulation with high Gluc concentrations (25mM) and TNFα (10ng/ml) induced an up to 5 fold increase in the Ttc39b mRNA content in VSMCs and ECs after 12 hours.

Conclusions: Our data suggest that Ttc39b causes a significant inflammatory response in VSMCs. Both, activity and expression of Ttc39b are regulated by Gluc and TNFα. Therefore, Ttc39b might play an important role in hyperglycemia-accelerated vascular inflammation and pathogenesis of atherosclerosis.

5740 | BENCH
Orphan receptor GPRC5b activates inflammatory signaling in vascular smooth muscle cells

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Purpose: Atherosclerosis is driven by an inflammatory process of the vascular wall. GPRC5b, a novel orphan G protein-coupled receptor (GPCR), is endogenously expressed in cells of the vascular wall, including vascular smooth muscle cells (VSMC), endothelia cells (EC) and macrophages. In diolethyl, the GPRC5b ortholog in zebrafish is anti-inflammatory and regulates Gluc-induced energy and lipid metabolism. Our hypothesis is that GPRC5b is involved in pro-inflammatory and pro-atherogenic signaling, particularly in hyperglycemia.

Results: Confocal microscopy demonstrated specific accumulation of overexpressed YFP-tagged GPRC5b at the plasmamembrane of murine VSMC and EC. Incubation with high Gluc (25mM) instead of low Gluc (5mM) for up to 20 min induced an internalization of GPRC5b, which is a characteristic feature of GPCR in response to their cognate ligand. The adrenovial expression of human GPRC5b in VSMCs activated nuclear factor kappa B (NFκB) 72 h post induction (171±10-fold, p<0.05, n=4) compared to EGFP control even at low Gluc. Increasing the Gluc concentration up to 25mM further enhanced NFκB activity by 2-fold. GPRC5b overexpression in VSMCs caused a strong enhancement of the monocyte chemoattractant protein-1 (MCP-1) expression in the presence of high Gluc (25mM) compared to EGFP control cells with the maximum detected after 4 h Gluc presence (GPRC5b: 202%±19% vs. EGFP: 50%±5.7%, p<0.05, n=4).

MAP-kinase Erk1/2 phosphorylation was increased in GPRC5b overexpressing cells compared to EGFP control cells in a Gluc-dependent manner (Gluc 0 min: +56%±45%, Gluc 90 min: +345%±56%, p<0.05, n=4). Furthermore, the expression of GPRC5b is regulated by Gluc and the inflammatory cytokine TNFα. Both stimulation with high Gluc concentrations (25mM) and TNFα (10ng/ml) induced an up to 5 fold increase in the GPRC5b mRNA content in VSMCs and ECs after 12 hours.

Conclusion: Our data suggest that GPRC5b causes a significant inflammatory response in VSMCs. Both, activity and expression of GPRC5b are regulated by Gluc and TNFα. Therefore, GPRC5b might play an important role in hyperglycemia-accelerated vascular inflammation and pathogenesis of atherosclerosis.

5741 | BENCH
HIF-1alpha mediated metabolic reprogramming critically regulates macrophage function in inflammatory conditions

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Background: Hypoxia is a pathological condition in which the tissue is deprived of oxygen supply in many cardiovascular diseases such as myocardial ischemia and atherosclerosis. Each cell exerts its own responses to hypoxia, and most of them are mediated through a transcription factor, hypoxia inducible factor 1α (HIF-1α). Macrophage, a key mediator of inflammation, accumulates in hypoxic area, and a HIF-1α mediated hypoxic responses of the macrophage could play a critical role in macrophage activation.

Method: We investigated the genome wide binding profiles of HIF-1α in hypoxia or LPS treated macrophages by chromatin immunoprecipitation (ChIP) sequence, and the gene expression profiles of macrophage treated with each stimulus by RNA sequence. The metabolic states of such activated macrophages were analyzed with the Extracellular Flux Analyzer.

Result: Chip-seq assay showed that hypoxia induced 2101 HIF-1α binding sites, whereas LPS elicited HIF-1α binding at 1396 sites. The comparing investigation of these data revealed most of HIF-1α binding sites of LPS treated macrophages were included in that of hypoxic macrophages (961/1396 sites). While hypoxia elicited HIF-1α bindings to the regulatory regions related to glycolysis, angiogenesis and cholestasis remodeling, LPS induced HIF-1α binding sites were confined to glycogenic enzymes.

To examine the roles of HIF-1α in macrophage activation, we analyzed the gene expression profiles of LPS treated wild-type and HIF-1α deficient macrophages. RNA-seq and gene ontology analysis demonstrated that LPS induced HIF-1α played a critical role in the expression of glycogenic enzymes. Metabolic assays with the Extracellular Flux Analyzer showed that metabolic reprogramming (from aerobic to anaerobic) in LPS treated macrophages was totally dependent on HIF-1α. And interventions in the reprogramming by enzyme inhibitors (e.g. dichloroacetate) crucially affected gene expression and cellular function of LPS treated macrophage.

Conclusion: LPS induced HIF-1α bindings were significantly enriched for the elements related to glycogenic gene, and HIF-1α mediated metabolic reprogramming could play a critical role in macrophage activation.
Lipid signalling and inflammation / Translational research and hot clinical topics in cardiomyopathies

5742 | BEDSIDE
Epigenetic signatures induced by methyltransferase Set7 drive endothelial dysfunction and vascular inflammation in patients with type 2 diabetes
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Purpose: In vitro studies have shown that mammalian methyltransferase Set7 mediates hyperglycemia-induced endothelial inflammation via epigenetic regulation of oxidative stress factors and NF-κB. The link between Set7 and vascular disease in patients with type 2 diabetes (T2DM) remains to be elucidated. This study was designed to investigate whether Set7 contributes to endothelial dysfunction and vascular inflammation in T2DM patients.

Methods: Set7-related epigenetic changes on NF-κB p65 promoter were assessed in peripheral blood monocytes (PBMC) isolated from 30 patients with T2DM and 20 age-matched controls. Chromatin immunoprecipitation assay (ChIP) was performed to investigate Set7-dependent epigenetic changes on human NF-κB promoter. Brachial artery flow-mediated dilation (FMD), urinary 8-isoprostaglandin F2α (8-isOPGF2α), expression of NF-κB downstream genes COX-2 and iNOS as well as plasma adhesion molecules VCAM-1, ICAM-1 and MCP-1 were also determined. Experiments in human aortic endothelial cells (HAECs) exposed to high glucose were performed to characterize the mechanisms of Set7-induced inflammation and co-expression between different variables were measured by Spearman’s analysis. Probability values less than 0.05 were considered statistically significant. Data are expressed as percentage or mean ± standard deviation.

Results: Set7 expression was increased in PBM from T2DM as compared with controls (275.1 ± 18% vs. controls, p < 0.01). Set7-dependent monomethylation of histone 3 at lysine 4 (H3K4m) was found on NF-κB p65 promoter of T2DM patients. This epigenetic mark was associated with upregulation of NF-κB-dependent pro-inflammatory (COX-2, iNOS) and inflammatory genes (VCAM-1, ICAM-1 and MCP-1). Indeed, Set7 positively correlated with gene expression of COX-2 (r = 0.40, p < 0.05), iNOS (r = 0.47, p < 0.05), VCAM-1 (r = 0.57, p < 0.01), ICAM-1 (r = 0.58, p < 0.01) and MCP-1 (r = 0.53, p < 0.01). In line with these findings, Set7 expression correlated with oxidative stress marker 8-isOPGF2α (r = 0.44, p < 0.05) and brachial artery FMD (r = 0.54, p < 0.01). In HAECs, gene silencing of Set7 suppressed H3K4m, NF-κB p65 expression and subsequent overexpression of oxidant and inflammatory genes.

Conclusions: Our findings demonstrate that a specific epigenetic signature induced by Set7 regulates NF-κB p65 expression, leading to dysregulation of oxidant and inflammatory genes and subsequent endothelial dysfunction. These results suggest that targeting Set7 may represent a promising approach to reduce oxidative and inflammatory burden in patients with T2DM.

5756 | BEDSIDE
Prevalence and clinical relevance of left ventricular outflow tract obstruction in patients with takotsubo cardiomyopathy
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Purpose: Takotsubo cardiomyopathy (TTC) is regarded a benign disease since left ventricular function returns to normal within a short time. However, a number of complications have been observed in patients (pts) with this enigmatic syndrome. The present study evaluated the frequency and clinical relevance of left ventricular outflow tract obstruction (LVOTO) in a large TTC registry.

Methods: From 37 heart centres, 324 pts (296 f, 28 m, age 68 ± 12 years) were included in a TTC registry according to the following criteria: 1) acute chest symptoms, 2) ischemic ECG changes, 3) reversible LV akinesia not corresponding to a single coronary artery territory, 4) absence of coronary artery stenoses. Complete data in a TTC registry was obtained from 7 pts (70%) and developed between day 3 and day 10 in 3 pts. Inotropic agents had been administered in 1 pt. Age, sex and symptoms were comparable in pts with or without LVOTO. The ECG on admission showed a higher heart rate in association with LVOTO (101 ± 15/min vs 87 ± 23/min, p = 0.05). Other ECG parameters (ST elevation, T wave inversion, Q wave, QTc) were not different. Cardiac markers were lower with LVOTO (CK 1.67 ± 1.2 vs 1.97 ± 4.1 upper limit of normal, Troponin 11.7 ± 9.4 vs 21.4 ± 6.3 x upper limit of normal, p = 0.05). Angiographic lesion fraction was comparable in both groups (50 ± 14% vs 51 ± 13%). LVOTO occurred with similar frequency in mid-ventricular and in apical ballooning (2/76 vs 8/133, p = ns). Transient mitral regurgitation (> grade II) was only seen in pts with LVOTO (2/10 vs 0/199, p = 0.002). RV involvement occurred only in pts with LVOTO (0/10 vs 48/199, p = 0.06). Other complications (LV thrombus, pulmonary edema, ventricular tachycardia, shock, death) were observed with similar frequency in both groups. Receiving betablocker therapy LVOTO resolved within 2–3 days in every patient.

Conclusions: LVOTO is well tolerated in a TTC pts and may be associated with high grade mitral reguralation. Since catecholamines can provoke or aggravate LVOTO in TTC pts, inotropic agents should be used only under echocardiographic guidance. Spontaneously or under betablocker therapy LVOTO resolves within 2 to 3 days.

TRANSLATIONAL RESEARCH AND HOT CLINICAL TOPICS IN CARDIOMYOPATHIES

5757 | BEDSIDE
Prevalence of TTR senile cardiac amyloidosis among elderly patients with cardiac heart failure

Introduction: Transthyretin (TTR) senile cardiac amyloidosis is usually not diagnosed as a cause of heart failure with preserved ejection fraction (HFPEF). More geographic incidence of TTR cardiomyopathy, related to genetic and geographic factors, has been described. Although no treatment has shown to improve survival in HFPEF patients, new drugs that stabilise TTR might be of use in this subset of patients. 99Tc-DPD scintigraphy has been shown to have a high sensitivity and specificity for the diagnosis of TTR cardiac amyloidosis in this setting.

Objective: We sought to determine the prevalence of TTR senile cardiac amyloidosis among elderly patients admitted due to HFPEF and to investigate if a 99Tc-DPD scintigraphy-based protocol is effective to diagnose TTR senile cardiac amyloidosis in this setting.

Methods: We prospectively recruited all consecutive patients >60 years old admitted due to HFPEF (LVEF<50%) with LV hypertrophy (>12mm) to the Departments Cardiology and Internal Medicine of our centre during a 28 months period and a 9 months period respectively. All eligible patients were offered a 99Tc-DPD scintigraphy during hospitalization and their clinical data were collected.

Results: We recruited 122 patients (61% women, mean age 83±19 years, median NT-proBNP 4067 pg/l (IQR 1471-9885), 56% admitted to Cardiology). 89 patients (73%) agreed to participate in the study and had a 99Tc-DPD scan done. No patient had any adverse event related to 99Tc-DPD scan. 15 patients (17%) showed intense uptake on 99Tc-DPD scintigraphy. All patients with a positive scan underwent genetic testing of TTR gene and no mutations were found. Moreover, an endomyocardial biopsy was performed in 3 patients confirming TTR amyloidosis. There was no significant difference in gender, history of heart transplantation, diabetes, AF, renal function or NT-proBNP between the 99Tc-DPD scan-positive group and negative group. Patients with TTR senile cardiac amyloidosis were significantly older, were more likely to have conduction disorders on ECG and have a more pacemaker, had lower voltage on ECG and higher wall thickness. There was no difference in the hypertrophic pattern neither in treatment between both groups.

Conclusions: Senile cardiac amyloidosis accounts for a significant number of diastolic heart failure cases and is probably underdiagnosed. A 99Tc-DPD scintigraphy-based protocol is safe and accurate to detect TTR senile cardiac amyloidosis among elderly patients admitted to hospital due to HFPEF.

5758 | BEDSIDE
Genetic basis of familial dilated cardiomyopathy undergoing heart transplantation. A NGS study
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Purpose: We sought to determine the genetic basis of heart transplant familial DCM and to establish the genetic uptake of modern NGS technologies in this setting.

Methods: 53 heart transplanted patients due to familial DCM underwent NGS by conventional genetic techniques. Moreover, genetic basis of DCM among patients undergoing HT. The high number of DCM-associated genes has made very difficult to study DCM by conventional genetic techniques. Moreover, genetic basis of DCM among patients undergoing HT is poorly characterized.

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genetic evaluation with a panel of 195 genes related with cardiac conditions (64 specifically related with DCM). Genetic variants found were classified as possible pathogenic variants (novel missense variants in a previously DCM-associated gene and not present in controls) or as pathogenic mutations (previously described as pathogenic or variants found in a DCM-associated gene, not found in controls) predicting premature truncation, frameshift or abnormal splicing of the protein). Final pathogenicity status of possible pathogenic variants was determined by familial cosegregation studies.

Results: Initially, 28 pathogenic mutations were found in 23 patients (43%); 3 pathogenic mutations exhibited possible pathogenic variants. 25 patients (47%) carried 29 possible pathogenic variants. 5 patients (9%) did not show any disease-causing mutations. Familial evaluation of 215 relatives confirmed pathogenicity in 13 patients with pathogenic mutations and allowed reclassification of possible pathogenic mutations in 17 patients and as non-pathogenic in 3 cases. In 5 patients with possible pathogenic variants familial evaluation was inconclusive or not possible. At the end of the study the DCM-causing mutation was identified in 40 patients (75%). Mutated genes included: EMD (14 patients), TNN (10), BAG3 (4), DSP (3), LMNA (2), FLNC (2), MYBPC3, MYH7, TNNT2, DMD, FLNC, PKP2, DSC2, TPM1, NCN and PSEN2. 5 patients (9%) harbor possible pathogenic variants in the following genes: DSC2, MYBPC3, MYH6, MURC, MYPN, PSEN2, and TNNT1. The causal mutation was not identified in 8 cases (15%).

Conclusions: Genetic spectrum of familial DCM undergoing heart transplantation is heterogeneous and multiple genes are involved. Current NGS technology plus detailed familial studies allow identification of causative mutations in the vast majority of familial DCM cases. Despite advances in genetic techniques, detailed familial studies remain critical to determine the pathogenicity of underlying genetic defects in a substantial number of cases.

5759 | BEDSIDE

Left ventricular systolic function but not the presence of late gadolinium enhancement independently predicts adverse cardiac events in muscular dystrophy patients

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Background: Cardiac involvement is a frequent finding in patients with X-linked recessive inherited muscular dystrophy type Duchenne (DMD) and Becker (BMD) and characterized by a myocarditis-like pattern of left ventricular (LV) myocardial fibrosis. It may be associated with dilated cardiomyopathy, progressive heart failure and arrhythmias, and represents an important cause of morbidity and mortality in this population.

Objective: Since the presence of myocardial fibrosis detected by late gadolinium enhancement (LGE) CMR was shown to be a strong and independent predictor of worse outcome in different non-ischemic myocardial diseases (such as myocarditis and dilative cardiomyopathy), we evaluated the prognostic value of different CMR parameters in patients with DMD/BMD.

Material and methods: Eighty-eight male MD (20 DMD and 68 BMD) patients (age 29±14 yrs) were prospectively enrolled. All patients underwent cine and LGE CMR imaging at inclusion and were followed up for adverse cardiac events. The primary endpoint was considered cardiac death and/or cardiac transplantation. The secondary endpoint was a combination of hospitalization for heart failure, unsustained ventricular tachycardia (VT), ventricular fibrillation (VF) and sudden death. Biventricular long sheath technique showed typical histopathological findings of CS in 4 patients (50%) (The figure is a typical case of positive biopsy result). Positive biopsy sites were lower voltage and longer total activation time than negative biopsy sites (0.73 vs. 1.84 ms and 132 vs. 77 ms, respectively). No complication occurred throughout the procedure.

Conclusions: EVM-guided EMB provides histological confirmations of sarcoidosis at high incidence, and is a safe and helpful in confirming the diagnosis of CS in probable CS patients who remain undiagnosed by traditional EMB.

5770 | BEDSIDE

Targeted endomyocardial biopsy using electroanatomical voltage mapping for patients suspected of cardiac sarcoidosis

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Purpose: Cardiac sarcoidosis (CS) may submit to life-threatening ventricular arrhythmias. Diagnosis CS is sometimes due to lack of typical signs, especially in isolated CS. Although histologic diagnosis is crucial, endomyocardial biopsy (EMB) is associated with low diagnostic yield caused by focal nature of the disease. We evaluated the diagnostic contribution of electroanatomical voltage mapping (EVM)-guided EMB in patients with CS.

Methods: We studied 8 consecutive patients (5 male, mean age 56±17 years, EF ≥40±18%) with a noninvasive probable diagnosis of CS according to current criteria (Japanese Diagnostic Standard and Guideline for Sarcoidosis 2006) and without specific histological findings of CS by traditional EMB. All patients underwent EVM-guided EMB.

Results: In all 8 patients, RV bipolar voltage mapping was performed with a 3-D electroanatomical mapping system (CARTO), and the low voltage area with 0.5-1.5 mV was identified at outflow tract and interventricular septum of the RV. Histological samples taken from the low voltage area by a standard biopsy technique showed typical histopathological findings of CS in 4 patients (50%) (The figure is a typical case of positive biopsy result). Positive biopsy sites were lower voltage and longer total activation time than negative biopsy sites (0.73 vs. 1.84 ms and 132 vs. 77 ms, respectively). No complication occurred throughout the procedure.

Conclusion: EVM-guided EMB provides histological confirmations of sarcoidosis at high incidence, and is a safe and helpful in confirming the diagnosis of CS in probable CS patients who remain undiagnosed by traditional EMB.

5771 | BEDSIDE

Tash in the elderly: a retrospective investigation in 1129 patients treated in a single centre

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Background: According to the 2012 AHA/ACCF guidelines TASH is recommended in particular for elderly patients with symptomatic HOCM. However only limited data exist, that report the safety and efficacy of alcohol ablation in elderly patients.

Methods: We retrospectively investigated the outcome after TASH in all patients who were treated in our hospital since 1996 and compared older patients of age >75 years with younger patients <75 years.

Results: A total of 1129 consecutive patients (mean age 58,7 years) were analysed. 139 (12%) of these patients were older than 75 years. Older patients had a significantly higher NYHA functional class pre TASH (3.1±0.6 vs. 2.7±0.67; p <0.0001) and higher resting gradients at baseline (58.3±35.7 mmHg vs. 50.4±35.7 mmHg; p=0.004). The amount of alcohol used in elderly patients was somewhat lower (41.5±11.1 ml vs. 43.1±11.0 ml; p=0.03) resulting in a comparable maximum CK activity after TASH (768.5±541.3 U/l vs. 819.1±579.0 U/l; p=0.493). Only 1 patient >75 years died in hospital due to an abrupt coronary no flow syndrome occurring during the intervention, which equals the mortality rate of the whole collective of 1.15%. At six months follow up the NYHA functional class improved in both groups but did not differ from each other (1.73±0.79 vs. 1.41±0.83; p=0.302), however, older patients had a more pronounced gradient reduction compared to the younger patients (improvement rate of gradients at rest: 40.9±45.5 mmHg vs. -27.4±32.8 mmHg; p <0.002).

Conclusion: TASH is safe and effective even in the elderly. In contrast to other coronary interventions with an age dependent risk and outcome, TASH leads to favourable results with a very low mortality rate especially in elderly patients.

INTRACORONARY IMAGING: INSIGHTS

5774 | BEDSIDE

Comparison of vascular response after everolimus-eluting stents and bare metal stents implantation in ST-segment elevation myocardial infarction assessed by optical coherence tomography

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Background: Implantation of drug-eluting stents (DES) in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) reduces in-stent restenosis compared with bare metal stents (BMS), however, the long-term risk of DES use in STEMI has
been pointed. Previous pathological and optical coherence tomography (OCT) study reported that first generation DES use in STEMI resulted in higher rates of uncovered and malapposed strut stents at follow-up. The long-term safety of second-generation everolimus-eluting stents (EES) use in STEMI remains unknown. We used OCT to examine vascular response including strut coverage and malapposition in patients with STEMI treated with EES and BMS.

**Methods:** We enrolled 102 patients with STEMI who underwent primary stenting and 10-month follow-up OCT (EES: 61 patients and BMS: 41 patients).

**Results:** A total of 21366 stent struts were analyzed. There were no significant differences in the percentage of uncovered and apposed struts and the percentage of uncovered and malapposed struts between 2 stents (1.6±2.3% versus 1.2±2.0%, P=0.379 and 0.6±1.2% versus 0.4±0.9%, P=0.596, respectively). The mean neointimal thickness was smaller in EES lesions (104±39 μm vs. 388±148 μm, P<0.001). Intra-stent thrombus was observed in 13% of EES lesions and 10% of BMS lesions (P=0.758). The frequencies of in-stent binary restenosis and incidence of intra-stent thrombus at 10-month follow-up between EES and BMS. Differences in the percentage of uncovered struts and malapposed struts, and the incidence of intra-stent thrombus at 10-month follow-up between EES and BMS. On the other hands, EES as compared with BMS significantly reduces neointimal hyperplasia. EES has a potential to achieve low late loss without sacrificing safety.

### 5775 | BEDSIDE

**Saphenous vein graft changes after coronary artery bypass graft surgery: insights from the cardiocalculation for bypass graft patency rate optimization (CABG-PRO) study**

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**Purpose:** To investigate changes in saphenous vein graft (SVG) morphology during the first postoperative year using serial intravascular ultrasound (IVUS) and optical coherence tomography (OCT).

**Methods:** IVUS and OCT measurements were performed in 13 and 10 SVGs, respectively, immediately after surgery and after 12 months. Minimum lumen diameter (MLD), lumen cross-sectional area (LCSA), vessel cross-sectional area (VCSA) were measured using the Echoplaque 4 software (Indec, Mountain View, CA). Wall thickness was calculated by the difference of average vessel lumen diameter and average lumen diameter divided by two. MLD, LCSA and VCSA were measured also for the OCT images with LightLab imaging software (St Jude, Version D.0.2). The presence of thrombus and SVG valves was also evaluated.

**Results:** Compared to immediately after CABG IVUS imaging 12 months later revealed significant changes in minLD (4.02±0.62 vs. 3.13±0.73 mm, p=0.0003), LCSA (14.56±4.58 vs. 9.10±4.67 mm², p=0.0005) and VCSA (22.08±4.68 vs. 18.45±4.99 mm², p=0.03), but increase in W (0.50±0.09 vs. 0.74±0.17 mm, p=0.0007). These measurements correlated well with OCT measurements (base-line LCSA r=0.84, p<0.0002 and follow-up LCSA r=0.84, p=0.0002). OCT imaging revealed a double layered appearance of the SVG wall in all the study grafts (mean thickness 0.25mm ± 0.08mm) giving the impression of neointimal formation within the original vein graft (figure 1). Additionally OCT demonstrated that the vein valves which were obvious in baseline images were fused into the graft wall one year post surgery.

**Conclusions:** During the first year post CABG, SVGs undergo significant lumen loss due to a combination of wall thickening and negative remodeling. These findings provide important insights into the pathogenesis of early SVG failure.

### 5776 | BEDSIDE

**Assessment of tissue prolapse after perforate coronary intervention and its relation with neointimal hyperplasia at follow-up by serial optical coherence tomography**

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**Purpose:** Tissue prolapse (TP) after stent implantation is sometimes observed on optical coherence tomography (OCT). However, the clinical significance of TP after percutaneous coronary intervention (PCI) on long-term outcomes has not been fully investigated. Therefore, we sought to evaluate the relationship between TP after PCI and neointimal hyperplasia (NIH) at the follow-up period by serial OCT examination.

**Methods:** We evaluated 83 consecutive lesions in 83 consecutive patients (38 patients with acute coronary syndrome (ACS); 45 patients with stable anginapectoris (SAP)) that underwent PCI with OCT examination. All lesions were treated with stent implantation (44 lesions with drug-eluting stents (DES); 39 lesions with bare metal stents (BMS)). Plaque morphologies at the narrowest culprit sites on OCT (CT) images were considered as the stent reference. TP in the struts and the incidence of NIH at follow-up angiography (angiography) (mean interval 12.2 months) were calculated. NIH volume measurements in each CSA and NIH volume throughout stented segments were also measured. The relationships between TP and NIH at follow-up angiography at the culprit sites were measured, and throughout the stented segments were evaluated.

**Results:** TP area at the culprit sites correlated with NIH area (r=0.31, p=0.02 and r=-0.30, p=0.02) and at the most protruding sites (r=0.38, p=0.01) and r=-0.41, p=0.002). At the culprit sites, NIH area at follow-up angiography (angiography) (mean interval 12.2 months) NIH area in each CSA and NIH volume throughout stented segments were also measured. The relationships between TP and NIH at follow-up angiography at the culprit sites were measured, and throughout the stented segments were evaluated.

**Conclusions:** In STEMI patients undergoing primary PCI, there are no significant differences in the percentage of uncovered struts and malapposed struts, and the incidence of intra-stent thrombus at 10-month follow-up between EES and BMS. The presence of thrombus and SVG valves was also evaluated.

### 5777 | BEDSIDE

**Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: pooled analysis at patient level of 4 registries**

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**Purpose:** We sought to investigate the clinical impact of the use of intravascular ultrasound (IVUS) during recascularization of patients with left main disease with DES in our country. A propensity score matching method was used to obtain matched pairs of patients with and without IVUS guidance.

**Methods:** We performed a level patient pooled analysis of 4 registries of patients with left main disease treated with DES in our country. A propensity score matching method was used to obtain matched pairs of patients with and without IVUS guidance.

**Results:** A total of 1,670 patients were included and 505 patients (30.2%) underwent DES implantation under IVUS guidance (IVUS group) by means of the matching method, 505 patients without the use of IVUS during recvascularization were selected (no-IVUS group). Survival free of cardiac death, myocardial infarction and target lesion recascularization at 3 years was 88.7% in IVUS group and 83.6% in no-IVUS group (p=0.04) for overall population and 90% and 80.7% respectively (p=0.03) for the subgroups with distal left main lesions. The incidence of definite and probable thrombosis was significantly lower in IVUS group (0.6% vs. 2.2%; p=0.04). Finally, IVUS guided recvascularization was identified as independent predictor for major adverse events in overall population (HR 0.70, 95% CI 0.52 – 0.99; p=0.04) and in the subgroup with distal lesions (HR 0.54, 95% CI 0.34 – 0.90; p=0.02).

**Conclusions:** The results of this pooled analysis show an association of IVUS guidance at PCI with better outcomes in patients with left main disease undergoing recvascularization with DES.
with 173 CTO lesions were scheduled for coronary intervention in a single center. All procedures were guided with intravascular ultrasound (IVUS). After successful guidewire crossing, lesions were classified according to IVUS evaluation into 2 groups: (1) true lumen group and, (2) subintimal stenting group; and compared with regards to in-hospital and long term clinical outcomes.

**Results:** In 154 lesions, DES were deployed in the true lumen; and in 19 (11%) lesions, DES were deployed in the subintimal space (95% confidence interval: 6.3% to 15.6%) with a success rate of 96% and 82.4%, in antegrade and retrograde approaches, respectively. IVUS showed that the prevalence of dissection was two times and intramural hematoma (IMH) was four times as higher in the subintimal stenting group (p<0.001 and p<0.02, respectively). Subintimal stenting was associated with a non-significant increase in Peri-procedural myocardial infarction (5.3% vs. 2.6%), major dissections (10.5% vs. 3.2%), and perforations (10.5% vs. 5.8%). Kaplan-Meier analysis revealed similar rates of binary revascularization in this small patient group (Table 1). As expected, proliferation parameters were significantly higher after 6 months (Relative Proliferation Volume: 5.1±7.8 vs. 13.2±7.4 mm³/cm, p=0.002).

**Conclusion:** The application of paclitaxel by a DES induces a positive vessel remodeling in the target lesion, which is in combination with bare metal stenting an advantageous since it creates pronounced stent strut malaposition. Therefore, shortening of dual antiplatelet therapy below 6 months following a BMS + DEB procedure should be strictly avoided.

### PREDICTING OUTCOMES IN HEART FAILURE – WHAT IS NEW?

#### 5785 | BEDSIDE

A novel risk score for predicting 30-day mortality in heart failure patients undergoing non-cardiac surgery


**Background:** Heart failure is an established risk factor for poor outcomes in patients undergoing non-cardiac surgery; yet risk stratification of these patients remains a clinical challenge. We developed an index for 30-day mortality risk-prediction in this particular group.

**Methods and results:** All individuals with heart failure undergoing non-cardiac surgery between October 23, 2004 and October 31, 2011 from Danish administrative registers (n=16,827) were identified and randomly divided into derivation and validation cohorts (2:1 ratio). By stepwise logistic regression modeling, factors associated with 30-day mortality were chosen and combined in a weighted risk score. Total in-hospital, 30 days. 39 risk factors were considered and 24 were retained with P<0.05 by multivariable logistic modeling. Risk factors included age, male gender, emergent surgery, body mass index, non-ischemic etiology of heart failure, chronic obstructive pulmonary disease, prior acute myocardial infarction, renal disease, peripheral artery disease, cerebrovascular disease, atrial fibrillation, cancer surgery, use of insulin, statins, furosemide ≥80 mg/d, major orthopedic surgery, intra-abdominal surgery, plastic surgery, intracranial surgery, venous-lymphatic surgery, pulmonary surgery, and artery surgery. Mortality rates ranged from 1.0% (26/2729) for the lowest risk score to 57.1% (36/63) for the highest risk score. The model had good calibration and discrimination (c statistic 0.80, Hosmer and Lemeshow p=0.89 for validation cohort). A low risk score could with a specificity of 97.6% rule out mortality in 1320/1335 (98.9%) of the patients in validation cohort.

**Conclusions:** For patients with heart failure, this index can accurately identify those at low risk for perioperative mortality.

#### 5786 | BEDSIDE

Transient anemia also affects long-term prognosis in heart failure patients

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**Background:** It is well known that anemia carries worse prognosis in heart failure (HF). Less evidence exists on how haemoglobin monitoring influences outcomes during long-term follow-up. Aim: To examine whether serial haemoglobin levels measured 6 months apart have an impact on survival in a cohort of HF outpatients followed in a structured HF clinic. Haemoglobin (Hb) was determined at first visit and after 6 months. Anaemia was defined according to WHO criteria (Hb<13 g/dL for men and Hb<12 g/dL for women). Patients were classified relative to their Hb values as: non-anemic (both determinations normal), transiently anaemic (anaemia at first visit but not at 6 months), newly anaemic (non-anaemia initially but anaemia at 6 months) and permanently anaemic (anaemia in both determinations). The study included 1174 consecutive patients (71.7% men, mean age 66.8 ± 10 years) were included in the study. The majority of patients were of ischemic aetiology (54%). Mean initial LVEF was 33% ± 13. Most patients were in NYHA class II (64.5%) or III (29.7%). Mean Hb was 12.8 ± 1.9 at first visit and 12.8 ± 1.7 at 6 months. According to the defined classification 477 patients (40.6%) were considered

<table>
<thead>
<tr>
<th>fu (days) / uncovered struts</th>
<th>Relative Proliferation Volume (mm³)</th>
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<tbody>
<tr>
<td>8 weeks / (n=8)</td>
<td>63.9±14.7</td>
</tr>
<tr>
<td>6 months / (n=8)</td>
<td>249.1±100.4</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001*</td>
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fu, follow-up; ISA, incomplete stent apposition.
Results: Among patients considered underweight based on BMI strata, 60% and 100% were undernourished by definitions #1 and #2, respectively; These figures were 31% and 1% among normal-weight, 4% and 11% among overweight, and 30.72%, or other cardiovascular or bleeding outcomes. There was a marginally-significant excess of heart failure hospitalisation in HFpEF (RR 1.29, 95% CI 1.01-1.64, p=0.042; 4 studies, n=28,583).

Conclusions: Persistent, new, and even transient anaemia carry worse long-term prognosis in a large cohort of ambulatory HF patients.

5787 | BEDSIDE Nutritional status in outpatients with heart failure: a prognostic determinant beyond body mass index
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Background: Nutritional assessment may help to explain the reportedly increased mortality of HF patients that are not completely understood. The obesity paradox in heart failure (HF) is based on body mass index (BMI).

Objective: To assess the prognostic influence of undernourishment in HF outpatients.

Patients and methods: Two published definitions of undernourishment were used to assess 214 ambulatory HF patients (mean age 67.7±11.1 years, 75.2% male, 54.7% of ischemic etiology, L VEF 36.7±12.7). Definition #1 includes albumin, total lymphocyte count, tricipital skinfold (TS), subscapular skinfold (SS), and arm muscle circumference (AMC). Two or more below normal define undernourishment. Definition #2 only involves TS, AMC and albumin. One or more below normal define undernourishment. Patients were also stratified by BMI and percentage of body fat, and followed for two years. All cause death or HF hospitalization was the primary end-point.

Results: Among patients considered underweight based on BMI strata, 60% and 100% were undernourished by definitions #1 and #2, respectively. These figures were 31% and 44% among normal-weight, 4% and 11% among overweight, and 14.5% among obese patients, respectively. Undernourishment using both definitions was significantly associated with lower event-free survival. In multivariable analysis age, NYHA functional class, diabetes mellitus, NT-proBNP, and undernourishment (HR 2.25 [1.11-4.56] and HR 2.24 [1.19-4.21] for definitions #1 and #2, respectively) remained in the model. In this cohort BMI and percentage of body fat did not independently predict event-free survival at two years.

Conclusion: Nutritional status has a very significant prognostic role in HF beyond BMI. Proper undernourishment assessment should become routine in HF patients.

5789 | BEDSIDE Predictors for the transition to de novo heart failure in stage B asymptomatic patients -A report from the CHART-2 Study-
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Background: Increasing prevalence of heart failure (HF) is an urgent public health issue worldwide. Although the clinical guidelines emphasize the importance of the transition from asymptomatic to symptomatic HF, useful predictors for the development of de-novo HF in patients with cardiovascular disease remain to be elucidated.

Method: We analyzed the predictors for the development of de novo HF in 4,463 consecutive Stage B patients out of 10,219 patients registered in our Chronic Heart Failure Analysis and Registry in the Tohoku District 2 (CHART-2) study. Stage B was defined as asymptomatic cardiac structural and/or functional diseases according to the ACC/AHA guidelines.

Results: Mean age was 67±12.4[SD] years old, and male patients accounted for 71%. Regarding etiologies for asymptomatic cardiac structural abnormalities, the prevalence of ischemic heart disease, valvular heart disease, and cardiomyopathy was 51, 19, and 10%, respectively. During the median follow-up period of 3.0 years, 280 deaths (6.0%) and 165 de novo HF requiring hospitalization (3.5%) were noted. A stepwise Cox regression analysis with Akaike's information criterion (AIC) revealed that development of de novo HF in Stage B patients could be predicted by age (hazard ratio (HR) 1.02, P=0.020), diastolic blood pressure (DBP) (HR 0.98, P=0.021), atrial fibrillation (AF) (HR 2.05, P<0.001), left ventricular (LV) diastolic diameter >50 (HR 1.58, P<0.035), LV ejection fraction <50% (HR 2.10, P<0.001), anemia (HR 1.73, P=0.005), chronic kidney disease (HR 1.70, P=0.007) and BNP levels (HR 1.04 (per 100 pg/ml), P=0.004). A Classification and Regression Tree analysis showed the first split point of BNP to discern development of de novo HF was 90.1 pg/ml. In a sub-analysis of 5 groups divided according to BNP levels (G1: <49, G2:50-89, G3:90-149, G4:150-199, G5: >200 pg/ml), the multivariate Cox proportional hazard model revealed that patients with BNP >90 pg/ml (G3, G4, G5) had significantly higher risk for de novo HF.
been shown to be higher than that reported for healthy volunteers. The aim of the study was to evaluate the superiority of Ticagrelor 180 mg crushed tablets versus Ticagrelor 180 mg integral tablets in decreasing residual platelet reactivity in patients undergoing primary percutaneous coronary intervention (PCI).

Methods: Eighty-two consecutive patients with STEMI were randomized to receive Ticagrelor 180 mg as integral tablets (n=41) or as crushed tablets (n=41) before PCI. The primary study end-point was residual platelet reactivity by P2Y12 Reversibility Units (PRU) VerifyNow 1 hour after ticagrelor LD. Secondary end-points were: 1) The percent of patients with a high residual platelet reactivity (HRPR, PRU >180, 1 hour and 2 hours after ticagrelor LD); 2) Major and minor bleeding events (TIMI criteria); 3) Occurrence of dyspnoea or symptomatic bradycardia.

Results: PRU 1 hour after the LD was 68 (61-251) and 252 (167-301) in crushed and integral group, respectively (p=0.006). PRU values did not significantly differ between crushed and integral tablet groups at 2, 4 and 8 hours from LD (p=NS for all). HRPR was found in 35% and 63% patients (p=0.011) at 1 hour and in 20% and 28% patients (p=0.431) at 2 hours, respectively. There was no significant difference in bleeding, arrhythmias or dyspnea episodes in the 2 groups.

Conclusions: The administration of ticagrelor crushed tablets in STEMI patients is feasible and safe, and allow to achieve earlier platelet inhibition as compared with standard integral tablets.

ClinicalTrials.gov Identifier: NCT01992523

5801 | BEDSIDE
Reversibility of clopidogrel, prasugrel and ticagrelor- ex vivo study
Technische Universität Dresden, Heart Center Dresden, University Hospital, Dresden, Germany.

Background: In addition to clopidogrel (CI) two new P2Y12 inhibitors prasugrel (Pr) and ticagrelor (Ti) have been approved for clinical use.

In contrast to CI, Pr and Ti inhibit ADP-induced platelet activation more rapidly, more consistently and to a higher extent. Furthermore, in acute coronary syndromes Pr and Ti showed a significant reduction of major adverse cardiac events compared to clopidogrel, although increasing rates of bleedings. Compared to thienopyridines, Ti needs no further metabolism and has a different binding site from ADP, making it an allosteric antagonist with reversible blockade of the P2Y12 receptor.

In case of acute bleedings or emergent surgical procedures, the platelet inhibitory effect has to be reversed rapidly.

The aim of this study was to examine ex vivo whether platelet inhibition induced by CI, Pr and Ti could be reversed after administration of platelets. Furthermore, differences of CI, Pr and Ti as well as the quantity of platelet transfusion in order to achieve normalization of platelet function should be determined.

Methods: 61 blood samples of patients with acute coronary syndromes (24hours after initial loading dose with CI, Pr or Ti) have been investigated after administration of increasing amounts of platelet rich plasma (PRP) or pooled platelet concentrates (PP). The inhibition of the P2Y12-receptor was determined by Platelet Reactivity Index (PRI-VASP).

Results: Initial PRI-VASP values were within therapeutic range with significant lower values in the Pr and Ti-groups compared to CI (Pr 12,9±6,4%, Ti 18,3±13,2% and CI 22,6±13,3%; p<0,001 Pr/Ti vs. CI). After addition of PRP a significant increase in all 3 groups could be determined (CI 29,6±14,8% to 56,2±12,0%; p<0,001, Pr 12,9±6,4% to 46,5±12,7%; p<0,001, and Ti 14,8±2,6% to 36,7±13,2%; p<0,001). The increase was less pronounced in the Ti-group.

Addition of PP there was no significant increase of the PRI-VASP in the CI and Pr-groups Prasugrel (37,1±9,4% to 56,4±6,2%; p=0,005; 12,9±6,9% to 44,8±9,1%; p<0,001). In the Ti group there was only a non-significant trend to higher PRI-VASP values (13,4±9,8% to 19,5±10,0%; p=0,542).

Conclusion: The present study demonstrated that addition of both PRP and PP ex vivo are effective to partially reverse the platelet inhibitory effect on the P2Y12-receptor, whereas this effect is lowest for ticagrelor. These results support the current practice to administrate platelets in acute bleedings or emergent surgical procedures. If this approach leads to a reduction of bleeding complications in vivo has to be proven in further clinical studies.

5802 | BEDSIDE
Similar risk of cardiovascular events in diabetic patients with acute coronary syndromes managed medically with prasugrel vs clopidogrel: findings from the TRILOGY ACS trial
1Milpark Hospital, Johannesburg, South Africa; 2Shaharzade Medical Center, Jerusalem, Israel; 3Duke Clinical Research Institute, Durham, United States of America; 4University of Texas Southwestern Medical School, Dallas, United States of America; 5National Institute of Cardiology, Warsall, Poland; 6Brimgham and Women’s Hospital, Boston, United States of America; 7Ell Lilly and Co., Indianapolis, United States of America; 8Universities of Aberdeen, Edinburgh, United Kingdom.

Purpose: A prior analysis of diabetic subjects in the TRITON trial presenting with acute coronary syndrome (ACS) and undergoing percutaneous coronary intervention (PCI) showed enhanced benefit with prasugrel vs clopidogrel, but the
impact of this treatment comparison in medically managed ACS patients with diabetes remains uncertain.

Methods: The TRILOGY ACS trial compared prasugrel vs clopidogrel in non-ST-elevation ACS patients managed medically, without revascularization, compared baseline characteristics and treatment-related outcomes among 3539 patients with diabetes (1111 were treated with insulin) vs 5767 patients without diabetes.

Results: Patients with diabetes were younger, more commonly female, more likely to have known cardiovascular (CV) risk factors, and more frequently had a history of revascularization before the index ACS event compared with patients without diabetes. The frequency of ischemic events through 30 months was higher among patients with diabetes vs no diabetes; within the diabetic group, CV event frequency was higher among patients with insulin treatment vs those without (Table). No differences in bleeding rates were observed. All event rate comparisons by treatment (prasugrel vs clopidogrel) were statistically similar (p < 0.05) except for a marginally lower rate of myocardial infarction with prasugrel vs clopidogrel among insulin-treated diabetic patients (p = 0.044).

Conclusions: We observed a higher risk of ischemic events during long-term follow-up among patients with ACS and diabetes who were managed medically, but no significant treatment-related differences for ischemic and bleeding events with prasugrel vs clopidogrel were demonstrated.

5803 | BEDSIDE
Incidence and impact of dual antiplatelet therapy cessation among diabetic patients receiving drug eluting stents: a “real-world” analysis from the PARIS registry
D. Giacoppo1, M. Aquino1, J. Yu1, M.W. Kruczel2, D.J. Moliterno3, D.J. Cohen4, S. Pocock5, G. Weisz6, J.B. Hermiller7, R. Mehran1 on behalf of PARIS.

Methods: The PARIS registry was a multicenter, prospective, observational study from the PARIS registry of patients undergoing PCI with stent implantation. The study was designed to examine whether adenosine reuptake inhibition by ticagrelor and another adenosine antagonist had a significant impact on neutrophil chemotaxis in the presence of erythrocytes

Results: Among 5031 patients enrolled in the PARIS registry, we identified 1430 (33.0%) diabetic patients who received DES. During 2 year follow-up, the rates of any DAPT cessation, discontinuation, interruption and disruption were 50.2%, 32.6%, 11.5% and 12.4%, respectively. The cumulative incidence of major adverse cardiac events (MACE) was 9.2%, with most of these events occurring among those (76.4%) vs off (23.6%) DAPT. While discontinuation or brief interruption of DAPT appears safe among such patients, the risk following DAPT disruption remains substantial.

Conclusions: Among diabetic patients receiving DES, most adverse events occur while patients are on rather than off DAPT. While discontinuation or brief interruption of DAPT is safe among such patients, the risk following DAPT disruption remains substantial.

5804 | BEDSIDE
Cangrelor reduces large, prognostically important, myocardial infarctions in patients undergoing PCI: findings from CHAMPION-PHOREX
M. Cavender1, D. Bhagat1, G. Stone2, H. White2, G. Leonard2, J. Prats3, T. Liu4, T. Li5, J. Day5, K. Mahaffey6, R. Harrington1, B. Brigham and Women’s Hospital, Boston, United States of America; 2 Columbia University Medical Center, New York, United States of America; 3 Green Lane Clinical Center, Auckland, New Zealand; 4 Policlinic Foundation San Matteo IRCCS, Pavia, Italy; 5 The Medicines Company, Parsippany, United States of America; 6 Stanford University, Palo Alto, United States of America

Purpose: Cangrelor is an intravenous P2Y12 inhibitor that reduces the composite rate of death, myocardial infarction (MI), ischemia-driven revascularization, or stent thrombosis in patients undergoing percutaneous coronary intervention (PCI) at 48 hours. We characterized the effects of cangrelor on the type and size of MI that occurred within 48 hours after randomization in the CHAMPION-PHOREX trial.

Methods: 11,145 randomized patients were treated in a double-blind, double dummy fashion with either cangrelor or a loading dose of clopidogrel. CK-MB was to be measured every 6 hours and analyzed by an independent core laboratory. An independent clinical events committee adjudicated all potential MI. The association of MI and 30-day mortality was modeled with adjustment for known predictors of death. MI was further classified into type and size.

Results: A total of 462 patients (4.1%) undergoing PCI had a MI within 48 hours following randomization. The majority of MI were peri-procedural (Type 4a) (n=433, 94%). Cangrelor, as compared with clopidogrel, reduced MI with an elevation of CK-MB ≥5xULN by 20% (3.8% vs. 4.7%, HR 0.80, 95% CI 0.67-0.97).

There were consistent effects on MI with a 25% reduction in MI with CK-MB ≥5xULN and a 34% reduction in MI with CK-MB ≥10xULN (Figure). The occurrence of MI with a rise in CK-MB ≥3x, ≥5x, and ≥10x ULN was associated with increased odds of 30-day mortality (ORadj 6.7 [95% CI 3.2, 14.1], 9.0 [95% CI 4.3, 18.7], and 10.1 [95% CI 4.2, 24.5], respectively).

Conclusions: In patients undergoing PCI, the occurrence of peri-procedural MI was associated with significant risk of death. Cangrelor, when compared with clopidogrel, significantly reduces MI, including large MI.

5805 | BENCH
Tacroligec and dipyridamole potentiate adenosine-induced stimulation of neutrophil chemotaxis in the presence of erythrocytes
K. Alsharif, H. Judge, V. Ridger, R.F. Storey, University of Sheffield, Cardiovascular Science, Sheffield, United Kingdom

Introduction: Tacroligec is a dual inhibitor of platelet P2Y12 receptors and cellular adenosine receptor.

Methods: Neutrophils and erythrocytes were isolated from healthy volunteers using Histopaque ficoll gradient centrifugation. Concentration-dependent effects of adenosine on neutrophil chemotaxis were investigated and the involved adenosine receptors identified using adenosine receptor antagonists. The effects of cangrelor (another P2Y12 inhibitor), ticagrelor and dipyridamole on IL-8-stimulated neutrophil chemotaxis were determined over 30 minutes in the presence or absence of i) erythrocytes and/or ii) adenosine.

Results: Low-concentration adenosine (10 nM) caused a significant increase in IL-8 stimulated chemotaxis (1.4 ± 4.4 vs. 2.2 ± 0.8), P < 0.01. An independent in response to IL-8 through the low-affinity A1 receptor, whereas the high-affinity receptor A2a could reverse this action in the presence of high-concentration adenosine 10 μM (22.8 ± 3.6 vs. 21.5 ± 8.0, P < 0.05). Erythrocytes attenuated the effects of adeno-
Sine on neutrophil chemotaxis in the presence of cangrelor or control whereas ticagrelor and dipyridamole both preserved this effect of adenosine in the presence of erythrocytes (Figure).

Conclusion: Inhibition of adenosine reuptake by ticagrelor and dipyridamole leads to potential the effects of adenosine on neutrophil chemotaxis in the presence of erythrocytes. This represents a potential mechanism by which ticagrelor could influence host defence against bacterial lung infection.

RISK ASSESSMENT IN ATRIAL FIBRILLATION: WHAT REALLY MATTERS?

5831 | BEDSIDE
Stroke is often the first clinical manifestation of atrial fibrillation. The FibStroke study
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Purpose: Atrial fibrillation (AF) is often asymptomatic and may remain undiagnosed and lead to stroke when no anticoagulation is used.
Methods: We analyzed the timing of 1,471 ischemic strokes and transient ischemic attacks (TIA) in relation to the diagnosis of AF in 1,310 patients treated in 4 centers during 2003-2012. The patients were divided into 2 groups according to the history of AF: (1) patients with a history of AF and (2) patients with a new diagnosis of AF at the presentation of stroke or TIA.
Results: AF was diagnosed for the first time at the time of stroke/TIA in 384 (26.1%) patients. Patients with a history of AF were significantly older and they had more often heart failure, vascular disease, history of stroke and chronic AF (Table).

Clinical characteristics

<table>
<thead>
<tr>
<th>Previous AF (n (%))</th>
<th>New AF (n (%))</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (% of all events)</td>
<td>1087 (73.9)</td>
<td>384 (26.1)</td>
</tr>
<tr>
<td>Age, yr (95% CI)</td>
<td>76.7 (9.3)</td>
<td>74.8 (9.3)</td>
</tr>
<tr>
<td>Female gender</td>
<td>601 (55.3)</td>
<td>204 (53.1)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>221 (20.2)</td>
<td>37 (9.6)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>241 (22.2)</td>
<td>76 (19.8)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>698 (64.2)</td>
<td>245 (63.8)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>432 (39.7)</td>
<td>91 (23.7)</td>
</tr>
<tr>
<td>History of stroke</td>
<td>359 (33.0)</td>
<td>60 (15.6)</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>406 (44.0)</td>
<td>197 (50.1)</td>
</tr>
</tbody>
</table>

Conclusions: Stroke is often the first manifestation of AF. More effective measures to screen for asymptomatic AF are needed.

5832 | BEDSIDE
Cost-effectiveness analysis of screening for atrial fibrillation in pharmacies using an iPhone handheld ECG (SEARCH-AF)
N. Lowres1, G. Saikeld2, L. Neubeck3, C. Martinez4, C. Wallenhorst4, N. Lowres1, G. Saikeld2, L. Neubeck3, C. Martinez4, C. Wallenhorst4, N. Lowres1, G. Saikeld2, L. Neubeck3, C. Martinez4, C. Wallenhorst4, S. F. B. Freeman5, 1Dept of Cardiology, Concord Hospital & Anzac Institute, Sydney Medical School, University of Sydney, Sydney, Australia; 2University of Sydney, School of Public Health, Sydney, Australia; 3University of Sydney, The George Institute for Global Health, Sydney, Australia; 4Institute for Epidemiology, Statistics and Informatics GmbH, Frankfurt, Germany
Purpose: Identifying unknown atrial fibrillation (AF) in the community and subsequent anti-thrombotic treatment could reduce stroke burden. We aimed to determine the cost-effectiveness of community screening for unknown AF, using an iPhone ECG with an automated algorithm (iECG) in pharmacies.
Methods: Cost-effectiveness analysis from an Australian health funder perspective, comparing cost of ECG population-based AF screening, to diagnosed AF in an unscreened population, for age 65-84. Results are expressed as incremental cost-effectiveness ratio (ICER) per stroke avoided and per quality adjusted life year (QALY) gained. The model assumed a rate of unknown AF of 1.4% in target population; test sensitivity 97%; test specificity 92%; cost of warfarin treatment and monitoring $AUD303.80 ($421.73) pa; cost per screen $AUD20 ($10.49); and 5.09 QALYs gained per stroke avoided. Benefits of detecting AF are based on data obtained from the UK Clinical Practice Research Datalink using a subset of 5,587 patients with incidentally detected asymptomatic AF, with incidence rates projected out to 10 years following initial screening. Sensitivity analyses varied base assumptions for anticoagulant guideline- adherence rate.
Results: The ICER of extending iECG screening into the community, based on 55% warfarin prescription adherence, would be $AUD5,951 ($3,122) per QALY gained and $AUD30,290 ($15,892) for prevention of one stroke. Sensitivity analysis indicated cost-effectiveness improved with increased treatment adherence. Conclusions: Screening with iECG in pharmacies is cost effective for stroke prevention and gaining QALY, and well within a range fundable on a population basis, using either warfarin or novel oral anticoagulants. Guideline recommendation of community iECG screening for AF should be considered.

5833 | BEDSIDE
Comparison of ATRIA and CHA2DS2-VASc risk stratification schemes for the prediction of stroke in the individual patient with atrial fibrillation and the impact on treatment decisions
H.A. Van Den Ham1, O.H. Klungel1, D.E. Singer2, H.G.M. Leufkens1, T.P. Van Staa1 on behalf of IMI PROTECT. 1Utrecht Institute for Pharmaceutical Sciences, Pharmacoepidemiology and Clinical Pharmacology, Utrecht, Netherlands; 2Massachusetts General Hospital, Boston, United States of America; 3London School of Hygiene and Tropical Medicine, London, United Kingdom
Purpose: To compare the predictive ability of the currently recommended CHA2DS2-VASc ischaemic stroke risk score with the new ATRIA stroke risk score in patients with atrial fibrillation (AF).
Methods: Patients with AF, not using warfarin, were assembled from the Clinical Practice Research Datalink (CPRD) database. Patients were followed from date of AF diagnosis until occurrence of ischaemic stroke, prescription of warfarin, death or the end of study. Independent predictors of ischaemic stroke were identified with a Cox proportional hazard model by stepwise backward selection. The c-index assessed the discriminative ability of the risk schemes. Net reclassification improvement (NRI) assessed net correct risk reclassification using ATRIA versus CHA2DS2-VASc, using published point score cut-offs. As correct stroke risk thresholds for low/moderate/high risk, 1% and 2% per year were used.
Results: We included 60,594 patients. The overall stroke rate was 2.45% per year. Age and previous stroke were the strongest predictors of ischaemic stroke. Other independent predictors were hypertension (HR 1.25 CI 95%, 1.15-1.35) and diabetes (HR 1.27 CI 95%, 1.14-1.41). Vascular disease and heart failure were not significant predictors. For the full point scores, the c-index was 0.71 (95% CI, 0.70-0.72) for the ATRIA score and 0.69 (95% CI, 0.68-0.70) for the CHA2DS2-VASc score. The NRI was 0.38 for ATRIA compared to the CHA2DS2-VASc-score, resulting entirely from downward reclassification (Figure).

Abstract 5832 – Table 1. Sensitivity analysis (ICER/QALY gained)

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>40% Rx adherence</th>
<th>50% Rx adherence</th>
<th>55% Rx adherence</th>
<th>60% Rx adherence</th>
<th>70% Rx adherence</th>
<th>80% Rx adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>$4,610</td>
<td>$6,257</td>
<td>$6,896</td>
<td>$7,539</td>
<td>$8,182</td>
<td>$8,825</td>
</tr>
<tr>
<td>Deviations from base case</td>
<td>$0.00 per screen</td>
<td>$0.00 per screen</td>
<td>$0.00 per screen</td>
<td>$0.00 per screen</td>
<td>$0.00 per screen</td>
<td>$0.00 per screen</td>
</tr>
<tr>
<td>Treatment: 95% NOAC @ $1,510pa and 10% warfarin</td>
<td>$16,512</td>
<td>$14,674</td>
<td>$12,836</td>
<td>$11,006</td>
<td>$9,189</td>
<td>$8,375</td>
</tr>
<tr>
<td>Treatment: 95% NOAC @ $1,174pa and 10% warfarin</td>
<td>$16,512</td>
<td>$14,674</td>
<td>$12,836</td>
<td>$11,006</td>
<td>$9,189</td>
<td>$8,375</td>
</tr>
<tr>
<td>*2.75 QALYs gained per stroke avoided</td>
<td>$6,737</td>
<td>$5,273</td>
<td>$4,740</td>
<td>$4,297</td>
<td>$3,860</td>
<td>$3,423</td>
</tr>
</tbody>
</table>
| Rx: Treatment; NOAC: novel oral anticoagulant; $: $AUD (Purchasing Power Parity: $AUD1=$0.5247).

Conclusions: The ATRIA score had better discriminative ability than CHA2DS2-VASc. The CHA2DS2-VASc-score assigns most AF patients to the moderate and high risk categories, which could lead to overtreatment. In this community-based, low-risk cohort, the ATRIA score correctly reclassified patients as lower risk.
Using the CHA2DS2-VASc score for refining stroke risk stratification in low-risk Asian patients (ATRIA score 0-5) with atrial fibrillation

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Taipei Veterans General Hospital, Taipei, Taiwan; 2Birmingham City Hospital, Birmingham, United Kingdom

Background: A new scoring system, ATRIA score, was proposed for risk stratification in patients with atrial fibrillation (AF). Whether the ATRIA scheme can adequately identify patients who are at low-risk of ischemic stroke remains unknown. The goal of the present study was to compare the performance of ATRIA and CHA2DS2-VASc scores for stroke prediction.

Methods: This study used the “National Health Insurance Research Database” in Taiwan. A total of 186,570 AF patients without any antithrombotic therapy were selected as the study cohort. The clinical endpoint was the occurrence of ischemic stroke.

Results: During the follow-up of 3.7 years, 23,723 patients (12.7%) experienced ischemic stroke. The CHA2DS2-VASc score performed better than ATRIA score in predicting ischemic stroke as assessed by c-indexes (0.698 versus 0.629, p < 0.0001). The CHA2DS2-VASc score also improved the net reclassification index by 11.7% compared with ATRIA score (p < 0.0001). Among 73,242 patients categorized as “low risk” based on an ATRIA score of 0-5, the CHA2DS2-VASc scores ranged from 0.7 to 15.0 at one-year follow-up, and from 1.5 to 8.0% at 15-year follow-up. The Kaplan-Meier estimates of probability of remaining free of ischemic stroke according to the CHA2DS2-VASc score are illustrated in Figure 1. The c-indexes of CHA2DS2-VASc score (0.629) was significantly higher than that of ATRIA score (0.593) in this “low-risk” category.

Conclusions: Pts with AS and AF have significantly more frequent ischemic and bleeding events than pts without SVD. Given the small numbers of pts and events in AS group, conclusions regarding treatment effects need to be drawn with caution. This is the first study suggesting that efficacy and safety outcomes of pts with aortic stenosis on oral anticoagulation are distinctly different from pts without SVD.

Using the CHA2DS2-VASc score for refining stroke risk stratification in low-risk Asian patients (ATRIA score 0-5) with atrial fibrillation

P5835 | BEDSIDE

Patients with native aortic stenosis represent a high-risk subgroup in nonvalvular atrial fibrillation - Results from ROCKET AF

1University Hospital, Münster, Department of Cardiovascular Medicine, Division of Electrophysiology, Münster, Germany; 2University Hospital Münster, Department of Cardiovascular Medicine, Division of Adult Congenital and Valvular Heart Disease, Münster, Germany; 3Bayer HealthCare Pharmaceuticals, Montville, United States of America; 4Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 5Oregon Health & Science University, Portland, Oregon, USA

Background: ROCKET AF included patients (pts) with nonvalvular atrial fibrillation (AF) defined as the absence of mitral stenosis or artificial valve prostheses which allowed the inclusion of pts with native aortic stenosis (AS).

Aim: To compare characteristics and outcomes of pts with AS and pts without significant valvular disease (SVD), including the treatment effects with rivaroxaban or warfarin.

Methods and results: Cox regression was used to adjust comparisons for potential confounders. Of 14,264 pts included in the trial, 215 had diagnosis of AS (n=215), 12,179 had no SVD. AS pts were older (78 vs. 72 years), heavier (BMI 29 ± 8.2 kg/m²), had twice rates of persistent AF (80% vs. 81%), more peripheral artery disease (15% vs. 6%) and prior MI (30% vs. 16%), and had a slightly higher CHADS2 score (3.6 vs. 3.5) than pts without SVD. Independent of treatment allocation, efficacy outcomes in AS pts occurred approximately twice as often as in pts without SVD (Table). Bleeding events were also more frequent in pts with AS. When comparing rivaroxaban and warfarin groups, treatment effects were consistent across AS and no-SVD groups for all endpoints.

Conclusions: Patients categorized as “low risk” using an ATRIA score were not necessarily “low risk”, and the annual stroke rates can be as high as 2.95% at 1-year follow-up and 2.84% at 15-year follow-up compared to 1.06% to 13.3% at 1-year follow-up, and from 1.5 to 8.0% at 15-year follow-up. The Kaplan-Meier estimates of probability of remaining free of ischemic stroke according to the CHA2DS2-VASc score are illustrated in Figure 1. The c-indexes of CHA2DS2-VASc score (0.629) was significantly higher than that of ATRIA score (0.593) in this “low-risk” category.

Table 1. Efficacy and safety endpoints for AS and no-SVD patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Events/100 pt-yrs AS vs. no SVD</th>
<th>AS</th>
<th>No SVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke, SE, or vascular death</td>
<td>10.84 (41)</td>
<td>4.31 (982)</td>
<td>2.03 (1.47, 2.79)</td>
</tr>
<tr>
<td>Stroke, SE, vascular death, or MI</td>
<td>12.09 (45)</td>
<td>4.99 (1128)</td>
<td>1.91 (1.41, 2.59)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>3.68 (15)</td>
<td>1.96 (458)</td>
<td>1.70 (1.00, 2.39)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>11.22 (43)</td>
<td>4.39 (1002)</td>
<td>1.88 (1.38, 2.56)</td>
</tr>
<tr>
<td>Safety outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major or Non-CMR bleeding</td>
<td>24.36 (59)</td>
<td>14.16 (2431)</td>
<td>1.28 (0.98, 1.66)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>7.61 (21)</td>
<td>3.27 (625)</td>
<td>1.61 (1.03, 2.49)</td>
</tr>
</tbody>
</table>

Conclusions: Patients categorized as “low risk” using an ATRIA score were not necessarily “low risk”, and the annual stroke rates can be as high as 2.95% at 1-year follow-up and 2.84% at 15-year follow-up compared to 1.06% to 13.3% at 1-year follow-up, and from 1.5 to 8.0% at 15-year follow-up. The Kaplan-Meier estimates of probability of remaining free of ischemic stroke according to the CHA2DS2-VASc score are illustrated in Figure 1. The c-indexes of CHA2DS2-VASc score (0.629) was significantly higher than that of ATRIA score (0.593) in this “low-risk” category.
Results: Numbers of subjects who fulfilled the criteria were 9 (MF=5/4) (1:3,039) and 23 (MF=11/12) (1:2,255) in 6- and 12-year-old subjects, respectively. Genetic testing was performed in 8 subjects and mutation was determined in 4 subjects. All but one fulfilled the QTQ score criteria (criteria [a]). A 6-year-old girl had a score of 3 and a radical mutation (G745 fs+54X) in KCNQ2.

Conclusion: QTQ score of LQTS in 6- and 12-year-old subjects was about 1:3,000 and 1:2,250, respectively. Prevalence in 12 years olds was similar to the former report. The new QTQ scoring system is useful for clinical diagnosis of LQTS in both children and adolescents. These data may be a reference for the ECG screening programs.

P5838 | BENCH
A novel cardiac α-mysin heavy chain (MYH6) mutation impairing sarcomere structure responsible for familial sick sinus syndrome
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Purpose: Sick sinus syndrome (SSS) is a common arrhythmia often associated with aging or underlying structural heart diseases, but it may occur in a familial form. Mutations responsible for familial SSS have been demonstrated in several genes encoding sarcomere proteins such as α-MHC and HCN4, and recent genome-wide association studies have shown a rare variation (R721W) of the α-mysin heavy chain (α-MHC) gene MYH6 increasing susceptibility to SSS. α-MHC is a sarcomeric protein predominantly expressed in the atrium, and its knockdown animals showed impaired sarcomere structures and defective atrial contraction. Our goal is to identify genetic defects of MYH6 in familial SSS and elucidate the molecular pathophysiology underlying SSS with MYH6 mutations.
Methods: We genetically screened MYH6 in nine genotype-negative SSS families using PCR direct sequencing strategy. Since the mutations in MYH6 are linked to cardiomyopathy and a variety of congenital heart diseases and known to impair the myofilibrillation formation, we assessed the morphological changes of the sarcomere attributable to the MYH6 mutations.
Results: Frame 2bp deletion mutation delE933 (c.2797_2799delIGA) was identified in the exon 22 of MYH6 in a 62-year-old female who had a pacemaker implanted with a diagnosis of SSS. Her deceased mother also had a pacemaker implanted due to SSS. The delE933 was not identified in 400 healthy Japanese control subjects as well as in 1000 Genomes database or dbSNP. Echocardiography showed mild dilatation of left ventricle and right atrium, but there was no sign of cardiomyopathy, congenital heart diseases, or cardiac dysfunction. Immunofluorescence imaging of neonatal rat cardiomyocytes transfected with MYH6-R721W and delE933 showed brightly fluorescent speckles of α-MHC and lack of organized repeating units characteristics of myofibrils, demonstrating markedly impaired sarcomeric structural integrity. The residue E933 of MYH6 is located at the highly conserved region across different species for both α- and β-MHC isoforms. Co-immunoprecipitation study revealed that the delE933 α-MHC resulted in reduced binding affinity to myosin binding protein-C. Since E933 is highly conserved, this point mutation dominantly expressed in the atrium, it is suggested the variations or mutations of MYH6 may disrupt the sarcomeric integrity of the atrial muscle surrounding sinus node, which in turn progresses to manifest sinus node dysfunction.
Conclusion: DelE933 may define a new disease entity of inherited arrhythmias attributable to mutations in genes encoding sarcromere proteins other than cardiac ion channels or ion channel-associated genes.

P5839 | BEDSIDE
Genetic modifiers in the long QT3/Brugada overlap-syndrome caused by E1748K
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Purpose: Long QT syndrome (LQTS) and Brugada syndrome (BrS) are genetic arrhythmia disorders characterised by sudden death and highly variable penetrance. The E1748K mutation in SCN5A, the α-subunit of Nav1.5, causes a LQTS/BrS overlap phenotype and is the most commonly identified mutation in LQTS and BrS. The aim of this project is to identify genetic modifiers of the variable phenotype in an international cohort of E1748K carriers. Identification of genetic modifiers will increase our understanding of pathophysiology and may improve risk stratification.
Methods: We genotyped 88 caucasian E1748K mutation carriers from 14 families for 48 single nucleotide polymorphisms (SNPs) previously shown to be modifiers of different electrocardiographic (ECG) traits in the general population in large genome wide association studies. Association with PR interval, QRS duration, QTc interval, Brugada phenotype and time to occurrence of symptoms was tested using the R-package coxme (mixed effects Cox-models) with adjustment for age and sex. P-values are uncorrected for multiple testing.
Results: Eight SNPs showed significant association (p<0.05) with PR interval controlling for age and sex. One SNP showed difference in QTc intervals (change per minor allele) of -2.1 to +1.5 ms. Two SNPs were significantly (p<0.05) and one SNP was highly significantly (p=0.0022, rs251253, Chr 5) associated with QRS duration with effect sizes between -5.9 and +8.2 ms. Three SNPs showed association with QTC duration (p<0.05) with effect sizes of +1.1 to +3.4 ms. Four SNP rs1034 was significantly and five SNPs highly significantly (p<0.005) associated with the presence of the Brugada phenotype. Two SNPs (rs11047543, Chr 12 and rs17020136, Chr 2) were associated with the occurrence of symptoms (cardiac syncope, ventricular tachycardia, aborted cardiac arrest) with p-values of 0.0467 and 0.0154 and odds ratios of 3.35 and 2.61 respectively.
Conclusion: Several SNPs showed significant and highly significant association with different ECG traits and occurrence of symptoms in this cohort of E1748K carriers with a LQTS/BrS overlap disease. These results will require replication in additional cohorts, other ethnic groups and patient groups with LQT3 and Brugada syndrome. Functional studies will need to provide supporting evidence for the modifier function of highlighted genes and variants. However, these results provide promising initial evidence for the role of genetic modifiers in the phenotypic variation of LQT3 and BrS.

P5840 | BEDSIDE
Genetic markers of arrhythmia risk following acute coronary syndromes
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Background: Survivors of acute coronary syndromes (ACS) are at risk of ventricular arrhythmias, with a genetic component indicated both directly in markers of arrhythmia such as the QT interval. We investigated single nucleotide polymorphisms (SNPs) previously associated with the QT interval or arrhythmia for association with prolonged repolarisation & with sudden cardiac death/cardiac arrest (SCD/CA) in patients hospitalised for ACS.
Methods: Patients with ACS were enrolled in the prospective Coronary Disease Cohort Study & followed for clinical events for a median of 5.0 years (IQR 3.6, 6.8). Clinical, echo & neurohumoral data were collected for 12 months. 33 SNPs were genotyped & tested for univariate associations with time to SCD/CA, & with prolonged repolarisation (QTc interval >440ms, or if ECG LBBB & QRS duration >120ms, a JTc interval >370ms). After correction for multiple testing (false discovery rate), significant SNPs were tested in multivariable (MV) Cox or logistic regression models with pre-specified clinical predictors to determine whether the SNPs provided additional prognostic information (using an additive genetic model).
Results: 1657 Caucasian patients were included (104 SCD/CA events). Patients with SCD/CA were older (70 vs 67 years), were more likely to have diabetes, prior ACS & heart failure, renal dysfunction & LBBB on admission ECG than those without. 15 SNPs provided significant additional information. Four SNPs (KCNJ2), rs3864180 (GPC5), & rs876188 (C14orf64) were significantly associated with SCD/CA: rs17779747 with a decreased risk (HR = 0.66, 95% CI 0.48, 0.90, p=0.0008), & rs3864180 with an increased risk.
Results: Three SNPs were significantly associated with prolonged repolarisation at 12 months: rs10493466 and rs1214384 (NOS1AP), & rs7132154 (CAGNAC1). In a MV model with 12 month visit data (age, gender, NT-proBNP, LV end systolic volume, diabetes and LBBB) rs10494366 remained a significant predictor. No SNPs were significantly associated with prolonged repolarisation on the acute admission ECGs.
Conclusions: Three SNPs were associated with SCD/CA in patients following ACS, after adjustment for clinical covariates. Polymorphisms of the NOS1AP gene were associated with prolonged repolarisation 12 months post ACS, but not during the acute phase where the clinical predictors associated with the acute dominated the model.
sociation between atrial fibrillation (AF) and genetic variants in chromosome 4q25 which lie 120 kilobases from the nearest gene, PITX2 which has 3 known iso-
forms. PITX2c, which establishes the cardiac left-right axis, and PITX2a and b, which share a promoter and have unknown roles in cardiac development. In or-
der to investigate the mechanism of this association we mapped associations between single nucleotide polymorphisms (SNPs) and expression of PITX2 in human atrial tissue.

Methods: 122 right atrial appendage (RAA) and 12 left atrial appendage (LAA) samples were collected from patients undergoing cardiac surgery. 22 RAA sam-
pies and 6 LAA samples were from patients with a history of AF. In order to tag ge-
netic variation at the 4q25 locus, 42 SNPs were genotyped using the Sequenom platform. Expression of transcripts PITX2a/b and PITX2c were measured using TaqMan assays and normalised to three reference genes.

Results: The risk alleles of 3 variants associated with AF were associated with increased expression of PITX2a/b in RAA. rs17042711-A was associated with a 2.01-fold increase (p=5.34e-04), rs2200733 with a 1.95-fold increase (p=3.06e-03), and rs843082 with a 1.79-fold increase (p=1.13e-03). PITX2c expres-
sion was not associated with the risk SNPs. PITX2c expression was 3.32-
fold greater in LAA vs. RAA (p=5.56e-07), and PITX2c expression was 102-fold greater in LAA vs. RAA (p=3.20e-12).

Conclusions: Risk variants for AF are associated with markedly increased ex-
pression of PITX2a/b. This provides evidence for the overexpression of PITX2a/b as the underlying mechanism of the AF risk at this locus.

DEFINING PROGNOSIS IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

PS843 | BENCH

PITX2c gain-of-function mutation associated with atrial fibrillation

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Purpose: Genome-wide association studies have associated a genetic variant (rs2200733) located upstream of PITX2c with atrial fibrillation (AF), suggesting a potential role of PITX2c in AF. This study aimed to identify rare variants in PITX2c predisposing to AF.

Methods: The coding region of PITX2c was Sanger sequenced in two indepen-
dent AF cohorts.

Results: The p.Met207Val variant was identified in 5 patients in a European co-
hort of 402 patients with early-onset lone AF, but not in any of the 810 controls,
matched on ethnicity. The frequency of p.Met207Val was significantly higher in patients vs. 7031 controls (0.62% vs. 0.02%, OR=29.3, 95%, CI: 5.0 - 189.1, p=0.00002). The associations was replicated in an independent cohort of 462 Eu-
ropean American early-onset AF cases and 4760 controls (P=0.018). A pool ana-
yzes that included all 864 early-onset AF patients and all 11791 controls indicated a OR of 15.5 (0.46% vs. 0.03%, OR=15.7, 95%, CI: 5.0 - 50.8, p=1.9 x 10^-6).

Conclusions: We report a genetic association between the variant p.Met207Val and early onset AF, which is also replicated in an independent cohort. A pool anal-
yzes that included all 864 early-onset AF patients and all 11791 controls in-
dicated a OR of 15.5 (p=1.9 x 10^-6). This rare variant seems to be causing gain-of-function in PITX2c transactivation activity and in expression of genes re-
lated to AF.

PS844 | BEDSIDE

Incidences, determinants and prognosis of heart failure with normal ejection fraction in patients admitted for myocardial infarction; data from 91,360 patients in the SWEDEHEART registry


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Aim: To analyze the incidence and predictors of heart failure with normal EF (HFNEF) and its effect on outcome in acute myocardial infarction (AMI).

Design, setting and participants: The nationwide registry SWEDEHEART records baseline characteristics, treatments and outcome in consecutive patients with AMI admitted to all coronary care units in Sweden. In-hospital heart failure (HF) was defined as presence of crackles at admission (Killip class >1), or use of iv diuretics, or use of iv inotropics drugs during hospitalization. Reduced EF (REF) was defined as EF <50%; HFREF if there is HF with REF and NEF as <50% with out HF. All patients in the registry with AMI between 1998-2010 and an available EF were included in the analysis (n=91,360).

Results: Among patients with HF, the proportion of HFREF showed a relative in-
crease (18 to 31%). The incidence of HFREF in the total AMI population remained fairly unchanged (7.7 to 8.1%). The proportion of patients with HFREF declined dramatically (47 to 26%) as did the proportion of REF patients without HF (20 to 16%). AMI patients discharged with NEF without HF increased (25 to 50%). Age, female gender, diabetes, hypertension and renal failure were strong predictors of HFREF. Patients who developed HFREF had considerably higher mortality compared to patients without HFREF at any level of EF. (HR and 95% CI: REF without HF 1.6 [1.5-1.63], HFREF 3.3 [1.3-9.4] and HFREF 4.5 [4.4-4.6]) compared to patients with no HF and NEF, Fig 1).

Figure 1. Long-term mortality by type of HF.

Conclusion: The proportion of AMI patients with HFREF is unchanged over the years in contrast to a dramatic decline in the proportion of HFREF. Patients with
HFpEF have considerably worse prognosis compared to patients without HF regardless of EF. Clinical findings of HF are important to risk stratify patients after AMI.

P5845 | BEDSIDE
Prognostic impact of diastolic dysfunction in patients with heart failure with reduced ejection fraction: a cross-sectional analysis from the German Competence Network Heart Failure

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Background and purpose: In patients with heart failure with reduced ejection fraction (HFpEF), the presence of either systolic or diastolic left ventricular dysfunction is a well-acknowledged sign of an unfavourable prognosis. However, the detailed interaction of diastolic and systolic dysfunction (DD, SD) and its prognostic importance has not been systematically investigated so far.

Methods: From the German Competence Network Heart Failure, 1046 patients with HFpEF were analysed. Patients were grouped according to severity of left ventricular systolic dysfunction (SD: ejection fraction 35-50% (mSD) vs. ejection fraction <35% (SD)) and diastolic dysfunction (DD: E/E' <15 (mDD) vs. E/E' >15 (sDD)). Cumulative incidences of death and hospitalisation, mean time to hospitalisation or death, number of hospitalisations and length of hospital stay were studied during a median follow-up time of 5 years. Age-adjusted Cox regression was used to examine the prognostic utility.

Results: In patients with mSD (52.5% of the cohort), additional presence of sDD was associated with an absolute increase in overall mortality risk from 16.9% to 26.0% (p<0.004). Vice versa, in patients with mDD, additional sDD was associated with a risk increase from 16.9% to 34.0% (p<0.001). However, in patients with mSD, additional sDD hardly affected mortality risk (34.0 vs. 34.5%). With respect to cardiovascular death, similar results were demonstrated. Further, worse systolic function predicted endpoints as cardiovascular hospitalisation or cardiac death, numbers of hospitalisations, and length of hospital stay. Solely in patients with mSD mean time to cardiovascular hospitalisation or cardiac death showed a significant association with worsening diastolic function (p=0.017).

Conclusions: In patients with HFpEF, the evaluation of both, diastolic and systolic function, provides additional prognostic information. The degree of DD and its impact as a prognostic marker seems to be of higher relevance in patients with mid-to-severe SD.

P5846 | BEDSIDE
Outcome in heart failure with preserved ejection fraction strongly depends on right ventricular performance

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Background: Heart failure with preserved ejection fraction (HFpEF) is recognized as a major cause of cardiovascular morbidity and mortality. However, knowledge of risk factors in this specific patient population is scarce. Therefore, we aimed to improve risk prediction using a large variety of imaging modalities including hemodynamic, echocardiographic and cardiac magnetic resonance (CMR) imaging.

Methods: We prospectively included 142 patients with a definite diagnosis of HFpEF into our observational registry. Echocardiography, CMR and invasive hemodynamic assessments were performed in all patients. Hospitalization for heart failure and/or cardiac death as primary outcome was observed over a median follow-up of 10 months.

Results: We did not detect a significant association between imaging or functional parameters of the left ventricle and outcome in our adjusted analysis. However, the strongest risk factors were reduced right ventricular function measured using echocardiography (adj. HR 6.67; 95% CI 1.82-24.48; P<0.004) and systolic pulmonary arterial pressure using echocardiography (adj. HR per 1-SD 1.46; 95% CI 1.07-2.00; P=0.02) and invasive measurements (adj. HR per 1-SD 1.55; 95% CI 1.15-2.09; P=0.004). Kaplan-Meier analysis demonstrated a significant increase of the primary end-point in patients with significantly reduced right ventricular function (Fig. 1A; P<0.001). In patients with increased systolic pulmonary arterial pressure (Fig. 1B; P<0.001).

Conclusion: Outcome in patients with HFpEF does not correlate with left ventricular size or function but strongly depends on the performance of the right ventricle. For optimal clinical management thorough evaluation of the right ventricle is indispensable in affected patients.

P5847 | BEDSIDE
High prevalence of elevated high sensitivity troponin-T and reduction in levels by LCZ696 in heart failure with preserved ejection fraction in the PARAMOUNT trial

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Background: Elevation of high sensitivity troponin T (hs-TnT) has been shown to have prognostic significance in heart failure with reduced ejection fraction (HFpEF) but its significance in heart failure with preserved ejection fraction (HFpEF) is unclear.

Methods: We studied 296 patients from the Prospective comparison of ARNI with ACE inhibitor to Manage Outcome Of heart failure with preserved ejection fraction (PARAMOUNT) trial randomized to the angiotensin receptor neprilysin inhibitor LCZ696 or valsartan. We related troponin concentration to baseline clinical and echocardiographic measures and assessed the effect of randomized therapy on hs-TnT levels at 12 and 36 weeks.

Results: hs-TnT was elevated (>0.014 μg/L) in 55% of patients, and was associated with older age, a history of diabetes, higher NT-proBNP, lower eGFR, greater ventricular volumes and LV mass (Table). Treatment with LCZ696 led to a 12% reduction in hs-TnT at 12 weeks (p<0.05) and a 14% reduction at 36 weeks (p=0.03) compared with valsartan.

Characteristics by hs-TnT in HFpEF

<table>
<thead>
<tr>
<th>hs-TnT ≤0.014 μg/L</th>
<th>hs-TnT &gt;0.014 μg/L</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>70 (9)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>40 (30%)</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>684 (376-999)</td>
</tr>
<tr>
<td>eGFR (mL/min per 1.73 m2)</td>
<td>72 (21)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>113 (84%)</td>
</tr>
<tr>
<td>LA diameter (cm)</td>
<td>3.6 (0.4)</td>
</tr>
<tr>
<td>LV end diastolic volume (mL)</td>
<td>109 (30)</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>136 (33)</td>
</tr>
</tbody>
</table>
| LA, left atrial; LV, left ventricular; eGFR, estimated glomerular filtration rate.

Conclusion: Elevated hs-TnT is prevalent in HFpEF and is associated with other markers of disease severity. Neprilysin inhibition was associated with reduction in hs-TnT.

P5848 | BEDSIDE
References values for left ventricular diastolic function parameters: results from the NORRE study

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Purpose: Pulse Doppler and Tissue Doppler imaging (TDI) parameters have a fundamental role in the diagnosis of diastolic dysfunction. However, current guidelines do not take into account the possible differences related to age and gender. In this study, we reported gender and age specific differences in diastolic parameters in normal subjects.

Methods: The NORRE study is a multi-centre study investigating echocardiographic parameters in a large cohort of healthy population (n=734; 45.8±13.3years; 43.6% of male). E and A waves and isovolumetric relaxation time (IVRT) were measured. Mitral e' and a' wave velocities and IVRT were obtained from TDI at septal, lateral, inferior, anterior and posterior mitral annulus. Doppler parameters were analyzed according to gender and age (20-40; 40-60; >60 years).

Results: Higher E wave was observed in females (74.1 vs. 82.2 cm/s). No differences were found regarding A wave, E/A ratio and IVRT according to gender. Older patients showed a significantly lower E wave, E/A ratio, a higher A wave and longer IVRT. Regarding TDI parameters, there were no significant differences according to gender, except higher a' wave in males (10.4 vs. 9.2 cm/s). Older patients showed significant lower e', higher a' wave (8.7 vs. 10.1 vs. 11.3 cm/s) and longer IVRT in all the walls. There was a strong correlation between age and e'
Results: We also measured the ratio of mitral inflow velocity to e’ velocity (E/e’ ratio) and a’ wave (r=0.49, p<0.001). E/e’ ratio was also significantly higher in older patients.

Conclusions: Diastolic parameters are strongly influenced by age. This should be taken into account using individual parameters according to age categories in the evaluation of diastolic function.

P5854 | BESIDE
Which is better for improving diastolic function in patients with hypertension and left ventricular diastolic dysfunction, thiazide/ARB or CCB/ARB? Results of multicenter randomized trial
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Background: Hypertension is associated with an increased risk of diastolic dysfunction. In our previous studies, we demonstrated that reduction of blood pressure by a calcium channel blocker (CCB) or adding hydrochlorothiazide (HCTZ) to an angiotensin receptor blocker (ARB) is associated with improvement in left ventricular (LV) diastolic function in patients with hypertension and diastolic dysfunction. It remains unknown which combination is better to improve LV diastolic function, HCTZ/ARB or CCB/ARB. We conducted multicenter trial to compare the effects of HCTZ and CCB when used in combination with an ARB on LV diastolic function.

Methods: We enrolled 297 hypertensive patients with diastolic dysfunction from 31 sites. Patients received ARB monotherapy for at least 8 weeks, followed by additional use of HCTZ (n=149) or amlopidine (n=148) for 24 weeks after randomization. The primary end point is change in early diastolic mitral annular velocity (e’). We also measured the ratio of mitral inflow velocity to e’ velocity (E/e’ ratio) and brain natriuretic peptide (BNP).

Results: Blood pressure (BP) decreased from baseline to 24-week later in both groups (157/90 vs. 134/78 mmHg (P<0.001) in HCTZ/ARB; 156/88 vs. 130/75 mmHg (P<0.001) in CCB/ARB). There were no differences in magnitude of BP reduction and 24-week BP between both groups. The e’ velocity increased from 5.9 to 6.4 cm/s (Δ 0.5; P<0.001) in HCTZ/ARB and from 5.6 to 6.2 cm/s (Δ 0.6; P<0.001) in CCB/ARB. There was no difference in change in e’ velocity and 24-week e’ velocity between both groups. E’/e’ ratio was significantly improved only in HCTZ/ARB (E/e’: 11.4 vs. 10.2; log BNP 3.18 vs. 2.97, all P<0.001).

Conclusions: Both adding HCTZ or CCB to ARB are associated with improvement in LV relaxation (increase in e’ velocity). The combination of ARB and HCTZ may have a more beneficial effect on lowering BP increase (decrease in E/e’ ratio and BNP).

P5850 | BESIDE
Comparison of the echocardiographic definition of left ventricular diastolic dysfunction using the 2007 ESC and the 2009 EAE/ASE recommendations in metabolic syndrome patients
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Purpose: Identifying patients at risk for diastolic dysfunction (DD) may help prevent the occurrence of heart failure with normal ejection fraction (HFNEF), which is associated with high mortality and mortality. Currently there is no consensus on how to define DD. We compared clinical predictors of DD and diagnostic accuracy of DD in patients with metabolic syndrome (MetS) using the 2007 European consensus statement and the 2009 EAE/ASE recommendation.

Methods: Risk-diastolic heart failure (METR-DHF) is a cross-sectional cohort of 496 subjects with MetS (NCEP III criteria) and normal left ventricular (LV) systolic function - EF >50% and LV end-diastolic volume index <97 mm3/m2. Diastolic dysfunction was defined first, according to the 2007 European consensus statement on the diagnosis of HFNEF: as possible DD (E/E’>8) and definite DD (E/E’>15 or E’<15 + additional specified ECHO criteria, such as LV mass index >122 for women / >149 mm2/m2 for men), and secondly, according to the 2009 European EAE/ASE recommendation as: Septal E’<8 or Lateral E’<10 or Left atrial volume (LA >44 ml/m2), with seventy grading (grade 1, 2 or 3 or 4) additional ECHO criteria. A multivariable binary logistic regression analysis was used to assess clinical predictors of DD and diagnostic accuracy of DD.

Results: According to the 2007 ESC consensus, 231 (47%) patients had possible DD and 89 (18%) had definite DD. According to the 2009 EAE/ASE recommendation, 341 (69%) patients had DD, with 177 (36%) having mild, 162 (32%) moderate, and 4 (1%) severe dysfunction. Using the 2007 ESC consensus, multivariable analysis using either the criteria of possible or definite DD showed that older age, female sex, higher BMI, lower left ventricular (LV) systolic function and prescription of beta blockers were associated with a higher risk of DD. In addition, elevated heart rate and prescription of digoxin were associated with definite DD. Using the 2009 EAE/ASE recommendation only older age and non-prescription of digoxin were associated with a higher risk of DD. The C statistic was 0.79 (CI 0.75-0.83) for the 2007 ESC consensus, and 0.71 (CI 0.66-0.76) for the 2009 EAE/ASE recommendation.

Conclusions: In patients with MetS, only the use of the 2007 ESC consensus identified DD to be associated with MetS related risk factors. Furthermore, diastolic dysfunction should not be considered as a marker of cardiovascular risk and provides further support for the 2009 European EAE/ASE consensus rather than the 2007 ESC consensus. Future efforts to improve the diagnosis of DD with novel biomarkers should demonstrate accuracy superior to the 2007 ESC consensus.

NEWS FROM THE AORTIC VALVE

P5851 | BESIDE
Impact of periprocedural stroke on midterm mortality after transcatheter aortic valve implantation
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Purpose: Stroke occurrence in patients undergoing transcatheter aortic valve implantation (TAVI) has been reported among complications in several studies. The aim of this study was to assess the impact of periprocedural stroke on mortality at mid-term follow-up after TAVI.

Methods: Six-hundred-and-fifty-six patients with aortic stenosis underwent TAVI with the CoreValve system (92.8%) or the Edwards SAPIEN valve system (7.2%). Stroke and transient ischemic attack were defined according to the Valve Academic Research Consortium-2 consensus document. A cerebrovascular accident (CVA) was defined as any stroke or transient ischemic attack within 72 hours from the index procedure. Separate multivariable Cox regression analyses were performed to calculate hazard ratio (HR) with 95% confidence intervals (CI) for mortality for periprocedural stroke and periprocedural CVA, respectively.

Results: Periprocedural success occurred in 97.4% of patients. The incidence of any stroke and of CVA after the index procedure was 2.4% and 2.7%, respectively. Periprocedural strokes accounted for 56.2% of all strokes and occurred in 1.4% of patients, whereas in CVA occurred in 1% of patients. Periprocedural stroke or CVA were defined as stroke or CVA occurring within 72 hours from the index procedure. Separate multivariable Cox regression analyses were performed to calculate hazard ratio (HR) with 95% confidence intervals (CI) for mortality for periprocedural stroke and periprocedural CVA, respectively.

Conclusions: More than half of strokes and CVA following TAVI occur within the periprocedural period. Periprocedural stroke and CVA are independent predictors of all-cause mortality at mid-term follow-up. Strategies for periprocedural cerebrovascular events prevention are needed.

P5852 | BESIDE
Impact of aortic annulus size on valve hemodynamics and clinical outcomes following transcatheter and surgical aortic valve replacement: Insights from the PARTNER trial
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Purpose: The objectives of this study were to evaluate valve hemodynamics and clinical outcomes in those patients included in the PARTNER randomized con-
trolled trial (RCT) cohort A and the PARTNER non-randomized continued access (NRA) cohort according to aortic annulus size. **Methods:** Patients included the RCT (n=574) and NRA (n=1358) cohorts were divided in tertiles according to aortic annulus diameter (small, medium, large aortic annulus; SAA, MAA and LAA, respectively) as measured by transthoracic echocardiography. Moderate-to-severe paravalvular leak (PL) was defined as an effective aortic orifice area of <0.85 cm²/m². **Results:** In the RCT, patients who had TAVR in the SAA group had a lower incidence of PL (39% vs. 63%, *P*<0.01) with only a mild increase in moderate-to-severe PL. The leak rate was 0% in the SAA group, while no differences in PL were observed in other groups. **Conclusion:** In the RCT, the SAA was associated with lower PL. The results of the NRA were in line with those of the RCT. In conclusion, the SAA size should be considered in the evaluation of high-risk patients who are candidates for AVR, and the results of this study should be confirmed in future studies.

**P5853 | BEDSIDE**

Real-world multicenter prospective registry using the direct flow medical transcatheter aortic valve system for the treatment of severe aortic stenosis: comparison with the SAVR trial

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**Purpose:** To assess whether an echocardiographic marker of left ventricular (LV) filling pressure predicts future indication for aortic valve replacement (AVR) in patients with preserved LV function.

**Methods and results:** LV filling pressure was estimated by the ratio between early diastolic mitral inflow and mitral annulus velocity (E/e). The median follow-up time was 27 (IQR 20-44) months. Indication for AVR due to onset of symptoms was observed in 43 patients (41%). No SCD was observed. Aortic valve calcification grade 4, global longitudinal strain, E/e, and pro-brain natriuretic peptide (BNP) were strong univariable predictors of AVR. In a multivariable Cox proportional hazard regression model including age, gender and the above variables only E/e was significantly associated with future indication of AVR (HR: 1.10 (95% CI: 1.01 to 1.20), *P*<0.03). Figure 1 shows a Kaplan-Meier plot of event-free survival based on E/e dichotomized by the median (E/e median 12).

**Conclusion:** In the present study E/e is a strong predictor of indication for AVR in patients with asymptomatic AS and preserved LV EF. E/e as a marker of LV filling pressure could be an early marker of subclinical symptom development in asymptomatic AS.

**P5854 | BEDSIDE**

Prognostic value of left ventricular filling pressure in asymptomatic aortic valve stenosis

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**Purpose:** To assess whether an echocardiographic marker of left ventricular (LV) filling pressure predicts future indication for aortic valve replacement (AVR) in patients with asymptomatic aortic valve stenosis (AS) and preserved left ventricular ejection fraction (LVEF).

**Methods:** We recruited 104 asymptomatic patients with AS and preserved LVEF (>50%). A baseline research transthoracic echocardiography (TTE) was performed on all patients, and the results were blinded for the treating physician. LV filling pressure was estimated by the ratio between early diastolic mitral inflow and mitral annulus velocity (E/e). Outcome was defined as indication for AVR determined by the treating physician or sudden cardiac death (SCD).

**Results:** The mean (SD) age was 72 (9) years, 32% were women and mean AVA by TTE was 1.02 (0.28) cm². The median follow up time was 27 (IQR 20-44) months. Indication for AVR due to onset of symptoms was observed in 43 patients (41%). No SCD was observed. Aortic valve calcification grade 4, global longitudinal strain, E/e, and pro-brain natriuretic peptide (BNP) were strong univariable predictors of AVR. In a multivariable Cox proportional hazard regression model including age, gender and the above variables only E/e was significantly associated with future indication of AVR (HR: 1.10 (95% CI: 1.01 to 1.20), *P*<0.03). Figure 1 shows a Kaplan-Meier plot of event-free survival based on E/e dichotomized by the median (E/e median 12).

**Conclusion:** In the present study E/e is a strong predictor of indication for AVR in patients with asymptomatic AS and preserved LVEF. E/e as a marker of LV filling pressure could be an early marker of subclinical symptom development in asymptomatic AS.
Patients were dichotomized based on SVI (<35ml/m² vs. ≥35ml/m²) and LV GLS (<−15% vs. −15%). The end-point was all-cause mortality.

**Results:** During a median follow-up of 1.8 years (interquartile range 0.5–3), survival was better for patients with SVI ≥35ml/m² and GLS <−15% as compared to patients with SVI <35ml/m² and GLS −15% (log-rank p=0.01) (Figure). The addition of GLS (X² 18.00, p=0.02 and C-statistics 0.75) and SVi (X² 28.62, p=0.001 and C-statistics 0.69) improved the risk stratification of patients with LGeprEF severe AS undergoing AVR.

**Conclusion:** SVI and LV GLS are independently associated to survival after AVR in LGeprEF severe AS patients.

**P5857 | SPOTLIGHT**

High-sensitivity Troponin I concentrations are a marker of an advanced hypertrophic response and adverse outcomes in patients with aortic aortic stenosis


**Purpose:** High-sensitivity cardiac troponin I (cTnI) assays hold promise in detecting the transition from hypertrophy to heart failure in aortic stenosis. We sought to investigate the mechanism for troponin release in patients with aortic stenosis and whether plasma cTnI concentrations might predict long-term outcome.

**Methods:** In 122 patients with aortic stenosis (71 [65-77] years, 87% males, and aortic valve area 1.0 ±0.4 cm²), left ventricular (LV) mass and myocardial fibrosis (late-gadolinium enhancement (LGE) and T1 mapping) were assessed by 3T cardiac magnetic resonance, and aortic stenosis severity by echocardiography.

**Results:** From the Scottish Aortic Stenosis and Lipid Lowering Trial (SALTIRE) trial. Baseline plasma cTnI concentrations were measured in all 253 patients using a high-sensitivity assay.

**Results:** The indexed LV mass and extent of LGE were associated with cTnI concentrations independent of age, sex, coronary artery disease, aortic stenosis severity and diastolic function (P<0.01 for both) (Fig. 1A). Over a median follow-up of 10.6 years (1.178 patients-years), 24 patients died from a cardiovascular cause and 60 patients had an AVR. Plasma cTnI concentrations predicted AVR and cardiovascular deaths (HR 1.62; 95%CI 1.11–2.36) independent of age, sex, ejection fraction and aortic stenosis severity (Fig. 1B).

**Conclusions:** In patients with aortic stenosis, cTnI identifies an advanced hypertrophic response and replacement myocardial fibrosis, and predicts AVR and cardiovascular deaths.

**IMPROVING OUTCOMES IN STEMI PATIENTS**

**P5858 | BENCH**

Door to balloon time less than 30 minutes telemetry of 12 canal ecg in the prehospital phase of acute STEMI results for the period of 7 years from 2007 until 2013 including 1050 patients

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**Purpose:** For the acute ST-elevated myocardial infarction (STEMI) and the primary PCI with announcement there is a “door to balloon time” (DBT) less than 30 minutes demanded. In both Bavarian counties Traunstein and Berchtesgadener Land a “myocardial infarction network” for about 300,000 people with standardised preclinical and clinical procedures for the heart attack was established 2007. The preclinical derived 12-canal ECG is sent automatically to the receiving terminal of the cardio logical intensive care unit, is taken up there immediately by an experienced doctor and telephone contact to the emergency doctor is compounded. The aim of this study was to examine it whether a clear reduction of the DBT can be reached by the systematic preclinical use of the 12 canal ECG telemetry in our administrative districts. The period of the evaluation of the data applies was 7 years from January 2007 to December 2013.

**Methods:** All involved emergency doctors (n=70) were trained 2 x yearly about sense, purpose and use of the 12 canal ECG telemetry. The acceptance of using the telemetry was determined about the % of ECG with STEMI, which were send by telemetry in the years 2007 and 2013. The DBT time was automatically recorded from the time the patient arrived in the hospital until the time of the balloon-insufflation. Over the period of 7 years from January 2007 to December 2013 1050 patients with the diagnosis “STEMI” were enclosed in the study. Hereof were “STEMI with telemetry by the emergency doctor” (N=389 patients, 37%), without telemetry there are following groups: “STEMI sending from a peripheral hospital” (N=367 patients, 35%), “STEMI from patients come into the emergency room” (N=189 patients, 18%), “STEMI without telemetry by the emergency doctor” (N=105 patients, 10%).

**Results:** Because of intensive instruction of the emergency doctors the number of telemetry ECG in comparison from the years 2007 to 2013 could be increased from 40% up to 80%. The DBT for the “STEMI with telemetry by the emergency doctor” was in median 28 minutes (SD 14 minutes), for the group “STEMI without telemetry” the DBT was at least 72 minutes (SD 32 minutes). The data distinguished significant.

**Conclusion:** The telemetry of 12 canal ECG helps the emergency doctor with the diagnosis STEMI and is a very important tool for an optimal preclinical and clinical management for the acute coronary syndrome, above all it helps to prepare the catheter lab in time. With the use of 12 canal ECG telemetry it was possible to get a door to balloon time under 30 minutes (in median 28 minutes) over the period of 7 years.

**P5859 | BEDSIDE**

The importance of beta-2-agonists in myocardial infarction: findings from the eastern danish heart registry

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**Purpose:** β2-agonists are some of the most prescribed drugs worldwide and some studies have suggested that use of B2As is associated with an increased risk of myocardial infarction. Yet, angiographical coronary data and longitudinal outcomes data are sparsened.

**Methods:** Using a novel data-linkage of the Eastern Danish Heart Registry and nationwide administrative registries (Dec. 1998 to Dec. 2012), we identified a cohort of patients referred for acute coronary angiography due to ST-elevation MI (STEMI). B2A use was determined via prescription claims 12 months prior to date of admission. Clinical and angiographical findings compared between B2A users and non-users. Subsequent mortality associated with the use of B2A was estimated by Cox proportional hazard analyses.

**Results:** Of 91,124 patients undergoing coronary angiography, 10,521 were acutely referred due to STEMI. Of these, 948 (9%) patients used B2As and were...
characterized by older age (median age 68 years vs. 63 years; \(P < 0.0001\)) and fewer were men (males: 57% vs. 74%; \(P < 0.0001\)). The number of patients with peripheral vascular disease and hypertension was significant higher among B2A users but comorbidities were otherwise equally distributed in the two groups and so was the frequency of current smokers. For angiographical characteristics, B2A users more often had no acute coronary occlusion (16% in B2A vs. 10% in non-users; \(P < 0.0001\)). All-cause mortality during up to 14 years of follow up was significant higher among the B2A-user group compared to the non-user group (Hazard ratio 1.47, 95% CI 1.28-1.69; \(P < 0.0001\)).

Conclusion: Use of B2As is associated with an increased frequency of STEMI without an acute coronary occlusion compared with non-users. Yet, B2A use is also associated with greater long-term mortality.

P5860 | BESIDE

Does the right ventricular infarction actually increase the rate of mortality for PCI patients in the PCI era?

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Summary: The aim of the present retrospective observational study was to assess the efficacy of percutaneous coronary intervention (PCI) in patients with STEMI and right ventricular infarction (RVI). The main outcome for patients was in-hospital mortality, and secondary outcomes were heart failure, second-degree and complete AV block, and severe mitral regurgitation.

Methods: In total, we enrolled 535 patients with STEMI. RV involvement was identified from ECG and/or echocardiographic evidence of right ventricular wall motion abnormalities. RV involvement was diagnosed in 79% (33.5%) patients; 97 patients in the RVI group and 154 patients in the non-RVI group underwent PCI. Groups without PCI consisted of patients who refused the invasive procedure. Patients who had undergone fibrinolytic therapy were excluded from the study.

Results: There was no significant difference in in-hospital mortality between patients with and those without RVI (RVI 16.5% vs. non-RVI 12.6%; \(P > 0.01\)), but we found that patients with RVI without reperfusion had a higher mortality rate than patients without RVI (RVI 35.4% vs. non-RVI 21.6%; \(P < 0.02\)). In the RVI group, the heart rate failure (RVI 29.0% vs. non-RVI 15.4%; \(P = 0.0002\)), AV block II-III d. (RVI 17.9% vs. non-RVI 4.8%; \(P < 0.0001\)), and severe mitral regurgitation (RVI 21.2% vs. non-RVI 10.9%; \(P = 0.0001\)) were considerably higher than in the non-RVI group.

Conclusion: PCI in the RVI group was associated with a higher reduction of in-hospital mortality (RVI 21% vs. non-RVI 10.9%; \(P = 0.0001\)) than in the non-RVI group. PCI in the RVI group was associated with a higher reduction of in-hospital mortality rate (RVI PCI without reperfusion 14.5% vs. non-RVI PCI 9.4%; \(P = 0.0001\)) than in the non-RVI group (non-RVI PCI without reperfusion 21.6% vs. non-RVI PCI 8.3%; \(P = 0.0001\)). There was no relevant difference in mortality rates between PCI patients with and without RVI (RVI 8.2% vs. non-RVI 6.3%; \(P = 0.6\)).

P5861 | BENCH

Aspiration thrombectomy in ST segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: Meta-analysis of 16 randomized trials

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Objective: Primary percutaneous coronary intervention (PCI) has become the first line of therapy for acute ST elevation myocardial infarction (STEMI) due to providing effective epicardial and myocardial perfusion. However, mortality rate still high in some patients who underwent PCI because of ineffective epicardial and myocardial perfusion. The use of aspiration thrombectomy might be useful in this group but there is contradictory evidence in current trials. Therefore, we performed a meta-analysis that compared aspiration thrombectomy with primary PCI and PCI alone.

Methods: Sixteen trials comparing primary PCI (n=5262) and primary PCI plus aspiration thrombectomy (n=5256) were included in the meta-analysis. We calculated the risk ratio for epicardial and myocardial perfusion, and clinical outcomes. We performed a meta-analysis of association with risk ratios and 95% confidence interval. Risk ratios were calculated for mortality (all cause death, re-Infarction, target vessel/lesion revascularization, stent thrombosis and cerebrovascular accident) and composite major adverse cardiac outcome (all cause death, re-Infarction, target vessel/lesion of revascularization).

Results: In aspiration thrombectomy group post-procedural TIMI III flow, post-procedural MBG II-III flow and post-procedural ST resolution on ECG were more frequent than PCI alone group. The results revealed that all cause death incidence was comparable between thrombectomy group (2.9%) and conventional primary PCI group (3.4%) (HR: 0.861, 95% CI: 0.697-1.062, \(p = 0.16\)). Besides, re-infarction frequency was 0.8% in the thrombectomy arm and 1.3% in the conventional primary PCI arm (HR: 0.632, 95% CI: 0.433 to 0.923, \(p = 0.017\)). While TVR/TLR frequency was 3.9% in thrombectomy arm, it was 5.2% in the conventional primary PCI arm (HR: 0.795, 95% CI: 0.664-0.952, \(p = 0.013\)). MACE frequency was 7.3% in thrombectomy arm and it was 9.1% in the conventional primary PCI arm (HR: 0.797, 95% CI: 0.704-0.903, \(p < 0.001\)).

Conclusion: Aspiration thrombectomy improved epicardial and myocardial perfusion, reduced the rate of re-Infarction and target vessel / lesion of revascularization, however did not reduce the rate of mortality.
all STEMI and NSTEMI pts who underwent coronary angiography and/or (pri-
mary) PCI in the period January 2010 – December 2012. Primary endpoint was
30-day all-cause mortality. Choice of access was left to the discretion of the
cardiologist. All safety- and clinical parameters, were performed by 2 independent
investigators.

Results: Of the 3384 ACS pts, coronary angiography was performed in
2950/3384 (89%) and in 671/2950 (23%) pts by radial access. PCI was
performed in 2161/2950 (74%) of the pts. No differences in baseline or angiographic
characteristics were present between radial vs femoral access patients except
for diagnosis of STEMI: 54.6% vs 60.0%, p=0.011, IABP use: 1.1% vs 6.7%,
p<0.001, and Killip class: 2: 8.6% vs 12.9%, p=0.012. The primary endpoint
occurred less often in the radial group as compared to the femoral group (1.7% vs
4.8%, p<0.014). Also 30-day net adverse clinical events (NACE) occurred less
often in the radial group (6.3% vs 10.8%, p<0.001). After multivariable correction,
radial access remained an independent predictor for 30-day mortality (HR 0.433;
95% CI, 0.221 – 0.850, p=0.015, see Fig. 1).

Conclusions: Radial access in all comers ACS patients significantly reduced 30-
day mortality and 30-day NACE compared with femoral access, with similar PCI
success. Radial access remained an independent predictor for 30-day all-cause mortality.

P5866 | BEDSIDE
Surgical outcomes of patients with acute coronary syndromes undergoing coronary artery bypass grafting: Results from the North-Rhine-Westphalia surgical myocardial infarction registry
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Objectives: To evaluate in-hospital mortality of patients referred to urgent coro-
ary artery bypass grafting (CABG) with acute coronary syndromes (ACS), in-
cluding ST-elevation or non-ST-elevation myocardial infarction (STEMI/NSTEMI) or unstable angina.

Methods: Between 01/2010 and 05/2012 patients undergoing urgent CABG with ACS were prospectively entered into a registry by four participating cardiac surgery centers in North-Rhine-Westphalia. Demographic data and over one-
hundred perioperative variables were recorded, including in-hospital all-cause mortality. After univariate analysis, relevant perioperative variables were entered into a multivariable logistic regression model to identify independent predictors for in-hospital mortality.

Results: A total of 1197 patients (age 68±11 yrs, males 78%, log. EuroSCORE 24±21%) were admitted to CABG surgery with STEMl (25%), NSTEMI (65%) or UA (25%). Three-veesel coronary artery disease was present in 80% with main-
stem involvement in 46% of patients. On-pump CABG surgery was performed in
92% (CPB-time, 103±43 min, aortic cross-clamp time, 65.2±6 min; 53% blood
cardioplegia) with a mean of 2.5±0.7 bypass grafts and 91% LITA use. Overall
in-hospital mortality was 7.4%, with 12.7% in STEMI patients, 5.6% in NSTEMI
and 5.0% in patients with UA (P<0.001). Multivariable logistic regression analysis
revealed age, female gender, preoperative troponin I, LVEF, on-pump surgery and
the need for ECMO therapy to be independently predictive for in-hospital mortality
(P<0.05). Importantly, the preoperative use of aspirin/clopidogrel, β-blockers, or
statins, the use of preoperative IABP support as well as the type of cardioplegia
(crystalloid/blood) were not associated with in-hospital mortality.

Conclusions: CABG in patients with ACS is still linked to substantial in-hospital mortality. Especially for patients with STEMI reliable identification of preoperative predictors is mandatory to improve surgery outcomes.

TAVI: WHAT PREDICTS OUTCOME?

P5865 | BEDSIDE
Impact of mixed aortic valve stenosis on outcomes and postprocedural paravalvular aortic regurgitation in patients undergoing TAVI: results from the international multicentric registry PRAGMATIC
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Background: Residual postprocedural paravalvular aortic regurgitation (PPAR) is one of the main complications of transcatheter aortic valve implantation (TAVI) procedure. Only few data are available on the impact of baseline aortic regur-
gitation on clinical outcomes and PPAR.

Methods: Data from 4 experienced European centers were pooled together and analysed. AR grade was defined according to the European As-
sociation of Echocardiography (EAE) guidelines. Population was subdivided in patients affected by Pure Aortic Stenosis (PAS, <1+3+) and by Mixed Aortic Stenosis (MAS, >1+3+). Study objectives were the incidence of PPAR, Valve Academic Research Consortium 2 (VARG-2) outcomes at 30 days, 1 year and 2 years, and long-term follow-up total and cardiovascular mortality.

Results: In total, 1091 patients were included: 432 (39.5%) with MAS and 659 (60.5%) with PAS. At 30 days there were no differences in all-cause (6.4% vs. 6.3%; p=0.930) and cardiovascular mortality (5.5% vs. 4.2%; p=0.315), however a greater incidence of major bleeding (23% vs. 16.5%; p=0.011), spontaneous myocardial infarction (2% vs. 0.3%; p=0.019) and PPAR ≥1+3+ (43% vs. 27%; p<0.001) was observed in patients with MAS. Conversely, no differences were found in the incidence of PPAR ≥2+3+ (3% vs. 2%; p=0.137). Of note, MAS resulted an independent predictor of PPAR ≥1+3+ at multivariable analysis. At a median follow-up period of 421 days (IQR 252 – 710), patients with MAS had a greater all-cause mortality (30% vs. 24%; p=0.047) and cardiovascular mortality (17% vs. 12%; p=0.023).

Between MAS and PAS patients that developed PPAR ≥1+3+, no difference in mortality at 30 days and at long-term follow-up was present. Conversely, in pa-

Conclusions: The present cohort, baseline MAS has a high prevalence and is associated with a higher incidence of PPAR and increased all-cause and car-
diovascular mortality when compared to patients with baseline PAS at a median follow-up period of 421 days. In patients who developed PPAR ≥2+3+, baseline MAS trended to be associated with improved long-term survival.

P5866 | BEDSIDE
Risk factors and clinical significance of intra-procedural haemodynamic instability in patients undergoing transcatheter aortic valve implantation
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Objectives: The aim of this study was to investigate the causes, risk factors and clinical significance of haemodynamic instability (HI) during TAVI procedure.

Methods: From November 2007 to September 2013 all patients consecutively treated in our center were retrospectively analysed. HI was defined as a drop
of mean arterial pressure >20 mmHg with a heart rate (HR) >100 or <50 beats/min for ≥1 min. Causes of HI were broadly classified in those occurring post-preparatory balloon aortic valvuloplasty (PBAV), in patients whom a PBAV was performed, and post-valve implantation (VI). Each group was compared with a control group where intraprocedural HI did not occur.

Results: Overall, of 538 patients who underwent TAVI, 35 (7.4%) developed HI. Of these 18/453 (3.9%) developed HI after PBAV, while 19/538 (3.5%) developed HI after VI. Causes of HI after PBAV included severe aortic regurgitation (AR, 50%), undergoing atrial fibrillation (44.4%) and aortic annulus rupture (5.5%). Causes of HI after VI included aortic dissection (10.5%), cardiac tamponade (73.6%), cardi-
O PRA M A R I OB SAT ORY O NSE (10.5%) and severe AR (5.2%). Patients that developed HI after PBAV had higher all-cause and cardiovascular mortality at 30 days (respectively, 11.1% vs. 1%, p<0.001; and 11.1% vs. 1.8%, p=0.009), more frequently required urgent cardiac surgery (11.1% vs. 1.4%; p=0.002), a 2+ valve (12.5% vs. 3%; p=0.038), had higher incidence of atrial fibrillation (43.8% vs. 19.2%; p=0.016) and cardiac tamponade (12.5% vs. 2.7%; p=0.027). No differences were found in mortality at 2 years of follow-up. Predictors of post-procedural HI were BAV diameter, LVEDP and moderate-severe pulmonary hypertension.

Patients that developed HI after VI had higher rates of all-cause and cardiovas-
cular mortality at 30 days (respectively, 26.3% vs. 2.7%, p<0.001; and 21.1%
A reduction of the valve device price would increase the probability of groups of patients. In a European setting, the high cost of the valve in relation to effective compared to AVR. T AVI appears to be cost-effective in specific sub-

The main causes of HI after PBAV were severe AR and new-onset arhythmia, while after implantation was cardiac tamponade. HI after PBAV had a higher risk but did not affect significantly. HI after T AVI had a negative impact on both 30-day and long-term survival.

**P5868 | BEDSIDE**

Cost-utility of transcatheter aortic valve replacement compared with surgical aortic valve replacement in high-risk patients with severe aortic stenosis: Prospective observational study

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**Purpose:** Studies assessing cost-effectiveness of transcatheter Edwards Sapiens (ES) TAVI vs aortic valve replacement (AVR) are scanty, use data from a single randomized clinical trial and differ depending on the health system (US vs Europe). In addition there are no data concerning Medtronic Corevalve (MC). We sought to estimate the cost-utility of the two transcatheter TAVI modalities vs conventional surgery using data from “real life” patients.

**Methods:** Patients were recruited prospectively in 7 hospitals. Follow-up was performed at 1, 3 and 6 months after intervention. We measured utility from EQ5D data. We calculated differences in costs and QALYs between ES or MC versus AVR and the incremental cost-utility ratio (ICER) comparing ES vs AVR and MC vs AVR. Additionally, we performed net-benefit regressions on different willingness to pay threshold values (ranging from 0 to €50,000) and we estimated the adjusted ICERs. A willingness to pay threshold of 30,000 €/QALY was assumed for interpreting the results. Additional analyses were performed for different subgroups and scenarios.

**Results:** Data from 186 patients were analyzed: 48 in the ES-TAVI group, 86 in the MC-TAVI group and 52 in the AVR group. Mean logistic Euroscore (SD) was: ES: 14.3 (10.4), MC: 14.7 (9.9), AVR: 14.5 (6.9). Overall cost of ES-TAVI was €7,202 higher than AVR and the QALY benefit was 0.045, resulting in an ICER of 161,086 €/QALY. The adjusted ICER using the net-benefit approach was 131,000€/QALY. The cost of MC-TAVI was €7,476 higher than AVR and the QALY benefit was 0.003, resulting in an ICER of 2,451,568 €/QALY. The adjusted ICER was not estimable because MC-TAVI was non beneficial when adjusting for baseline characteristics. The results did not substantially change considering additional analyses except for: 1) in patients with preoperative higher severity in the ES-TAVI group 2) the adjusted ICER was 2,286 €/QALY for MC-TAVI; 2) a 30% reduction in the cost of the TAVI device lead to ES-TAVI being dominant over AVR; and 3) an increase of 30% in all costs except the price of the device lead to an adjusted ICER of 33,186 €/QALY for ES-TAVI. Considering TAVI group’s country setting, transcatheter TAVI is not likely to be cost-effective compared to AVR. TAVI appears to be cost-effective in specific subgroups of patients. In a European setting, the high cost of the valve in relation to global health care costs is the main determinant of the unfavorable cost-utility of ES-TAVI. A reduction of the valve device price would increase the probability of TAVI being cost-effective and spread its use.

**P5869 | BEDSIDE**

In-hospital events in a propensity matched cohort of percutaneous vs surgical aortic valve replacement patients

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**Background:** Transcatheter valve implantation (TAVI) is an option in patients (p) with severe aortic stenosis deemed inoperable or of high surgical risk. However, direct comparisons between surgical aortic valve replacement (SAVR) and TAVI are subject to several limitations, among them selection bias.

**Aim:** Evaluate baseline characteristics and in-hospital outcomes of p submitted to TAVI versus SAVR after propensity matching in a real world cohort.

**Methods:** 941 consecutive p submitted to AVR (TAVI n=49;biological SAVR n=892) were analysed. Multivariate logistic regression was used to determine baseline predictors of treatment by TAVI. These variables were used to create a propensity-score model of P were then submitted to nearest neighbour matching in a 1:4 ratio (1 TAVI p for 4 SAVR p).

**Results:** In pre-match analysis, significant differences were found on baseline characteristics regarding age (TAVI vs SAVR, 80.10;6.85 vs 73.52;6.04). Log Euroscore (15.93;9.31 vs 8.09;6.66), left ventricular (LV) dysfunction (53.06% vs 19.84%), chronic kidney disease (38.78% vs 19.17%) and chronic obstructive pulmonary disease (COPD; 26.53% vs 9.53%) - p<0.001 for all. In the SAVR group post propensity matching, there were no significant differences vs TAVI p (p=0.78, Log Euroscore: 17.06, LV dysfunction: 58.67, CKD:53.06, COPD: 27.55, p<NS for all).The results in in-hospital events are presented in Table 1:

<table>
<thead>
<tr>
<th>Group</th>
<th>TAVI</th>
<th>SAVR</th>
<th>post matching</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>49</td>
<td>188</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>9.16%</td>
<td>9.16%</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Length of ICU stay</td>
<td>6.68</td>
<td>6.05</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.00%</td>
<td>3.33%</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>12.24%</td>
<td>13.70%</td>
<td>0.0037</td>
<td>NS</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>26.53%</td>
<td>15.3%</td>
<td>-0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding with reintervention</td>
<td>4.08%</td>
<td>2.04%</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Infection</td>
<td>4.08%</td>
<td>2.04%</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

**Conclusions:** In this propensity-matched cohort of p submitted to TAVI and SAVR, in-hospital mortality was similar. Different complications were observed in the two groups, with pacemaker implantation more likely in the TAVI group and acute renal injury in the SAVR group. Both modalities were similar in respect to other in-hospital events.

**P5870 | BEDSIDE**

One year of outpatient percutaneous coronary intervention: safe, comfortable and money saving

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**Purpose:** To start an outpatient percutaneous coronary intervention (PCI) program and to analyse its safety, patient satisfaction and the potential cost reduction.

**Methods:** Patients submitted for coronary angiography and elective PCI were evaluated during 2013. Those older than 80 years, with left ventricular ejection fraction <35%, with renal glomerular filtration rate <30 ml/min and allergic to clopidogrel and other antiplatelet drugs were excluded. In case of non-high risk coronary anatomy and no PCI complications, they were selected for same-day discharge after 6 hours of clinical surveillance, checked the morning after and followed for 1 month. Then, we conducted a patient satisfaction survey.

**Results:** 72 patients were admitted as candidates for day-case PCI. 47 (65%) stayed overnight at hospital. Reasons for non-discharge included high-risk coronary anatomy and no PCI complications. 84% of patients were discharged home. None patient needed to call medical emergency
services during the night at home. The morning after, there were no complications at the puncture site, 2 patients showed negative T waves on electrocardiography and an asymptomatic new onset atrial fibrillation was diagnosed and solved with antiarrhythmic therapy. 4 patients had Troponin I levels above 1 ng/ml. At one month follow up there were 2 (8%) adverse events: 1 subacute bare-metal stent thrombosis at 1 month and 1 superficial infection treated to measure to diagnose of colon carcinoma. Both would not be avoided in case of in-hospital overnight observation.

Patients’ opinion: High patient satisfaction score (ranges from 1 to 5, mean 4.4±0.9) in the survey indicated that day-case PCI was popular with the patients. 22 patients (88%) would choose same-day discharge in case they should repeat PCI.

Expense: In our hospital, the mean cost of PCI is 2,480 €. A day of hospitalization costed 400 €, and as a day-case procedure the hospital costed 650 €. The study minimizes the problems of bed availability and reduces overall expense by 16 percent.

Conclusions: In selected patients, elective day-case PCI appears feasible and safe, well valued by patients and cost saving.

P5871 | BEDSIDE
Impact of very severe left ventricular dysfunction on outcomes after transcatheter aortic valve implantation
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Background: Transcatheter aortic valve implantation (TAVI) seems to have better outcomes on high-risk patients as compared to conventional surgery in patients with severe left ventricular dysfunction (LVEF<35%). However, the range of dysfunction included in the term “severe” is wide and up to 10% of TAVI patients present deeper LV dysfunction (<25%). There is a lack of data concerning this subgroup.

Objective: To determine prognosis of patients with severe LV dysfunction and to compare the outcomes with the subgroup presenting deeper dysfunction.

Methods: We enrolled 76 consecutive patients with severe aortic stenosis who underwent TAVI with severe LV dysfunction: 52 (68.4%) presented LVEF=35-25% and 24 patients (31.6%) LVEF<25%.

Results: 29.8% of 84.2% were in NYHA class III-IV. Mean LVEF was 29.1±6.6 and mean 3D LV end diastolic volumes in both preterm (r²=14%, P=0.003) and term cohorts (r²=2% P=0.22). In the preterm cohort with severe LV dysfunction (<25%) was significantly increased when measured from aorta to tibial artery (6.4 mm Hg (±0.6) and 6.1 mm Hg (±0.4), P=0.009) and carotid to femoral artery (5.8 mm Hg (±0.8) and 5.5 mm Hg (±0.6), P=0.001). However, CAVI and PWV adjusted for mean arterial pressure were not significantly different between groups. Reductions both in aortic and cardiac size are proportional in individuals born preterm. However the changes do not appear to explain the differences in blood pressure. When blood pressure is accounted for arterial stiffness is unchanged in preterm born individuals.

EPIDEMIOLOGY-NEW INSIGHTS

P5872 | BEDSIDE
Reduced aortic size without changes in arterial stiffness in young adults born preterm
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Preterm birth is associated with reduced cardiac size, likely due to premature shift from low resistance in-utero circulation to high resistance systemic circulation. We used cardiac magnetic resonance (CMR) and non-invasive measures of arterial stiffness to determine whether there are proportional reductions in aortic size in preterm born individuals which might lead to a change in arterial stiffness important to blood pressure. 204 individuals aged 20-30 years underwent detailed cardiovascular phenotyping. 102 had been followed prospectively since preterm birth and 102 were born at term to uncomplicated pregnancies. CMR imaging (Siemens 1.5T scanner) was performed to measure cardiac volumes and aortic structure at multiple levels of the thoracic and abdominal aorta. Blood pressure was assessed peripherally and centrally. Arterial function was assessed by Sphygmocor tonometry (to measure carotid-femoral pulse wave velocity (PWV)) and carotid-ankle vascular index (cAI) and pressure pulse wave height (PPWH) and a blood pressure algorithm to measure arterial stiffness.

The preterm cohort had a mean gestational age of 30.3 weeks (±2.5), birth weight 1297 g (±286) and current age of 25.1 years (±1.4), compared to the term cohort of 39.6 weeks (±0.9), 3460 g (±417) and 25.0 years (±2.6). Resting mean blood pressure was measured in the preterm cohort 89.1 mmHg (±7.4) compared to 83.5 mmHg (±7.1) in the term cohort (P<0.001). In the preterm cohort, the aorta lumen cross-sectional area was significantly smaller in the thoracic descending (1.21 cm²/ m² (±0.18) and 1.46 cm²/ m² (±0.24), P<0.0001) and abdominal aorta (0.70 cm²/ m² (±0.19) and 1.05 cm²/ m² (±0.19), P<0.0001) compared to the term cohort. The aorta luminal areas correlated with left ventricular end diastolic volumes in both preterm (r²=14%, P=0.0003) and term cohorts (r²=26% P<0.0001). However the blood pressure differences between groups were not associated with the degree of reduction in aortic size in the preterm (P=0.1 P<0.43) or term cohort (P=0.22). In the preterm cohort PWV was significantly increased when measured from aorta to tibial artery (6.4 m/sec (±0.6) and 6.1 m/sec (±0.4), P=0.009) and carotid to femoral artery (5.8 m/sec (±0.8) and 5.5 m/sec (±0.6), P<0.001). However, CAVI and PWV adjusted for mean arterial pressure were not significantly different between groups. Reductions both in aortic and cardiac size are proportional in individuals born preterm. However the changes do not appear to explain the differences in blood pressure. When blood pressure is accounted for arterial stiffness is unchanged in preterm born individuals.

P5873 | BEDSIDE
Aortic root diameter and risk of cardiovascular events in a general population: the PAMELA study
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Aim: Data on the association of aortic root diameter (ARD), as assessed by echocardiography, with incident cardiovascular morbidity and mortality in the general population are scanty and limited to elderly individuals. Thus, we investigated the value of ARD in predicting cardiovascular events in the PAMELA population.

Methods: A cohort of 1,850 subjects (mean age 50±14, 50.8% men) underwent extensive lifestyle and diagnostic testing including laboratory investigations, office and out-of-office blood pressure measurements (home and 24-hour ambulatory BP monitoring), and echocardiography. ARD was measured at the level of Valsalva’s sinuses and indexed to body surface area (BSA) and body area space (BAS).

Results: Over a 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, ARD indexed to BSA (HR for 1 standard deviation (SD) increase = 1.48, 95% CI 1.13-1.94, P=0.02) and ARD indexed to height (HR=2.69, 95% CI 1.21-5.97, P=0.01) but not absolute ARD (HR=1.38, 95% CI 0.85-2.24, P=0.19) predicted an increased risk of cardiovascular events.

Conclusions: Our results for the first time show that ARD indexed to body size is predictive of incident non-fatal and fatal cardiovascular events among middle-aged subjects in the community and support the view that assessment of ARD might contribute to refine cardiovascular risk stratification and preventive strategies in the general population.

P5874 | BEDSIDE
Longitudinal association of carotid atherosclerosis with depressive symptomatology in late life: the 3C study
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Purpose: Vascular disease has been hypothesized to increase the risk of depression in late life, but evidence form prospective studies is currently lacking. We investigated the longitudinal association of carotid atherosclerosis with depressive symptomatology in older adults.

Methods: A cohort of community-dwelling individuals 65 to 85 years of age was examined for carotid plaque presence (CPP) and common carotid artery intima media thickness (CCA-IMT) at baseline and followed up after 2, 4, 7 and 10 years. At baseline and follow-up examinations, depressive symptomatology was measured using the Centre for Epidemiologic Studies Depression Scale (CES-D). Depressive symptoms (DS) were defined using validated cut-offs (CES-D score > 16 in men and > 22 in women). We evaluated associations of CPP and CCA-IMT at baseline with CES-D score at follow-up examinations using linear mixed-mod-
Els. For a more clinical perspective, the likelihood of DS at follow-up associated with CPP and CCA-IMT at baseline was estimated using generalized estimating equations.

Results: Among 4,125 participants (mean age 73.4 years, 57.8% female) with- out lifetime major depression and free of DS and dementia at baseline, a total of 1,973 (47.8%) showed CPP and mean CCA-IMT was 0.71 (standard devi- ation [SD] 0.12) mm. Baseline CPP was associated with a significantly higher CES-D score at the 10-year follow-up in men (+1.40, standard error [SE] 0.38, p < 0.001), but not in women, after adjustment for age, study centre and antide- pressant use at follow-up examinations. Baseline CPP was also associated with a significantly increased likelihood of DS at follow-up examinations in men (odds ra- tio 1.36, 95% confidence interval 1.02-1.80), but not in women. One SD increase in baseline CCA-IMT was associated with a significantly higher CES-D score at the 10-year follow-up (+0.38, SE 0.19, p = 0.046) and women (+0.56, SE 0.20, p = 0.005). The association between baseline CCA-IMT and DS at follow-up examinations was non-significant in both sexes. Results were consistent when further adjusting for cardiovascular risk factors and cognitive functioning at base- line and for coronary heart disease and stroke events as well as incident dementia during the 10-year follow-up.

Conclusions: Baseline CPP was associated with a higher CES-D score and an increased likelihood of DS at follow-up in older men, and baseline CCA- IMT was associated with a higher CES-D score at follow-up in older men and women, consistent with the hypothesis that vascular disease increases the risk of depression in late life.

PS874 | BEDSIDE
Ethnic differences in the effect of the Framingham risk factors on atherosclerosis and cardiovascular events in the USE-IMT cohort
C.M. Gijsberts1, K.A. Groenewegen2, I.E. Hoefer1, G. Pasterkamp1, D.P. de Kleijn1, S.A.E. Peters2, M.L. Bots2, H.M. Den Ruijter1 on behalf of USE-IMT.
1University Medical Center Utrecht, Utrecht, Netherlands; 2Julius Health Center - Julius Gezondheidscentra, Utrecht, Netherlands; 3National University of Singapore, Surgery, CVRI, NUHS, Singapore, Singapore

Background: Cardiovascular disease (CVD) is an important cause of morbidity and mortality, not only in Caucasians, but also in other ethnic groups worldwide. Yet, it is unknown whether it is appropriate to use the same primary prevention pro- grams and risk scores are based on data derived from mostly or even exclusively Caucasian people. Therefore we investigated ethnic differences in the magni- tude of the relation of the Framingham risk factors with atherosclerosis (mea- sured by mean common carotid intima-media thickness (CIMT)) and cardiovas- cular events.

Methods: For our analyses we used the USE-IMT cohort, a large ongoing individ- ual participant data meta-analysis involving 17 population-based cohorts world- wide. From the entire cohort 60,211 participants were selected who were free from CVD at baseline and had known ethnicity (Caucasian, Black, Asian or His- panic). First, we applied linear regression and Cox regression on a model contain- ing the Framingham risk factors and ethnicity for mean common CIMT and CVD events.

Results: Eleven studies were included (332,267 participants, mean follow-up 20.1 months, 12 full-text articles) The pooled relative risks (RRs) for total CVD events and CV mortality were 0.86 (95% confidence interval: 0.76 to 0.97), 0.91 (95% CI: 0.86 to 0.98), respectively, for subjects with PV versus subjects without PV. For all CVD events and CV mortality in the elderly, the protective value of PV was statistically significant only in the elderly (RR: 0.90; 95% CI: 0.817 to 0.999 and RR: 0.88; 95% CI: 0.75 to 0.99, respectively). The protective ability of PV increased as the presence of CV and pulmonary disease increased, whereas whether patients were vaccinated for influenza did not influence the protective role of PV. Regarding MI and cerebrovascular events, the protective role of PV was statistically significant only in the elderly (RR: 0.90; 95% CI: 0.817 to 0.999 and RR: 0.88; 95% CI: 0.75 to 0.99, respectively).

Conclusions: Men and women of middle age have similar lifetime risks of CVD. Two out of three face some form of CVD during their lifespan, underlining that primary prevention of CVD is of paramount importance. Gender differences in the first manifestation of CVD are, however, large: CHD accounts for nearly half of the first CVD revelations in men, whereas CVD unveils itself with cerebrovascular disease or heart failure in over 70% of women. This emphasizes the priority of stroke and heart failure prevention in women.

PS875 | BEDSIDE
Association between pneumococcal vaccination and cardiovascular outcomes: a systematic review and meta-analysis of cohort studies
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Purpose: Streptococcus pneumoniae is the most common cause of community- acquired pneumonia (CAP) and CAP-related mortality in adults. It has been sug- gested that pneumococcal vaccination (PV) could protect patients from cardiovas- cular events by reducing pneumonia severity or even preventing it. We conducted a meta-analysis of cohort studies for determining the ability of PV to protect from the risk of CV events and to dissect factors influencing this ability.

Methods: A comprehensive search of electronic databases was conducted through January 2014. Cohort studies that reported relative risk (RR) estimates with 95% confidence intervals were included. Two reviewers extracted data inde- pendently and summary estimates of association were obtained using a fixed- or random-effects model.

Results: Eleven studies were included (332,267 participants, mean follow-up 20.1 months, 12 full-text articles) The pooled relative risks (RRs) for total CV events and CV mortality were 0.86 (95% confidence interval: 0.76 to 0.97), 0.91 (95% CI: 0.86 to 0.98), respectively, for subjects with PV versus subjects without PV. For all CVD events and CV mortality in the elderly, the protective value of PV was statistically significant only in the elderly (RR: 0.90; 95% CI: 0.817 to 0.999 and RR: 0.88; 95% CI: 0.75 to 0.99, respectively). The protective ability of PV increased as the presence of CV and pulmonary disease increased, whereas whether patients were vaccinated for influenza did not influence the protective role of PV. Regarding MI and cerebrovascular events, the protective role of PV was statistically significant only in the elderly (RR: 0.90; 95% CI: 0.817 to 0.999 and RR: 0.88; 95% CI: 0.75 to 0.99, respectively).

Conclusions: PV is associated with decreased risk of CV events and CV mortality, while the protective value of PV for total CV events increases at older ages and in high CV risk groups and decreases as the time elapses from the PV. PV decreases the risk of MI and cerebrovascular events in the elderly.
Comparison of carvedilol and other beta-blockers on long-term mortality

**Results:** For all drugs and devices included in the study, a direct correlation was observed between the patient population size and cost of treatment (R²=0.411). For all drugs and devices included in the study, a direct correlation was observed between the patient population size and mortality benefit (number needed to treat [NNT]) and treatment cost (R²=0.219 and 0.101, respectively). Similarly, when only CV drugs and devices were considered, there was a correlation between the patient population size and cost of treatment in both the US (R²=0.493) and Europe (R²=0.643). A correlation between NNT and cost of treatment was also observed for CV drugs and devices, although this correlation was stronger in the US (R²=0.504) than in Europe (R²=0.359).

**Conclusions:** The results of this analysis provide a unique insight into factors affecting value assessments for innovative in-hospital CV treatments, and highlight that consideration of patient population size and mortality benefit, including evaluation of NNT, plays an important role.

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**Evolving Indications and Prescription Patterns in Cardiovascular Pharmacotherapy**

**PS879 | BEDSIDE**

Comparison of carvedilol and other beta-blockers on long-term mortality in patients with acute myocardial infarction who performed percutaneous coronary intervention using drug-eluting stents

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**Purpose:** The use of beta-blockers is recommended for treatment of patients with acute myocardial infarction (AMI) in current guidelines. However, there was no recommendation one beta-blockers over another. The aim of this study is to compare the impact of carvedilol and other beta-blockers on long-term clinical outcome in patients with AMI who performed percutaneous coronary intervention (PCI) with drug-eluting stents (DES).

**Methods:** A total of 4,748 AMI patients undergoing PCI with DES were consecutively enrolled in the COREA-AMI (Convergent REGistry of cAthicol and chorn-nAm university for AMI) registry from January 2004 to December 2009. Among 4,748 patients, 1,163 patients who did not prescribe any beta-blockers were excluded. We divided into two groups: carvedilol group (n=2,921) and non-carvedilol group (n=2,607). Non-carvedilol group included bisoprolol, atenolol, betaxolol, and nebivolol. The primary endpoint was a cardiac death during 3-year follow-up.

**Results:** During 3-year follow-up, the rate of cardiac death was 7.6% in carvedilol group and 10.7% in non-carvedilol group (p=0.002), respectively. In multivariate model, the use of carvedilol reduced the rate of cardiac death (adjusted HR 1.776, 95% CI 1.244-2.537, p=0.002).

**Conclusions:** Carvedilol was associated with reduced cardiac death in patients with AMI treated with PCI using DES compared with other beta-blockers.

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**PS880 | BEDSIDE**

Hypertensive patients treated with beta blockers prior to surgery are at increased risk of major adverse cardiovascular events and death – a nationwide cohort study

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**Purpose:** The safety and efficacy of continued beta blocker therapy treatment in patients with a stable condition i.e. hypertension, undergoing non-cardiac surgery, is largely unknown.

**Methods:** Through nationwide registers we identified hypertensive patients undergoing non-cardiac surgery using a validated algorithm (treatment with at least two antihypertensive drugs; RAS-inhibitors, beta blockers, calcium antagonists or thiazides plus no prior cardiovascular or kidney disease). The risk of 30-day MACE (non-fatal AMI, non-fatal ischemic stroke and cardiovascular death) and 30-day all-cause mortality were calculated using Cox proportional hazard models adjusted for sex, age, type of surgery and surgery risk category (low, intermediate, and high).

**Results:** A total of 44,506 patients were included, 33,319 received RAS-inhibitors, 13,310 received beta blocker, 25,355 received calcium antagonists, and 24,273 received thiazides. The incidence of MACE and death in the overall population was 1.29% and 1.83%, respectively. Hazard ratios (95% confidence intervals) for single antihypertensive drugs and specific drug combinations are presented in Fig. 1.

**Conclusion:** Antihypertensive treatment with beta blockers prior to surgery is associated with increased risk of perioperative adverse outcomes.

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**PS881 | BEDSIDE**

Effectiveness of perioperative ivabradine in patients undergoing vascular surgery

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**Background:** Perioperative control of heart rate (HR) is important for achieving cardioprotection in high risk patients. However, effective HR control with β-blockers (BB) may be difficult to achieve and may be associated with increased risk especially when initiated <1 week before surgery.

**Aim:** To assess the effectiveness of ivabradine in reducing perioperative HR in patients undergoing vascular surgery.

**Methods:** Patients scheduled for elective open vascular surgery with HR >75 bpm and revised cardiac risk index (RCRI) score >2 were prospectively enrolled. Ivabradine was given to 45 patients (Ivab group) with any of the following: inadequate HR control despite BB therapy; contraindication to BB; or surgery scheduled less than a week. Another 26 patients received titrated doses of bisoprolol according to current guidelines (standard care group). Medications were continued for 30 days postoperatively. Cardiac troponin T (cTnT) was measured before surgery and on postoperative days 1, 3, and 7. Target HR was defined as <65 bpm. Thirty-day cardiac events were the composite of cTn release, death, and stroke.

**Results:** Both groups were similar in terms of age, RCRI score, and surgical procedure. HR was similar in both groups before therapy (86.4±5 vs. 85.4±5 beats/min) but was significantly lower in Ivab group preoperatively (64.4±4 vs. 71.9±9 beats/min, p<0.001) and at first postoperative day (66.8±8 vs. 78.±12 beats/min, p=0.007) with similar rates of clinically significant hypotension or bradycardia. More patients in Ivab group than in standard care group achieved target HR (66% vs. 31%, p<0.003). Thirty-day cardiac events were higher in standard care group (37%) versus Ivab group (9%, p=0.003); this was driven mainly by excess rate of cTnT release. Independent predictors of cardiac events were: RCRI score (odds ratio (OR) = 4.2, 95% confidence interval (CI): 1.8-5.7, p=0.013); lack of aspirin.
P5882 | BENCH
The right ventricle molecular changes associated with pulmonary arterial hypertension are attenuated by neuregulin-1 treatment
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Pulmonary arterial hypertension (PAH) leads to right ventricular (RV) failure and death. Neuregulin-1 (NRG-1) has been implicated in several processes regulating cardiac development, as well as cardiac and vascular homeostasis. It was previously shown, in an experimental model of MCT-induced PAH, that NRG-1 treatment is able to restore PAH-induced severe abnormalities in cardiac function and structure. This study investigated the underlying molecular mechanisms to the beneficial effects of NRG-1 in myocardial function, in the same animal model of induced PAH. Male Wistar rats randomly received monocrotaline (MCT, 60mg/kg, sc) or vehicle. After 14 days, animals received NRG-1 (40 μg/kg/day) or vehicle, resulting in 4 groups: CTRL; CTRL+NRG-1; MCT; MCT+NRG-1. RV sample collection for were performed 21-24 days after MCT administration. Only significant results (mean±SEM, p<0.05) are given.

NRG-1/ErbB system components expressions in MCT animals are changed. We observed increased levels of NRG-1 in RV (11.1±2.8 vs 1.0±0.3 AU, MCT vs CTRL), which were reversed by NRG-1 treatment (MCT+NRG-1: 1.7±0.5 AU), and decreased levels of ErbB4 in all MCT animals (MCT: 0.6±0.2 and MCT+NRG-1: 0.7±0.15 AU). We also found increased levels of ErbB2 (2.0±0.3 AU), ADAM-17 (2.1±0.3 AU) and ADAM-19 (2.7±0.3 AU), and increased NF-κB expression (2.0±0.3 AU) in the RV of MCT animals that did not reversed with NRG-1 treatment. MCT treatment led to altered GLUT1 expression (4.1±0.5 AU) and NRG-1 treatment attenuated this increase (1.7±0.3 AU), GLUT1 was increased in all animals treated with NRG-1 (CTRL+NRG-1: 1.4±0.1; MCT+NRG-1: 1.5±0.2 AU). Increased RV caspase 3 (MCT: 4.4±0.4 AU) and plasmatic expression of IL-6 and TNF-α (IL6: 2.7±0.7 AU; TNF-α: 1.7±0.3 AU) were attenuated by NRG-1 treatment (caspase 3: 1.7±0.3 AU; IL6: 2.0±0.4 AU; TNF-α: 1.5±0.4 AU). Moreover, we found that the increased expression of BNP (17.5±2.2 AU), ET-1 (5.0±1.2 AU) and HIF-1α (4.3±1.1 AU) observed in MCT animals was attenuated or reversed with NRG-1 treatment (MCT+NRG-1: 5.6±1.9; 1.7±0.7; 1.4±0.1 AU, respectively).

In conclusion, we show that NRG-1 treatment is able to restore the changes in expression of markers of cardiac overload, hypertrophy and hypoxia induced by PAH. These beneficial effects of NRG-1 are associated with the modulation of different signaling pathways, namely apoptotic, metabolic, survival/proliferation, and inflammation pathways.

P5883 | BENCH
Ivabradine in pulmonary arterial hypertension
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Background: Pulmonary arterial hypertension (PAH) is a disabling chronic disorder of the pulmonary vasculature, which is characterized by increased pulmonary artery pressure as a result of increased pulmonary vascular resistance. We therefore sought and verify clinical differences between PAH patients in ivabradine treatment vs controls and verify a possible functional improvement after ivabradine treatment.
Methods: Between 1st July 2009 and 1st July 2013, a total of 28 consecutive patients with PAH in specific therapy were evaluated in our ambulatory for diagnosis and treatment of PAH. Non-invasive cardiac evaluation included: clinical evaluation, ECG, and echocardiography, with estimation of the PdP. Functional capacity was assessed through six minute walking test (6MWT). Finally, RHC was required to confirm the diagnosis of PAH. Ivabradine, a selective inhibitor of the sinus node If channels, was added to all patients with a HR over 100 bpm or those in NYHA III-IV functional class. After 14 days, animals received NRG-1 (40 μg/kg/day,ip) or vehicle, result-
pain for the acute coronary syndrome (ACS) scenario or shortness of breath for acute heart failure (AHF) scenario. Further information was provided only if asked for by the pharmacist. The other investigator observed the conversation and after each visit collected the data using standardized data collection form. 

**Results:** Of 600 pharmacies, 360 (63.3%) pharmacists advised the simulated patient to seek medical care, more so with the ACS scenario (70.3% vs. 58.3%, p < 0.001). The pharmacists were likely to advice patients to seek medical advice during weekdays than weekends, and during the morning hours than during the evenings or nights. Pharmacists sought more information regarding other symptoms and comorbidities with the simulated ACS patients (59.7% vs. 48.7%, p < 0.009 and 46.3% vs. 37.3%, p = 0.031 respectively). Only 28 pharmacists (4.7%) inquired about drug allergies and 14.3% gave instructions on treatment duration, with no significant differences between the two scenarios.

**Conclusion:** The use of simulated case scenarios by community pharma-

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**ENDOTHELIAL CELL FUNCTION: BEDSIDE TO BENCH**

P5886 | BEDSIDE

**Dietary nitrate improves endothelial function, vascular stiffness and modifies platelet markers of atherogenesis in hypercholesterolemia**

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**Purpose:** Recent evidence suggests that orally ingested inorganic nitrate undergoes sequential chemical reduction in vivo first to nitrite and then to nitric oxide (NO) within the circulation. The provision of NO within the vasculature improves platelet and endothelial reactivity in healthy volunteers. We sought to examine whether nitrate may be effective in improving endothelial and platelet function in a cohort at risk of cardiovascular disease i.e. hypercholesterolemics.

**Methods:** 67 otherwise healthy non-diabetic untreated hypercholesterolemics completed this randomised double blind placebo controlled parallel study of a once daily dietary nitrate dose for 6 weeks (n=33, Nitrate: 400 mg, juice, 250 ml of 24.1±7.7 mM) vs Placebo (n=34, nitrate-depleted juice, 250 ml of 0.05±0.1 mM). The primary end point was endothelial function determined using ultrasound flow-mediated dilation (FMD) at baseline and at 6 weeks. Pulse wave analysis (PWA) and pulse wave velocity (PWV) were also measured and blood taken for assessment of plasma cholesterol, platelet P-selectin expression and platelet monocyte aggregate (PMA) formation using flow cytometry. Plasma, urine and salivary nitrate and nitrite measurements were conducted using ozone chemiluminescence. Values shown are mean±SEM.

**Results:** Plasma levels of nitrate increased ~8-fold from a baseline of 26.7±2.3 μM (p = 0.0001) and nitrite 2.5-fold from 0.3±0.1 μM (p = 0.0001) in the Nitrate limb, whilst no changes occurred in the Placebo limb. LDL cholesterol was similar in both groups. Even small increase in nitrate levels of total CD4+ T cells (631±108) vs Placebo (466±107, p < 0.001) vs a trend to decrease in the Placebo group (45.2±10.3% vs 43.0±10.3% p = 0.07). A small improvement in PWV (8.3±2.2 to 8.1±2.0 μM/s, p = 0.02) and PMA expression (5.7±2.0 to 4.9±2.0, p = 0.07) and a decrease in nitrite levels of total CD4+ T cells (4.6±0.4 μM/l vs 4.7±0.5 μM/l, p < 0.001) vs a trend to increase in the Placebo group (45.2±0.3% vs 43.0±0.3% p = 0.07). A small improvement in PWV (8.3±2.2 to 8.1±2.0 μM/s, p = 0.02) and PMA expression (5.7±2.0 to 4.9±2.0, p = 0.07) and a decrease in nitrite levels of total CD4+ T cells (4.6±0.4 μM/l vs 4.7±0.5 μM/l, p < 0.001).

**Conclusions:** Once daily dietary nitrate ingestion improves endothelial function, vascular stiffness and platelet markers of atherogenesis in hypercholesterolemics. Dietary nitrate may be useful in a potential preventative strategy in the battle against atherosclerosis.

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**ENDOTHELIAL CELL FUNCTION: BEDSIDE TO BENCH**

P5887 | BEDSIDE

**The role of vascular function in patients with diabetic retinopathy**

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**Purpose:** Diabetic Retinopathy (DR) is a complication of diabetes mellitus and remains a leading cause of irreversible blindness. Measurement of endothelial function and arterial stiffness are well validated in large population studies as strong predictors of adverse cardiovascular outcomes. We investigated the possible association of DR with endothelial function, arterial stiffness and inflammation.

**Methods:** We enrolled 100 consecutive subjects with DR (mean age 69±9 years) at the diabetic clinic and 100 healthy subjects with diabetes (mean age 68±10 years) and 100 healthy subjects (mean age 63±11 years). Endothelial function was evaluated by flow mediated dilation (FMD) in the brachial artery, carotid-femoral pulse wave velocity (PWV) was measured as an index of arterial stiffness and augmentation index (Alx) as an index of reflected waves. Creatinine clearance, glycosylated hemoglobin, and C reactive protein were measured.

**Results:** Patients with DR compared to NDR patients and healthy subjects had impaired FMD (3.55±1.23% vs. 7.11±1.92% vs. 7.54±3.06%, p < 0.001), PWV (11.06±2.75/sec vs. 9.16±1.97/sec vs. 8.41±1.75/sec, p < 0.001) and increased Alx (27.85±8.15% vs. 24.12±7.96% vs. 22.52±8.00%, p < 0.001). In diabetic patients, we applied a forward logistic regression model, which revealed that impaired FMD was the strongest predictor of the presence of DR [Odds ratio 0.24, 95% CI (0.23, 0.51), p < 0.001]. As many confounders may exist, we applied a second logistic regression model which revealed that impaired FMD was independently associated with the presence of DR [Odds ratio 0.17, 95% CI (0.07, 0.39), p < 0.001] even after adjustments for confounders such as age, glycosylated hemoglobin and common CVD risk factors including diabetes, body mass index, type of treatment and the presence of arterial hypertensia and dyslipidemia. Moreover, among diabetes mellitus patients ROC curve analysis revealed that FMD has sufficient discriminative ability to detect DR [AUC=0.85, 95% CI 0.80 to 0.91, p < 0.001] and an FMD value below 4.35% has a sensitivity of 82%, and a specificity of 79% for the diagnosis of DR. Importantly, the negative predictive value of an FMD above 4.36% was estimated at 85%.

**Conclusion:** This study showed that DR patients have significantly impaired en-
thelial function and increased arterial stiffness compared to NDR patients and suggests that endothelial function in a cohort at risk of cardiovascular disease i.e. hypercholesterolemics.

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**ENDOTHELIAL CELL FUNCTION: BEDSIDE TO BENCH**

P5888 | BEDSIDE

**Adaptive immune responses and endothelial function in young adult survivors of childhood acute lymphoblastic leukemia**

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**Purpose:** Adult survivors of childhood malignancy are at increased risk of early atherosclerosis and late cardiovascular complications. Innate and adaptive im-
mune mechanisms play an important role in atherogenesis. Macrophages and effector T cells produce proinflammatory mediators and contribute to the progres-
sion of atherosclerotic plaques. The aim of the study was to assess endothelial function and T lymphocytes subsets in young adult survivors of childhood acute lymphoblastic leukemia (ALL).

**Methods:** We examined 27 (age 18-28, median 20) ALL survivors who had completed chemotherapy at least 5 years prior to the study and 20 healthy controls. Endothelial function was assessed using flow mediated dilation (FMD) of brachial artery. Flow cytometry was used to identify naive, central memory, effector mem-
ory and effector T cells among CD4+ and CD8+ subsets of lymphocytes.

**Results:** FMD of 15 patients vs 61±4.6% controls, p = 0.71, and a uniform cardiovascular risk factors were comparable except for lower HDL cholesterol (1.5±1.0 vs 1.8±0.5 mmol/l; p = 0.02) in the study group. ALL survivors had lower levels of total CD4+ T cells (631±166 ul vs 758±249 ul; p < 0.048), which was dependent on decreased naive T cells and central memory T cells. Naive T cells, central memory T cells, memory CD4+ T cells and central memory CD4+ T cells in ALL survivors and associated with the magnitude of en-
thelial dysfunction as assessed by flow mediated dilation. Decreased naive helper T lymphocytes may result from enhanced differentiation of naive T cells into T cells which migrate from blood into irima and participate in the maintenance of chronic inflammatory responses with the vascular wall, which might contribute to endothelial dysfunction on a long-term basis.

**Conclusions:** Adaptive immune dysfunction reflected by lower levels of CD4+ T cells was present in ALL survivors and associated with the magnitude of en-
thelial dysfunction as assessed by flow mediated dilation. Decreased naive helper T lymphocytes may result from enhanced differentiation of naive T cells into T cells which migrate from blood into irima and participate in the maintenance of chronic inflammatory responses with the vascular wall, which might contribute to endothelial dysfunction on a long-term basis.
inadequate vascular repair mechanisms predispose to atherosclerosis in patients with a family history of CAD compared to age- and sex-matched controls.

**Methods:** Sixteen patients (51±5 years; 94% male) with premature CAD (<50 years old) and a family history of CAD (first degree relative) and 16 healthy, age- and sex-matched controls (50.8±8 years) with normal coronary arteries underwent a detailed assessment of vascular function. Bilateral forearm blood flow was measured before and during unilateral intra-brachial arterial infusion of acetylcholine (5 - 20 μg/min) and sodium nitroprusside (2 - 8 μg/min). Vascular endothelial cells were isolated and cultured from venous biopsies of superficial forearm veins and aorta. CD34+, CD34+CD133+, or CD34+CD133+KDR+ cells in blood between patients and controls, but endothelial outgrowth appeared later in patients (patients vs. controls = 10.30±0.81 vs. 7.94±0.54 days; P=0.03). The level of CD133 expression on vascular ECs was reduced in patients compared to controls (P=0.001).

**Results:** Endothelial-dependent vasodilation was impaired in patients with premature CAD compared to controls (P=0.03) but endothelial-independent vasodilation was unchanged (P=0.37). There were no differences in the number of CD34+, CD34+CD133+, or CD34+CD133+KDR+ cells in blood between patients and controls, but endothelial outgrowth appeared later in patients (patients vs. controls = 10.30±0.81 vs. 7.94±0.54 days; P=0.03). The level of CD133 expression on vascular ECs was reduced in patients compared to controls (P=0.001). Vascular ECs from patients displayed reduced adhesion to collagen compared to controls, but no differences were observed in the migration of vascular ECs compared to circulating ECs in controls (P=4.04). No differences were observed in the migration of vascular ECs compared to circulating ECs in controls (P=4.04). No differences were observed in the migration of vascular ECs compared to circulating ECs in controls (P=4.04).

**Conclusion:** Patients with premature CAD and a family history of CAD have deficiencies in both endothelial vasomotor function and in the proliferation, adhesion and migration of vascular and circulating endothelial cells. These mechanisms suggest the genetic basis of premature CAD may be mediated in part by inherited defects in endothelial function and vascular repair.

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**PS5890 | BENCH**

**Association between NADPH oxidasex activity and NO bioavailability in atherosclerotic plaques**

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**Purpose:** Oxidative stress and the generation of reactive oxygen species (ROS), including superoxide (O2·-) are thought to play a critical role in pathophysiology of atherosclerosis. NADPH oxidase (NOX) synthesis may be considered as the pivotal sources of ROS contributing to a decreased NO bioavailability in the endothelium, leading to endothelial dysfunction. This study was established to determine whether NADPH oxidae-derived O2- can contribute to a decrease production of bioactive NO by eNOS in the endothelium overlaying the arterial atherosclerotic plaques.

**Methods:** The endothelial cells, that were harvested from atherosclerotic and non-atherosclerotic (control tissue) regions of carotid arteries isolated from patients scheduled to carotid trans-endarterectomy, were used for further investigation. The protein expression of NADPH oxidase subunits (NOX 4 and p47phox) was analyzed by Western blot technique. The NADPH oxidase activity was measured with lucigenin (5 μM) based assay for O2- production. Concurrent kinetics of NO, O2- and ONOO- radicals released from single endothelial cells were measured with highly sensitive electrochemical nanosensors.

**Results:** The reduced release of NO (55±6 vs. 214 nmol/L) with simultaneous increased releases of both O2- (21 vs. 71 nmol/L) and ONOO- (288 vs. 648 nmol/L) were observed in endothelium from atherosclerotic arteries in comparison to control tissue. Moreover, in comparison to control, the endothelial cells overlaying the atherosclerotic plaques released a significant increase of NADPH oxidase activity (0.27±0.05 vs. 0.14±0.03 RLU/min/mg) as well as an increased expression of total and membrane fractions of p47phox subunit. Additional the NOX4 subunit expression showed no differences in total and membrane-bound fractions of the endothelial cells retrieved from atherosclerotic and non-atherosclerotic regions of the arteries.

**Conclusion:** We have provided the direct evidence that a reduction of NO bioavailability and a change in the oxidative-reductive balance in human atherosclerotic plaques is due to the elevated O2- production by over expressed NADPH oxidase. Re- action between NO derived from eNOS and O2- derived from NAPDH oxidase is responsible for ONOO- overproduction in the endothelium of atherosclerotic plaques.

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**PS5891 | BENCH**

**In vivo vascular function assessment in living mice using high resolution ultrasound: a translational model**

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**Purpose:** To test the hypothesis that lowering levels of angptl2 improves endothelial cell stress resistance and prevents endothelial dysfunction induced by a sub- dually expressed pro-inflammatory ligand. Lack of angptl2, as shown in KD mice, protects against angII-induced endothelial dysfunction in mice. In vivo vascular function assessment in living mice using high resolution ultrasound: a translational model promises to allow longitudinal studies on eNOS-dependent endothelial function in mouse models that can be directly translated to humans as the methodology is almost identical with the clinical read-out.

**Methods:** In 22-week-old angptl2 knock-down mice, the main vasodilator NO contributed similarly in both KD and WT mice. This response was completely abolished by L-NAME in eNOS-KO mice. COX inhibition by indomethacin, arginase inhibition with ornithine and L-arginine, and endothelium-derived hyperpolarizing factor inhibition by sulfaphenozole had no effect on FMD. Furthermore, using our approach, we showed that eNOS-dependent FMD was age-dependently decreased, whereas the eNOS-independent component of FMD as assessed after L-NAME infusion remained unaffected. In ApoE-KO mice, an established accelerated atherosclerosis model, FMD measured weekly, progressively decreased upon initiation of a high cholesterol diet along with an increase in pulse wave velocity and aortic collagen content, confirming progressive atherosclerosis.

**Conclusion:** This model promises to allow longitudinal studies on eNOS-dependent endothelial function in mouse models that can be directly translated to humans as the methodology is almost identical with the clinical read-out.

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**PS5892 | BENCH**

**Lack of angioptlein like-2 protects against angiotensin II-induced endothelial dysfunction in mice**

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**Purpose:** Cardiovascular diseases are characterized by chronic low-grade inflammation, oxidative stress and endothelial dysfunction. Angiopoietin like-2 (angptl2) is a recently identified pro-inflammatory protein that is elevated in atherosclerotic patients, but knowledge on its role in regulating endothelial function in a pro-inflammatory and pro-oxidative environment is limited.

**Methods:** To test the hypothesis that lowering levels of angptl2 improves endothelial cell stress resistance and prevents endothelial dysfunction induced by a sub-dually expressed pro-inflammatory ligand. Angptl2 is responsible for ONOO- overproduction in the endothelium of atherosclerotic plaques.

**Results:** In cerebral arteries of saline-treated KD and WT mice, ACh-induced vasodilation were similar; however, while dilation depended on eNOS activation in both groups (inhibited by L-NNA), eNOS-derived H2O2 (sensitive to PEG-catalase) contributed to vasodilation in WT, and only eNOS-derived NO (P<0.001) was involved in KD mice. In contrast, in the aorta of saline-treated mice, the main vasodilator NO contributed similarly in both KD and WT mice. An induced endothelial dysfunction in cerebral arteries of WT mice only (P<0.01), evidenced by a 60% reduction in maximal dilation induced by ACh. The impaired dilation was reversed (P<0.05) acutely by the antioxidant N-acetylcysteine (10 μM), apocynin (10 μM), a non-selective NADPH oxidase inhibitor, or indomethacin (10 μM), a non-selective cyclooxygenase inhibitor. Global endothelial function was maintained in the aorta after ang II infusion in all groups; however, ang II infusion revealed prostatocystin-mediated relaxation in KD (P<0.01) but not in WT mice. Finally, in angII-treated KD mice only, apocynin bluntly blunted relaxation in both the cerebral arteries and aorta (P<0.01) suggesting a global remodelling of the NOX systems, possibly by revealing the protective role of NOX4, an isoform that produces predominantly H2O2 in mediating relaxation.

**Conclusion:** Lack of angptl2, as shown in KD mice, protects against angII-induced endothelial dysfunction: it favours the production of NO and prostacyclin, likely increasing endothelial cell resistance to oxidative stress and maintaining relaxation, while recruiting a potential compensatory dilatory NOX pathway.
Our study confirms that SSc patients exhibit biventricular systolic and diastolic dysfunction and increased sPAP, with a further deterioration at 3-year follow-up, and suggests that currently available drugs have no protective effect on the course of SSc-HD.

PS589 | BENCH
Systolic and diastolic biventricular function in systemic sclerosis: a novel long-term assessment
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Objectives: To investigate by standard echocardiography (SE) and pulsed tissue Doppler imaging (TDI) the course of systemic sclerosis (SSc) – heart disease (HD) and its correlation with epidemiological, clinical and serological features of the disease and drug treatment.

Methods: Seventy-four consecutive patients with SSc (69 female, aged 19-71 years, disease duration 1-43 years) and 71 age- and sex-matched controls underwent cardiac assessment at baseline and at 3-year follow-up.

Results: At baseline, SSc patients showed an impaired left (LV) and right ventricular (RV) systolic function compared to controls (Em/Am 0.85±0.04 vs 1.5±0.7, p<0.00001; E/e’ 29.2±9.1 vs 15.4±3.2 cm/sec, p<0.001; St 14.4±3.5 vs 15.7±4.7 cm/sec, p<0.05). Pulmonary artery systolic pressure (PAP) was significantly higher in SSc patients than in controls (26.1±6.0 vs 24.3±5.1, p<0.0013).

At 3-year follow-up, SSc patients showed a further deterioration of biventricular diastolic and systolic function and a further increase in sPAP. At multiple regression analysis performed to assess the impact of LA strain parameters with the severity of MetSyn and logistic regression analysis performed to assess the relationship of low LA strain with MetSyn.

Conclusion: MetSyn is associated with reduced LA strain and LA strain reparation, LA reservoir and pump function, respectively. Furthermore, LA mechanical function decreases even more with the increasing severity of the MetSyn.
Methods: One hundred sixty-three consecutive patients (IMF = 101:62, age = 56±15 years, LV Ejection Fraction [LVEF] = 49±15%) who underwent 2D echocardiography were enrolled. Patients with moderate to severe mitral regurgitation, mitral stenosis or atrial fibrillation were excluded. LA minimum (LA volume at LV end-diastole, LAVmin) and maximum (LA volume at LV end-systole, LAVmax) volumes were measured using biplane disc method. LA reservoir function was estimated by calculating LA filling fraction (LAFr) during LV systolic period; LAFr = 100 × (LAVmax − LAVmin)/LAVmin. Peak velocity of pulmonary vein systolic flow (PVS) was also measured.

Results: LAFr showed a strongly positive correlation with LVEF (r = 0.734, p < 0.001) and also showed significant correlations with both LVMi and E/e′ (r = -0.569, p < 0.001; r = -0.534, p < 0.001, respectively). And LVEF was strongly correlated with PVS (r = 0.639, p < 0.001). In a multivariate regression analysis, LVEF resulted to be a strong significant predictor of LAFr (β = 0.593, p < 0.001) and PVS (β = 0.646, p < 0.001).

Conclusions: Our data supports that LV systolic function which influences LA enlargement and subsequent LA stretching might be a strong determinant of LA reservoir function during systole. LV dysfunction which is proportionally compromising LA reservoir function may be of important contributing factors of LV filling impairment.

P5899 | BEDSIDE
Synergistic effects of left atrial deformation and left ventricular diastolic function on physical fitness in elderly men
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Background: Both atrial function and ventricular diastolic function are important in exercise performance. However, the interactions between left atrial (LA) and left ventricle (LV) diastolic function on functional capacity have never been studied. We studied the influences of both LA function and LV diastolic function on physical capacity in elderly.

Methods: We recruited 269 community-based, apparently healthy elderly men who were 65 years and older (mean age 74±6 years) without structural heart disease. LA function was evaluated by 2-dimensional speckle tracking echocardiography. Average peak systolic strain of LA (LAS) during atrial filling was used as index for LA function. The ratio of peak early filling velocity (E) of mitral in-flow to average early diastolic annulus velocity (e′) of the annulus (E/e′) was used as index for LV diastolic function. Physical capacity was assessed by 2 methods including time for 15-foot walking test and time for 8-foot up-and-go test.

Results: Time for 15-foot walking test was significantly correlated with age (r = -0.287, p < 0.001), E/e′ (r = -0.208, p < 0.001), mitral left ventricular ejection fraction (EF) (r = -0.155, p = 0.016), and LAS (r = -0.230, p < 0.001). Time for 8-foot up-and-go test was significantly correlated with age (r = -0.265, p < 0.001), E/e′ (r = -0.224, p < 0.001), and LAS (r = -0.268, p < 0.001). Multivariate regression analysis showed age (β = 0.278), E/e′ (β = 0.229), LAS (β = 0.207), and EF (β = -0.159) were independent factors for 15-foot walking test. Age (β = 0.227), E/e′ (β = 0.238), and LAS (β = 0.199) were independent factors for 8-foot up-and-go test. We further divided subjects into two groups according to LV diastolic function or median level of LAS. Subjects with both impaired LV diastolic function (E/e′ > 18) and lower LAS (LAS ≤ -38.2%) had the poorest functional capacity than subjects with normal LV diastolic function and higher LAS represented by time for 15-foot walking test (5.1±2.4 vs. 4.7±1.3 sec, p=0.003) or time for 8-foot up-and-go test (10.1±1.5 vs. 7.5±2.0 sec, p=0.001).

Conclusion: Both LA function and LV diastolic function are independently correlated with time for 15-foot walking or 8-foot up-and-go tests. They have synergistic effects on physical fitness in elderly men.

5924 | BENCH
raAAV mediated Thymosin beta4 overexpression induces therapeutic neovascularisation in a porcine model of chronic myocardial ischemia
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Induction of neovascularization using vascular growth factors has emerged as a promising novel approach for promoting cardiac repair and regeneration. Thymosin β4 (Tß4), a small 4.9 kDa peptide influences cell motility, migration and differentiation. We investigated the role of long-term Tß4 overexpression using recombinant adeno-associated vector Tß4 (rAAV Tß4) in a pig model of normo- and hypercholesterinemic diet in chronic myocardial ischemia.

Methods: Chronic ischemia was induced via reduction stent graft in the circumflex artery, leading to a total occlusion on day 28 (d28). Regional application of saline or rAAV Tß4 (5x10E12 viral particles, d28) was compared with Tß4 transgenic pigs. Global myocardial function (EF, LVEDP) was obtained and regional myocardial function (GLS, LVESV/LVSV) was measured using biplane echocardiography. We investigated the role of long-term Tß4 overexpression using recombinant adeno-associated vector Tß4 (rAAV Tß4) in a pig model of normo- and hypercholesterinemic diet in chronic myocardial ischemia.

Background: Ventricular-arterial (VA) coupling has reported to have the critical role in heart failure with preserved ejection fraction (HFpEF), however, its association with left ventricular (LV) systolic dysfunction and left ventricular (LV) circumferential strain (GCS) is still uncertain in clinical setting.

Methods: Among 457 heart failure patients who require hospitalization were analyzed from ICAS-HF registry. No-option patients with ischemic heart disease, patients who underwent 2D echocardiography were enrolled. We further divided subjects into two groups according to the median value of GCS (%) ≤ 15%. VA coupling was defined as the ratio of LV end-systolic volume to stroke volume by echocardiography.

Results: The demographic and clinical characteristics showed no significant difference between GLS (-15%) and GCS -15% groups as follows; age 78±7, 73±11 years, systolic blood pressure 127±19, 118±20 mmHg, LVEF 62±8, 58±7%, BNP 235±220, 302±349 pg/mL, respectively. But, GCS had markedly deteriorated in impaired GLS (< -15%) than that in preserved GCS (-15%) patients (-15.2±0.4% vs. -19.0±0.9%; p = 0.0196). Furthermore, VA coupling was significantly correlated with GLS (R = 0.29; p = 0.0060) and GCS (R = 0.46; p < 0.0001).

Conclusion: Global longitudinal strain and global circumferential strain may reflect abnormal VA coupling in clinical settings of HFpEF.
5926 | BENCH
Downregulation of von willebrand factor prevents angii-induced endothelin-1 expression independently of enos activation in porcine endothelial cells

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Purpose: Angiotensin II (AngII) generated under conditions of myocardial ischemia and reperfusion increases endothelial levels of endothelin-1 (ET-1), von Willebrand factor (vWF) and anion superoxide (O2-), which lead to progressive coronary endothelial dysfunction. Recent study described that vWF blockade improves endothelial function in coronary patients, but the mechanisms are still unknown. Our study investigated whether the downregulation of vWF modulates the ET-1 level, eNOS activity and O2- production without affecting endothelial function. Our findings support the usefulness of vWF as upstream modulator of ET-1 expression under oxidative microenvironment.

Conclusions: We demonstrated, for the first time, that barleary-derived β-D-glucan promotes adult angiogenesis under oxidative microenvironment through increased histone H4 acetylation. These findings uncover a novel and unexpected role for dietary β-D-glucan as a critical epigenetic activator of antioxidant activity governing adult angiogenic response.

5928 | BENCH
Induction of superoxide dismutate-2 (MnSOD) by apoptosis signal kinase-1 (ASK1) via activation of NFκB in endothelial cells

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Purpose: Endothelial cell apoptosis precedes myocardial apoptosis in ischemic myocardium, as well as during the reperfusion of ischemic myocardium. Although it remains unclear as to how the endothelial cells undergo apoptotic death during myocardial ischemia-reperfusion, activation of apoptotic signaling could be a major contributor to endothelial cell death and could be crucial in the acquisition of tolerance to ischemia. TNFα, which induces MnSOD, it also activates ASK1. We hypothesize that ASK1 signaling is a major contributor to endothelial cell death in the ischemic myocardium.

Methods: Human microvascular endothelial cells (HMVEC) were cultured in EGM-2MV with supplements. pcDNA3-ASK1, pcDNA3-3.5A5 (constitutively active form), and dnASK1 (dominant-negative ASK1) were transfected into HMVEC using Fugene-6 transfection reagent (Roche). In addition, cells were co-transfected with pcDNA3-ASK1 and pcDNA3-JNK-APF, pcDNA3-MKK4 or pcDNA3-MKK7 to determine the transcription of ASK1 signaling mechanism. We also determined the activation of NFκB due to ASK1 expression using electrophoretic mobility shift assay (EMSA).

Results: To our surprise, transfection of ASK1 induced the MnSOD gene expression in endothelial cells, but transfection of dnASK1 did not induce MnSOD. In addition, transfection of pcDNA3-3.5A5 also induced MnSOD gene expression and MnSOD protein. In contrast, in the presence of JNK inhibitor SP600125 or co-transfection of dominant-negative JNK expression construct resulted in repression of MnSOD expression. Our findings suggest that transfection of ASK1 into the HMVEC induced NFκB activation and pSEMTubl, a superpressor of NFκB was able to abrogate NFκB activation by ASK1.

Conclusion: We concluded that apoptotic signaling by ASK1 induces antiapoptotic gene expression, possibly by a MAP3K, MnSOD, which is crucial in the acquisition of tolerance to ischemia. Our findings suggest that ASK1 signaling is a major contributor to endothelial cell death in the ischemic myocardium.

Funding: The study is supported by NIH grants HL109337 and HL107588 to K. Das.
5930 | BENCH Inflammatory molecules are involved in the regulation of endothelial senescence via Notch signaling.


Introduction: Accumulation of senescent vascular cells occurs in aged vessels, leading to reduced bioavailability of NO and endothelial functions. These data also demonstrate for the first time, that increased insulin signaling in the endothelium, leading to reduced bioavailability of NO and endothelial functions. These data also demonstrate a state of enhanced oxidative stress in the endothelium.

Methods: Western blotting and RT-PCR were carried out on tissues and isolated endothelial cells from lungs to confirm the presence of human insulin receptor protein levels and mRNA expressions, respectively. NADPH-dependent lucigenin-chemiluminescence assay was performed to measure superoxide anion levels. Isolated thoracic aortic rings suspended in organ baths were used to determine vasoconstrictor function. eNOS activity was examined by citrulline assay with 14C-labelled L-arginine. HIRECO were compared to wild type littermates (WT).

Results: Over-expressing human insulin receptors in the endothelium has no effect on development, metabolic phenotypes or blood pressure in HIRECO. Plasma insulin levels were similar following an overnight fast, but were decreased in the HIRECO after glucose challenge. HIRECO mice demonstrated significant endothelial dysfunction measured by a blunted endothelium-dependent vasorelaxation to acetylcholine. Basal NO release was decreased in HIRECO. Endothelium-independent response to sodium nitroprusside remained unchanged. The impaired aortic response to acetylcholine was normalized by the specific NADPH oxidase inhibitor gp91ds-tat, as well as the superoxide dismutase mimetic MnTmPyP. HIRECO demonstrated significant increase in superoxide anion production compared to WT. This data was supported by a concomitant increase in NADPH oxidase isoform, NOX2 protein expression. Both basal eNOS and Akt phosphorylation levels and mRNA expressions, respectively. NADPH-dependent lucigenin-chemiluminescence assay was performed to measure superoxide anion levels. Isolated thoracic aortic rings suspended in organ baths were used to determine vasoconstrictor function. eNOS activity was examined by citrulline assay with 14C-labelled L-arginine. HIRECO were compared to wild type littermates (WT).

Conclusions: These data demonstrate a state of enhanced oxidative stress in the endothelium, leading to reduced bioavailability of NO and endothelial functions. These data also demonstrate a state of enhanced oxidative stress in the endothelium, leading to reduced bioavailability of NO and endothelial functions.

5931 | BENCH Notch signaling regulates the lifespan of vascular endothelial cells via a p16-dependent pathway.


Introduction: Rapid turnover of vascular endothelial cells occurs in aged vessels, leading to reduced bioavailability of NO and endothelial functions. These data also demonstrate a state of enhanced oxidative stress in the endothelium, leading to reduced bioavailability of NO and endothelial functions.

Methods: Western blotting and RT-PCR were carried out on tissues and isolated endothelial cells from lungs to confirm the presence of human insulin receptor protein levels and mRNA expressions, respectively. NADPH-dependent lucigenin-chemiluminescence assay was performed to measure superoxide anion levels. Isolated thoracic aortic rings suspended in organ baths were used to determine vasoconstrictor function. eNOS activity was examined by citrulline assay with 14C-labelled L-arginine. HIRECO were compared to wild type littermates (WT).

Results: Over-expressing human insulin receptors in the endothelium has no effect on development, metabolic phenotypes or blood pressure in HIRECO. Plasma insulin levels were similar following an overnight fast, but were decreased in the HIRECO after glucose challenge. HIRECO mice demonstrated significant endothelial dysfunction measured by a blunted endothelium-dependent vasorelaxation to acetylcholine. Basal NO release was decreased in HIRECO. Endothelium-independent response to sodium nitroprusside remained unchanged. The impaired aortic response to acetylcholine was normalized by the specific NADPH oxidase inhibitor gp91ds-tat, as well as the superoxide dismutase mimetic MnTmPyP. HIRECO demonstrated significant increase in superoxide anion production compared to WT. This data was supported by a concomitant increase in NADPH oxidase isoform, NOX2 protein expression. Both basal eNOS and Akt phosphorylation levels and mRNA expressions, respectively. NADPH-dependent lucigenin-chemiluminescence assay was performed to measure superoxide anion levels. Isolated thoracic aortic rings suspended in organ baths were used to determine vasoconstrictor function. eNOS activity was examined by citrulline assay with 14C-labelled L-arginine. HIRECO were compared to wild type littermates (WT).

Conclusions: These data demonstrate a state of enhanced oxidative stress in the endothelium, leading to reduced bioavailability of NO and endothelial functions. These data also demonstrate a state of enhanced oxidative stress in the endothelium, leading to reduced bioavailability of NO and endothelial functions.
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CCT A was a mean of 6.5 days (± 8.2). Subjects with IMA graft failure had less diabetes, a lower grade LAD stenosis, and worse graft quality. After adjustment, predictors for IMA graft failure were diabetes (OR: 0.55, 95% confidence interval [CI]: 0.36-0.83, p=0.004), and LAD stenosis >75% (OR: 1.76, 95% CI: 1.20-2.16, p=0.004). LAD stenosis, but not diabetes remained predictive in an alternative model in which IMA failure was defined as a composite of either >75% stenosis or death before angiography. The model for clinical outcomes found that IMA failure was associated with a significantly higher incidence of subsequent acute (<14 days of angiography) events and a trend towards more subsequent remote events (see Figure 1).

Conclusion: Patients with less severe pre-operative LAD stenosis are at higher risk for IMA graft failure. While the long-term clinical implications are less clear, IMA graft failure is associated with increased early adverse clinical events.

5941 | BESIDE
Can serial cardiac troponin I measurements following coronary artery bypass grafting be used to identify early graft occlusion?

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Purpose: The aim of this study was to determine if serial measurements of cardiac troponin I (cTnI) following coronary artery bypass grafting (CABG) can be used to identify early graft occlusion.

Methods: From September 2011 to June 2012 patients with stable angina pectoris and 2-3-vessel disease, undergoing elective on-pump CABG were considered. Blood samples for cTnI measurements were taken 9 times pre- and postoperatively. Tomoses were performed in the 34 patients. CCT A demonstrated a total of 12 occluded grafts in 8 patients. Three patients had a myocardial infarction (MI) in the period time from CABG to CCT A. Two of the MIs occurred -72 hours following CABG. Only in one MI patient an occluded graft was found. The peak cTnI value did not differ significantly between the 8 patients with one or more occluded grafts (10850 ng/L) and the 26 patients without graft occlusion (10950 ng/L) (p=0.935).

Conclusion: Patients with stable angina pectoris undergoing elective CABG, serial postoperative measurements of cTnI were not useful in identifying patients with early graft occlusion.

5942 | BESIDE
Mortality impact of previous coronary angioplasty in the long-term follow-up of patients with acute coronary syndromes submitted to coronary artery bypass surgery during the same hospitalization


Purpose: There is strong evidence in the literature suggesting that previous percutaneous intervention (PCI) in the non-operated patients (pts) submitted to coronary artery bypass graft surgery (CABG). However, the evidence regarding pts with ACS and/or long-term outcome data for this population, the purpose of this study, is very scarce.

Methods: We analyzed retrospectively a non-selected population of 461 pts (mean age 64.5 years, 70.9% men) with ACS submitted to CABG during the same hospitalization, out from 4100 ACS pts included prospectively in a dedicated databank. The mean (± SE) follow-up (FU) time was 4.56±0.18 years (maximum 13.9 years). The Pearson Chi-square and the Tarone-Ware tests were applied as indicated. Adjusted models utilizing the Cox stepwise regression method were developed in order to adjust for confounder baseline and in-hospital factors.

Results: During the in-hospital phase the Odds-Ratio (OR) for mortality according to presence/absence of previous PCI was 1.3 (P=0.45). During FU, the Kaplan-Meier survival time (mean ± SE) for the groups with presence or absence of previous PCI were, respectively, 8.43±0.68 years and 9.70±0.34 years (P=0.085). Excluding pts with interventional septum defect (IVSD) and cardiac tamponade - CT (N=14), the figures for pts with or without previous PCI were, respectively, for in-hospital mortality OR=1.38, P=0.07; mean survival times 8.50±0.68 years and 9.90±0.34 years (P=0.047). In the adjusted models, for the whole population the following variables correlated significantly and independently with mortality: age (P<0.001, HR per year=1.049), in-hospital cardiac troponin I shock (P=0.001, HR=4.55), early graft occlusion (P=0.018, HR=1.63), previous stroke (P=0.006, HR=2.83), CT (P=0.031, HR=3.12), and ST-elevation MI (P=0.046, HR=0.67). Excluding IVSD and CT, the results were: age (P<0.001, HR per year=1.049), in-hospital cardiac troponin I shock (P=0.001, HR=2.83), previous stroke (P=0.006, HR=2.28), previous PCI (P=0.027, HR=1.59) and ST-elevation MI (P=0.041, HR=0.65).

Conclusion: The presence of previous PCI correlates with worse prognosis in patients with acute coronary syndromes submitted to surgical coronary revascularization during the same hospitalization.

5943 | BESIDE
Comparison of euroscore i, ii and acef for risk prediction after on-pump and off-pump cabs

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Purpose: The role of new scores in risk prediction after CABG is not defined. Our aim was to evaluate the predictive properties of ES II and ACEF, as compared to ES I, after on-pump and off-pump CABG.

Methods: We included 1220 pts. Mean ES I, ES II and ACEF predicted risk were 3.75%, 1.63% and 2.41%. Global all-cause mortality was 3.0%. Off-pump had lower mortality (1.7% vs 4.7%, p=0.001, lower PO bleeding (1.0% vs 3.0%, p=0.035) and stroke rate (3.9% vs 6.7%, p=0.015), but more new revascularization (1.5% vs 0.2%, p=0.006). Multivariable analysis showed that On Pump (OR=3.08, ICS 1.22-8.4, p=0.017) and EuroSCORE II (OR=1.29, ICS 1.04-1.60, p=0.023) were independent predictors of in-hospital/30 days mortality. Performance of ES I and ES II and ACEF in the 4 risk strata was measured by O/E ratio (ES I: 1.19, 0.60, 0.99 and 0.61; ES II: 0.85, 2.54, 2.06 and 1.50; ACEF: 2.26, 0.67, 0.91 and 1.26). ES II was best in low and very high risk, and ACEF was adequate in high and very high risk groups. ES I was adequate only in low risk. The best performance was ES II in Off-pump group (O/E 1.11, 95 IC 1.03-1.22). Calibration in the entire cohort was poor for ES I and adequate for ES II and ACEF ( Hosmer-Lemeshow p=0.20, 0.158 and 0.567, respectively). In Off-pump ES 2 and ACEF were also well calibrated (p=0.251 and 0.69). Accuracy of ES II was higher than ES I and ACEF in the entire cohort, off-pump and on-pump groups (C stat= 0.71, 0.652 and 0.724 (ES II); 0.650, 0.518 and 0.699 (ES II); 0.663, 0.575 and 0.689 (ACEF) respectively; DeLong test p<0.05 for the 3 comparisons). ES II greatly improved risk classification compared to ES I and ACEF in the 4 risk strata. In the 3 comparisons, ES II was better than ES I and ACEF, and improved risk reclassification in many patients. ES II is the best risk score for risk prediction after CABG.
5944 | BEDSIDE
Is pulmonary function assessment before coronary artery bypass graft surgery always necessary?
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**Purpose:** Postoperative pulmonary complications (PPC) contribute significantly to overall morbidity and mortality of coronary artery bypass graft surgery (CABG). An attempt to prevent PPC, pulmonary function tests (PFTs) are routinely used as a standard-of-care for preoperative risk assessment. We aimed to determine whether preoperative PFTs are predictive of PPC.

**Methods:** This retrospective study was conducted in consecutive patients who underwent non-urgent CABG, between 2003 and 2008, in our tertiary care institution. Pulmonary function was evaluated through clinical and functional assessment. PPC was defined as any clinically significant pulmonary abnormality (disease or dysfunction) that adversely affected the clinical course.

**Results:** Of the 203 patients included in the study, 50 (24.6%) had a pathologic pattern: 18 (8.9%) had PFTs consistent with at least class II chronic obstructive pulmonary disease and 1 (0.5%) had a pure restrictive pattern. We identified 14 (6.9%) postoperative PPC. Patients with preoperative abnormal clinical exam and/or chest x-ray did not present significantly more PPC (4/42 [9.5%] vs 10/161 [6.2%], p=0.4); patients with abnormal PFTs did not significantly differ from that of patients with normal or sub-normal ones (2/19 [10.5%] vs 12/184 [6.5%], p=0.63). We found no significant difference when we compared the group presenting abnormal clinical exam/chest x-ray and PFTs, and the group with normal clinical exam/chest x-ray and PFTs (3/14 [21.4%] vs 0/15/6 [6.4%], p=0.26).

**Conclusions:** PFTs were not useful to predict the incidence of postoperative PPC. Therefore, it does not seem to be relevant to perform these tests systematcially before CABG.

5945 | BEDSIDE
The transplants conundrum in cardiac surgery: does age matter?
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1 University of Foggia, Foggia, Italy; 2 Città di Bari Hospital CBH, Cardiovascular Surgery, Bari, Italy; 3 Dept. Cardiovascular Surgery and Transplant V Monaldi Hospital, Naples, Italy

**Purpose:** Red blood cells (RBCs) transfusion is a well-known predictor of acute kidney injury (AKI) and death after cardiac surgery procedures. This study explored whether a similar effect existed among octogenarians.

**Methods:** Study population included 1765 consecutive adult patients undergoing cardiac operations on cardiopulmonary bypass from 2011 to 2013 in a single centre (age: 67±10.3; female: 33.1%; redo: 6.2%; urgent/emergent: 12.9%; isolated valve: 40.1%; isolated CABG: 30.4%; combined: 26.7%). The relationship between RBCs with both survival and AKI, and any interaction by age (<80 years versus ≥80 years) was estimated. A propensity score for the patients younger than 80 years (52.8% versus 39.7%; p<0.01) was calculated. Multivariable logistic models for study outcomes.

**Result:** The incidence curve was developed to seek for the interaction between this propensity score in octogenarians was 0.53±0.3 vs 0.39±0.3 in younger patients (p<0.0001) with a twofold increase in the relative risk for transfusion. Anyhow, age did not independently predicted the need for RBCs. AKI and fatality rates were significantly higher in transfused subset irrespective of age. Nevertheless older age per se did not prove an independent predictor of AKI and fatality.

**Conclusions:** Octogenarians receive RBCs more often than do younger patients. Frailty and not age per se confers an increased risk of RBC transfusion and worse outcomes. Careful evaluation of preoperative patient profile is mandatory in octogenarians referred for cardiac surgery.

5946 | SPOTLIGHT
Assessment of performance and communication of results to add quality in heart surgery

**Introduction:** One of the main challenges of current hospital management is the assessment of the medical team. The medical team performance assessment model should favor evidence-based comparisons.

**Method:** In 2011, a performance assessment related with the medical team performance was designed to comply with medical ethical standards and to follow internal guidelines. A meeting was held to disseminate the assessment model among the heart surgery teams, in which we had 100% compliance and agreement from physicians. The assessment was divided into three categories of indicators: outcomes, processes and compliance with institutional protocols, goals based on international indicators and each indicator was scored (10 to 50).

**Results:** As shown in the table below.

<table>
<thead>
<tr>
<th>Assessed item</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death rate</td>
<td>0</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Readmission</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>Discharge within 5 days</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>LOS - 14 days</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Medications</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
</tbody>
</table>

**Conclusion:** The assessment of the performance of heart surgical teams is a tool used to improve outcomes and clinical care, has a positive impact as it enables the creation of improvement strategies that engage the surgical teams and the organization’s managers.

5947 | BEDSIDE
Mortality reduction with IABP prior to emergency CABG in patients with cardiogenic shock
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**Objectives:** Patients with cardiogenic shock undergoing coronary artery bypass graft (CABG) surgery have been supported by intraaortic balloon counterpulsation (IABP) therapy, according to the recommendations. Recently, the benefit of IABP support has been doubted, and the optimal starting point for IABP therapy, i.e. before or after surgical revascularization, remains questionable.

**Methods:** In a single-center retrospective study consecutive patients with cardiogenic shock undergoing emergency CABG in 2008, 2009 and 2010 were supported by IABP therapy either beginning before (“IABP-before” group) or after (“IABP-after” group) revascularization, with 150 patients in each group. In the IABP-before group, IABP support was started either prior to or at the beginning of the CABG operation, in the IABP-after group at the end of the CABG operation. All patients (average age 68 years; 32% women) received the best available therapy with cardiogenic shock with the aim of early CABG. After CABG, the duration of IABP support in the IABP-before group was 4.2±1.9 and in the IABP-after group 5.6±1.4 days.

**Results:** At 30 days post CABG operation (POD 30), all-cause mortality was significantly lower in the IABP-before group, albeit without significance, than in the IABP-after group (33% vs. 37%, respectively). Conversely, after 1 year the IABP-before group showed a significantly lower all-cause mortality rate than the IABP-after group (41% vs. 52%, respectively; p=0.02). Complications such as major bleeding, peripheral or intestinal ischemia, sepsis and stroke did not differ significantly between the two groups.

**Conclusion:** IABP support initiated before surgical revascularization markedly reduced the 1-year mortality in patients with cardiogenic shock undergoing early CABG revascularization in contrast to IABP therapy beginning after surgical revascularization. These beneficial effects were not obvious at 30 days. Initiation of IABP therapy before CABG did not cause an increase in IABP-related complications. IABP support does benefit patients in cardiogenic shock due to acute onset of ischemic origin with urgent need for coronary revascularization.

5948 | BEDSIDE
Endothelial progenitor cell homing in human myocardium in patients with coronary artery disease
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**Purpose:** Endothelial progenitor cells (EPCs) are mobilized from bone marrow

**Results:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>Discharge within 5 days</th>
<th>Readmission</th>
<th>LOS - 14 days</th>
<th>Medications</th>
<th>Medication score in octogenarians</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50%</td>
<td>440</td>
<td>250 (57%)</td>
<td>220 (50%)</td>
<td>410 (93%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| ≥ 50% | 1054 | Predictors of outcome in coronary artery bypass grafting / Improving diagnosis of stable coronary disease

**Conclusion:** The assessment of the performance of heart surgical teams is a tool used to improve outcomes and clinical care, has a positive impact as it enables the creation of improvement strategies that engage the surgical teams and the organization’s managers.

**Conclusions:** The assessment of the performance of heart surgical teams is a tool used to improve outcomes and clinical care, has a positive impact as it enables the creation of improvement strategies that engage the surgical teams and the organization’s managers.
into peripheral blood, contributing to the revascularization of ischemic areas, to endothelial repair and to the physiological maintenance of vascularization. EPC mobilization and homing has been primarily linked to inflammation and infection presence. While the presence of circulating EPCs has been widely evaluated in different diseases, few studies tried to evaluate the presence of EPCs in human vital myocardium. Aim of our study was to investigate EPC levels both in peripheral blood and in myocardium in the same patients at the same time, evaluating the correlation with coronary artery disease (CAD) presence.

Methods: 36 consecutive patients admitted either for valve replacement surgery or ascending aorta substitution (n=14, group A) or for coronary artery bypass grafting surgery (n=22, group B) were enrolled for the study. Group A patients (4 males, 10 females, age 75.1±7.0 years) had no-ischemic heart disease with no evidence of CAD presence, while Group B patients (13 males, 9 females, age 76.2±4.5 years) comprised mono- (9 out of 22), bi- (7 out of 22), or tri- (6 out of 22) diseased coronary vessels (CAD presence, evaluated as a stenosis >75%). EPC (CD34+KDR+) levels were assessed before the intervention by flow cytometry on whole blood (circulating EPCs) and by immunohistochemistry on a right appendageal segment collected during cardioplegia induction (tissue EPCs).

Results: In myocardial tissue, EPCs were primarily located inside the endothelium or the interstitium at epicardial level. A significant increase of tissue EPCs (p<0.001), accompanied by a significant reduction of circulating EPCs (p<0.01) was observed in the Group B patients (characterized by CAD presence), as compared to Group A patients (tissue EPCs: Group A 0.218±0.052 vs. Group B 0.533±0.211 EPCs/mm²; circulating EPCs: Group A 87.5±16.6 vs. Group B 57.4±6.9 EPCs/ml).

Conclusion: Our data show an opposite effect of CAD presence on circulating and tissue EPCs. The presence of CAD disease and the consequent chronic ischemia could represent a trigger to increase EPC recruitment through mobilization from bone marrow and homing in myocardium, supporting the hypothesis of EPC mobilization and homing in myocardium or the interstitium at epicardiac level. A significant increase of tissue EPCs (p<0.001) was observed in Group B patients as compared to Group A patients (tissue EPCs: Group A 0.218±0.052 vs. Group B 0.533±0.211 EPCs/mm²)

5949 | BEDSIDE
Proprotein convertase subtilisin/kexin type 9 (PCSK9) concentrations predict event-free survival in patients with stable coronary disease on statins

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Background: Proprotein convertase subtilisin/kexin type 9 (PCSK9) increases LDL-C concentrations by enhancing degradation of hepatic LDL-receptors. Therefore, PCSK9 inhibitors emerge as a new option to lower LDL and as therapeutic tool in the prevention of cardiovascular (CV) disease. The association of PCSK9 and event-free survival has not been clarified prospectively in high-risk patients. This prospective cohort study analyzes risk prediction with PCSK9 serum concentrations in patients with stable coronary artery disease (CAD) on statin treatment.

Methods and results: Fasting PCSK9 concentrations were measured in 504 consecutive patients with stable CAD confirmed by angiography. The median age was 68 years, 63% of patients were male and 95% were treated with statins. Oral glucose tolerance tests were performed in all patients without known diabetes for metabolic characterization. PCSK9 concentrations correlated strongly with fasting glucose tolerance tests (R=0.33, p<0.0001) and PCSK9 was associated with statin treatment, age, hypertension, hyperlipidemia, C-reactive protein, hemoglobin A1c, fasting insulin and total cholesterol. No association was observed with body mass index, waist circumference, LDL- or HDL-cholesterol (linear regression analyses were not freely circulating miRs predicts the occurrence of cardiovascular events in stable CAD patients.

Conclusion: Expression of microvesicle-incorporated miR-126 and miR-199a but not freely circulating miRs predicts the occurrence of cardiovascular events in stable CAD patients.

5951 | BEDSIDE
Association between plaque vulnerability and eicosapentaenoic acid in non-hypercholesterolemia patients


Background: Recent reports suggest that eicosapentaenoic acid to arachidonic acid ratio (EPA/AA ratio) is a new risk marker for coronary artery disease. The aim of this study was to evaluate the relationship between EPA/AA ratio and coronary plaque vulnerability in non-hypercholesterolemia patients.

Methods: Consecutive non-hypercholesterolemia patients with stable anginapectoris (n=76) without any lipid lowering therapies were divided into two groups based on the presence of in vivo thin cap fibroatheroma (TCFA) in de novo target vessels assessed by virtual histology intravascular ultrasound (VH-IVUS). VH-TCFA+ (group n=18) vs. VH-TCFA- (group n=58).

Results: Total cholesterol, low-density lipoprotein cholesterol, high-density cholesterol, and triglyceride levels were similar between the two groups. On the other hand, EPA/AA ratio was significantly lower in Patients with in vivo TCFA than patients without in vivo TCFA (0.39±0.18 vs 0.51±0.23, p<0.05). In addition, docosahexaenoic acid level was also significantly lower in Patients with in vivo TCFA (117±29.5 vs. 140±35.4, p<0.05). Percent necrotic core volume was significantly higher in TCFA group (25.3±5.2% vs 19.6±4.3%, p<0.01).

Laboratory data

<table>
<thead>
<tr>
<th></th>
<th>T.CHA (mg/dl)</th>
<th>LDL-C (mg/dl)</th>
<th>HDL-C (mg/dl)</th>
<th>TG, (mg/dl)</th>
<th>EPA, μg/ml</th>
<th>AA, μg/ml</th>
<th>DHA, μg/ml</th>
<th>EPA/AA</th>
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</thead>
<tbody>
<tr>
<td>T.CHA</td>
<td>174±36.4</td>
<td>179±36.1</td>
<td>107±19.1</td>
<td>42.9±14.5</td>
<td>111.2±71.1</td>
<td>117.4±29.5</td>
<td>0.39±0.18</td>
<td>0.29</td>
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<tr>
<td>LDL-C mg/dl</td>
<td>107±19.1</td>
<td>108±18.7</td>
<td>42.9±14.5</td>
<td>111.2±71.1</td>
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<tr>
<td>HDL-C mg/dl</td>
<td>42.9±14.5</td>
<td>45.0±11.0</td>
<td>111.2±71.1</td>
<td>117.4±29.5</td>
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<tr>
<td>TG, mg/dl</td>
<td>127.4±66.2</td>
<td>112.1±35.4</td>
<td>117.4±29.5</td>
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<tr>
<td>EPA, μg/ml</td>
<td>54.3±73.3</td>
<td>72.6±38.5</td>
<td>136.6±32.1</td>
<td>136.6±32.1</td>
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<tr>
<td>AA, μg/ml</td>
<td>136.6±32.1</td>
<td>142.4±28.0</td>
<td>136.6±32.1</td>
<td>136.6±32.1</td>
<td>0.04</td>
<td>0.04</td>
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</tr>
<tr>
<td>DHA, μg/ml</td>
<td>117.4±29.5</td>
<td>140.4±35.4</td>
<td>117.4±29.5</td>
<td>117.4±29.5</td>
<td>0.01</td>
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<tr>
<td>EPA/AA</td>
<td>0.39±0.18</td>
<td>0.51±0.23</td>
<td>117.4±29.5</td>
<td>117.4±29.5</td>
<td>0.05</td>
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</tbody>
</table>

Conclusion: Low EPA/AA ration and low docosahexaenoic acid level might...
be associated with coronary plaque vulnerability even in patient with non-hypercholesterolemia.

5952 | SPOTLIGHT
CPET in the diagnosis of CAD – a new approach
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Purpose: Prospective study to examine the diagnostic accuracy of a new exercise-based parameter (abrupt steepening of HR response) in late exercise to diagnose macro-vascular CAD.

Method: 1000 CPX performed in symptomatic patients & 50 Angiograms in a single centre.

Results: Patients without inducible ischemia have a linear HR response as a function of VO2 throughout exercise (Fig. 1). Patients with inducible ischemia develop mechanical dysfunction and a compensatory steepening of HR response (curvilinear) (Fig. 2); this signifies clinically significant global ischemic burden. Fifty consecutive patients with an abnormal response underwent angiography. The sensitivity and specificity for significant large vessel atherosclerosis (one or more vessels with >50% stenosis) was 92% (Table 1).

Table 1. CPX relationship to coronary angiogram

<table>
<thead>
<tr>
<th>Coronary angiogram (Gold Standard)</th>
<th>NPV negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Test outcome positive</td>
<td>35 (TP)</td>
</tr>
<tr>
<td>Test outcome negative</td>
<td>3 (FN)</td>
</tr>
<tr>
<td>Sensitivity = 92%</td>
<td></td>
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<tr>
<td>Specificity = 92%</td>
<td></td>
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<tr>
<td>Accuracy = 92%</td>
<td></td>
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<tr>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Test outcome positive</td>
<td>1 (FP)</td>
</tr>
<tr>
<td>Test outcome negative</td>
<td>11 (TN)</td>
</tr>
<tr>
<td>Sensitivity = 78.5%</td>
<td></td>
</tr>
<tr>
<td>Specificity = 92%</td>
<td></td>
</tr>
<tr>
<td>Accuracy = 92%</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: In the contracting Ischemic Myocardium, an oxygen supply-demand mismatch results in diastolic dysfunction causing the stroke volume response to deteriorate and HR response to steepen with a progressively increasing work rate past the ischemic threshold. This methodology is seen far more frequently than ST depression and is highly sensitive to the presence of a physiologically significant ischemic burden.

5953 | BEDSIDE
Diagnostic yield of invasive coronary angiography in the workup of patients suspected of coronary artery disease: referral strategies in a tertiary care hospital
R. Ladeiras-Lopes, N. Bettencourt, J. Almeida, T. Dias, R. Fonseca, V. Gama. Hospital Center of Vila Nova de Gaia/Espinho, Department of Cardiology, Vila Nova de Gaia, Portugal

Purpose: Invasive coronary angiography (ICA) is an important exam in the diagnostic workup of patients suspected of stable coronary artery disease (CAD). However, recently published studies describe 30-45% rates of normal coronary arteries. We sought to describe the referral strategy for ICA in a tertiary care hospital in comparison to the 2013 ESC guidelines.

Methods: All elective diagnostic ICAs performed in a tertiary care hospital from 2008 to 2012 to evaluate patients suspected of having CAD were reviewed. Patients with known CAD or unstable presentation were excluded from the analysis. We collected data on patient’s clinical status and symptoms and non-invasive diagnostic tests performed before referral for ICA. Pretest probability (PTP) was calculated with the 2011 modified Diamond-Forrest model. The ICA was classified as normal if there was no epicardial coronary stenosis ≥70%, non-obstructive CAD if the stenosis was >30% but <70% (-50% for left main stenosis) and obstructive CAD for left main stenosis ≥50% or other epicardial coronary stenosis ≥70%. The non-invasive diagnostic test performed before ICA was classified as positive, negative or inconclusive. Results are presented as mean ± standard deviation or proportion of cases.

Results: From the 13,864 ICAs performed in the 5-year period, we identified a total of 2,818 ICAs fulfilling the inclusion criteria. Sixty-nine percent were male and the mean age was 63.6 ± 9.9 years. Most patients (64.2%) demonstrated typical angina and 7.9% complained of symptoms other than chest pain. One patient had a low PTP of CAD. From the 2,755 (97.7%) patients with intermediate PTP, 468 (17%) didn’t perform any prior non-invasive stress test. Most patients (69.4%) performed one non-invasive test, 13.5% 2 tests and only 0.3% 3 tests before ICA. The most common non-invasive evaluation was performed by treadmill exercise test (63%), followed by SPECT (22.3%), CTA (10.6%), stress echocardiography (1.1%) and stress CMR (only 11 patients). Five percent of the total population was directly referred for ICA after CTA. A total of 986 ICAs (33.5%) showed normal coronary arteries and 14.3% non-obstructive CAD. On the other hand, an obstructive coronary stenosis was present in 1538 ICAs (52.3%), mostly 1-vessel disease (728 ICAs).

Conclusion: We report a 34% rate of normal ICAs in a tertiary care hospital population investigated for possible CAD. According to the current 2013 ESC guidelines, there is a need for improvement in patient referral for ICA in order to maximize its potential in the diagnosis and treatment of obstructive CAD.

5954 | BEDSIDE
Periprocedural myocardial infarction - does it really matter?
M.K. Christensen1, H. Huang1, C. Torp-Pedersen2, T. Trydal3, J. Ravnkle1.
1 Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark; 2 Aalborg University, Department of Health Science and Technology, Aalborg, Denmark; 3 Aalborg University Hospital, Department of Clinical Biochemistry, Aalborg, Denmark

Purpose: Cutoff values for troponin to define periprocedural myocardial infarction (type 4a) have been defined by consensus, but the prognostic value of this definition has not been carefully evaluated. The purpose of this study was to determine the incidence of elevated biomarkers after elective PCI using the cut off set by the expert consensus document and ESC clinical practice guideline “The Third Universal Definition of Myocardial Infarction” and to clarify whether this carries independent prognostic significance.

Methods: We performed a historical prospective follow up study of a cohort of patients with stable angina pectoris who underwent elective PCI in a single high volume center from 2000 to 2013. To link and follow the patients we used multiple national Danish registries. We aligned older values of Troponin T concentration (cTnT) to modern high sensitive values in ng/L.

Results: Of the included 2760 patients, 1064 (38.5%) patients had elevated cTnT above 5 x the 99th percentile upper reference limit (URL) after PCI. Follow-up was mean 5.8 years and a total of 15891 years. In stratified analysis of the hazard rates for time until death after peak post-PCI cTnT there was no statistically significant difference regarding all-cause mortality or the combined end-point of death or new onset heart failure. Figure 1 shows Kaplan-Meier plot of peak post-procedural cTnT in five groups. There was also no significant difference in multivariable analysis adjusting for gender and age.

Conclusion: The incidence of elevated biomarkers above the defined 5x URL in our population was high, but this carries no apparent independent prognostic value. Our data suggest that routine measurement of cTnT or CK-MB after elective PCI is not relevant barring procedural complications.
Gender differences in the management of stable angina pectoris

Aim and methods: We followed 6,040 patients (27% women) with suspected SAP referred for first-time coronary angiography in Eastern Denmark during 1999–2009 who had obstructive (>50% stenosis) coronary artery disease (CAD). All patients were free of prior cardiovascular disease. Outcomes were a composite of percutaneous coronary intervention and coronary artery bypass grafting and medical treatment categorized by drug group all within 1 year of angiography and found by registry linkage.

Results: Severity of CAD differed by sex. Women had more single-vessel disease (48% vs 19%), and men had more three vessel disease (68% vs 35%) (P < 0.001 for distribution difference). In total, 1,074 women and 3,328 men were revascularized within 1 year of angiography. Women were less likely to be revascularized within 1 year of angiography. Women were less likely to be revascularized (66% vs 76% in men, P = 0.001). Conventional risk factors (except for hypercholesterolemia) and anatomical testing were all independent predictors of obstructive CAD, with adjusted odds ratios (95% confidence interval) of 3.62 (3.00–4.36) for male gender, 1.04 (1.03–1.05) for age, 2.09 (1.52–2.87) for current smoking, 1.53 (1.25–1.87) for diabetes, 1.27 (1.00–1.61) for hypertension, and 1.99 (1.69–2.39) for coronary CT angiography.

Conclusion: Necessarily 40% of patients without known CAD undergoing elective ICA did not have obstructive lesions, even though more than 4/5 had a positive noninvasive test. Functional tests were more often used but appear to be outperformed by anatomical testing as gatekeepers for ICA.

Combination of global longitudinal strain and late gadolinium enhancement predicts left ventricular reverse remodeling in patients with non-ischemic dilated cardiomyopathy

Purpose: In non-ischemic dilated cardiomyopathy (DCM), left ventricular reverse remodeling (LVR) is a marker of a favorable prognosis, and has been reported to be predicted by the absence of late gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR). The aim of this study was to investigate whether global longitudinal strain (GLS) by two-dimensional speckle-tracking echocardiography (2DSTE) has a predictive value for LVR in combination with LGE in DCM patients.

Methods: We studied 129 consecutive patients with DCM (age ≥15 years, 88 males, LV ejection fraction (EF) ≥30%). All patients underwent CMR and echocardiography with conventional assessment including left atrial (LA) volume and mitral regurgitation (MR) grade and with 2DSTE analysis. After the optimal medical therapy for 12 months, echocardiography was repeated for assessment of LVR which defined as an absolute increase in LVEF ≥10% accompanied by a decrease in LV end-diastolic volume ≥10%. Cardiac death and heart failure hospitalization were defined as cardiac events.

Results: LVR was observed in 76 patients (59%), significantly associated with LGE, LA volume, MR grade, and GLS (all p < 0.05), and strongly associated with a favorable long-term outcome (Follow-up period 1585±835 days, 29 cardiac events, p = 0.01). Multivariate regression analysis showed that GLS was an independent predictor of LVR (HR, 1.20. 95%CI: 1.07–1.34, p = 0.003). Dividing all patients into 4 groups with LGE and GLS cut-off value of 8.5% derived from ROC curve analysis, we found the significant difference in the prevalence of patients with LVR among them (p = 0.01).

Conclusion: GLS is significantly associated with LVR, particularly predicts LVR in combination with LGE, and can indicate a favorable outcome in DCM patients.
5969 | BEDSIDE
Characterisation of transmural longitudinal and circumferential mechanics by multi-layer strain analysis in hypertrophic cardiomyopathy
D. Murano1, F. Valente2, P. Aruta1, G. Cavalli1, G. Calore1, S. Mihaila1, D. Peluso1, P. Melacini2, S. Illecito1, L.P. Badano1, University of Padua, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; Hospital District of Santarém, Serviço de Cardiologia, Santarém, Portugal
Purpose: Until recently, the application of two-dimensional speckle-tracking (2DSTE) in asymptomatic hypertrophic cardiomyopathy (HCM) has been hampered by the impossibility to adjust the region of interest (ROI) to the variations in LV wall thickness. This study aimed to characterise the transmural mechanics in HCM pts using a novel software which allows multi-layer strain analysis and an adjustable ROI.
Methods: In 40 HCM pts and 40 controls matched for age, gender, body size and LVEF, longitudinal (LS) and circumferential (CS) strain at LV endo-, mid- and epicardial layers were analysed using EchoPAC BT13 (GE Vingmed, N). Global and segmental transmural gradients (LSepi-endo and CSepi-endo) were calculated. LVEF and mass were measured by 3D echo.
Results: In HCM pts, global LSendo, LSmid and LSeto were significantly impaired with respect to controls (p < 0.001), and were inversely correlated with LV mass (r = -0.57, p = 0.001). Thus, LSeto-endo was larger in pts vs controls (5.9±1.5% vs 5.5±0.9%, p = 0.11). While CSendo was similar, CSepi was significantly lower in magnitude in HCM pts (Table), and was related with LV mass (r = 0.57, p = 0.001). Thus, CSepi-endo was larger in pts vs controls (20.8±5.4% vs 14.5±3.2%, p < 0.001). A ROC curve analysis, LSendo, LSmid and LSeto (AUC 0.90-0.92), and CSepi and CSepi-endo (AUC 0.84 for both) had the best discriminative power to separate HCM pts from controls.
Conclusions: Multi-layer strain analysis with adjustable ROI may provide objective insights into HCM pathophysiology and disease course. Characterisation of transmural mechanics appeared to be more advantageous for CS than for LS.

5970 | BEDSIDE
Usefulness of speckle myocardial imaging modalities for the differential diagnosis of left ventricular non-compaction of the myocardium
Introduction: Current diagnostic criteria for left ventricular non-compaction (LVNC) may result in overdiagnosis of this disease. Analysis of strain and left ventricular (LV) rotation have reported abnormal results in patients (pts) with LVNC. In our study we evaluate the role of speckle imaging (strain and rotation) in the differential diagnosis of LVNC.
Methods: We have included in our study all pts that between January 2012 and February 2014 fulfilled currently accepted echocardiographic criteria for LVNC in a tertiary hospital non-invasive cardiology laboratory. A control group of healthy subjects with preserved LV ejection fraction (EF), LVM, and a normal LV rotation pattern (-19±50%) were used for comparison. From a total of 220 patients (45±14 years, 54.1% female) were followed for an average of 14 years.
Results: LVEF was significantly reduced in HCM pts compared with controls (p < 0.05), and were younger, compared to those with LVEF >50%. All but 14.5% of LVNC pts, with preserved LVEF, had a normal LV rotation pattern (-19±50%). We observed a significant pattern (HR: 2.112, 95% CI 1.119-3.986, P = 0.021) and it was four times higher in those with concomitant diastolic dysfunction (HR: 4.783; 95% CI 2.863 to 7.990, P < 0.001) as compared to patients with septal thickness ≥12 mm.
Conclusion: In patients with FAP V30M-TTR, the progression of cardiomyopathy is associated with increased risk of death. The combination of septal thickening and diastolic dysfunction increases significantly the risk.

5971 | SPOTLIGHT
Progression of cardiomyopathy in familial amyloid polyneuropathy - impact on prognosis
Introduction: The cardiomyopathy in familial amyloid polyneuropathy (FAP) V30M-TTR is due to progressive infiltration of amyloid in the heart causing diastolic dysfunction in the early stages and myocardial thickening in the more advanced stages of the disease. The temporal evolution and the prognostic significance of these changes are not well known.
Aims: To analyze the progression of cardiomyopathy by conventional echocardiography and to determine its prognostic impact.
Methods: A retrospective study of consecutive V30M-TTR mutation carriers followed annually with echocardiography and conventional Doppler. The predictive value of echocardiography in the risk of death from any cause was evaluated by multivariate Cox regression analysis with adjustment for age and Kaplan-Meier survival analysis (considering multiple tests per patient).
Results: A total of 220 patients (45±14 years, 54.1% female) were followed for a median of 56 months and performed 745 tests. With aging there was a progressive increase in the thickness of the septum and posterior wall, in the left atrial dimension, in the A wave deceleration time and in the pressure half-time and a decrease in the E/A ratio. With the increase in symptoms duration, similar changes were observed. The risk of death increased by 13% for each 1 mm increment of the septal wall (HR: 1.127, 95% CI 1.059-1.198, P < 0.001). The presence of diastolic dysfunction (E/A ratio < 1 or > 2.5) improved the accuracy of prognostic stratification. The risk of death duplicated in patients with septal thickness ≥12 mm (HR: 2.112, 95% CI 1.119-3.986, P < 0.021) and it was four times higher in those with concomitant diastolic dysfunction (HR: 4.783; 95% CI 2.863 to 7.990, P < 0.001) as compared to patients with septal thickness <12 mm.
Conclusion: In patients with FAP V30M-TTR, the progression of cardiomyopathy is associated with increased risk of death. The combination of septal thickening and diastolic dysfunction increases significantly the risk.

5972 | BEDSIDE
Consistency of independent estimates between two assessors of 2D global strain by a novel multi-layer analysis technique using transthoracic echocardiography in HCM with preserved LV ejection fraction
K. Ozawa, N. Funabashi, H. Takaoka, T. Kamata, F. Nomura, Y. Kobayashi. Chiba University Graduate School of Medicine, Chiba, Japan
Purpose: To evaluate the consistency with which different assessors estimated two-dimensional (2D) left ventricular global longitudinal (GLS) and circumferential (GCS) strain analysis by the A wave layer analysis technique using transthoracic echocardiography (TTE), we acquired data from hypertrophic cardiomyopathy (HCM) subjects with preserved LV ejection fraction (EF).
Methods: A total of 22 HCM subjects (16 male, 61±15 yrs, LV EF >50%) underwent TTE (Vivid E9, GE Healthcare) to measure 2D multi-layer global strain in LV myocardium using ECHOPAC software. Apical 4-, 2-, and 3-chamber views were acquired for GLS and parasternal short-axis views at the level of mitral valve, papillary muscle, and apex were acquired for GCS. Quantitative strain measurements of 1) all layers, 2) endocardial myocardial layer only and 3) epicardial myocardial layer only, were performed for both GLS and GCS.
Results: Correlation coefficients (CC) of estimates of 2D GLS in all layers, endocardial and epicardial layers at 4-, 3- and 2-chamber views by the two assessors were 0.872, 0.872 and 0.872 between the contacts (2-chamber view), 0.679, 0.561, 0.742 (2-chamber view), and 0.866, 0.817, 0.878 (3-chamber view), respectively. CC of estimates of 2D GCS in all layers, endocardial and epicardial layers at the level of mitral valve, papillary muscle, and apex by the two assessors were 0.471, 0.478, 0.487 (mitral valve).
PLATELETS AND THROMBOSIS

5977 | BENCH
Uridin triphosphate (UTP) and its analogue are potent antagonists for platelet and endothelial P2Y12 receptors: effect on platelet aggregation and endothelial barrier
M. Aslam, C. Troidl, H. Nef, C. Hamm, D. Guenduez. Cardiology and Angiology, Internal Medicine I, Justus Liebig University, Giessen, Germany

Background: Platelets express two ADP receptors namely P2Y1 and P2Y12 which regulate ADP and agonist-induced platelet shape change and aggregation, respectively. Moreover, we have found that human endothelial cells also express both P2Y1 and P2Y12 receptors. The aim was to characterise the pharmacological profile of the P2Y12 receptor for uridine triphosphate (UTP) and its analogue 2-thio-UTP (S-UTP) in platelets and human endothelial cells.

Methods: The study was carried out on platelet rich plasma freshly isolated from blood donated by healthy volunteers and freshly isolated human umbilical vein endothelial cells (HUVEC).

Results: Both UTP and S-UTP inhibited ADP-induced platelet aggregation in a conc.-dependent manner, S-UTP being more potent. The IC50 values against ADP (10 μM)-induced platelet aggregation were 32±9and 0.36±0.05 μM for UTP and S-UTP, respectively. Likewise, both nucleotides potently antagonised collagen (2 μg/ml)- and epinephrine (10 μM)-induced platelet aggregation. However, both UTP and S-UTP had no effect on ADP- and MRS2693 (P2Y1 receptor agonist)-induced platelet shape change suggesting their inactivity at P2Y1 receptors. PCR data showed that HUVEC also express both P2Y1 and P2Y12 receptors. ADP reduced basal as well as antagonised thrombin-induced endothelial hyperpermeability in a conc.-dependent manner with IC50 8±2 μM. This barrier protective effect of ADP was abolished with a specific P2Y1 receptor antagonist (MRS2500; 10 μM) suggesting a P2Y1 receptor-dependent phenomenon. Both UTP and S-UTP increased endothelial cAMP levels and antagonised thrombin-induced hyperpermeability by 30±5% and potentiated the barrier protective effects of ADP. Similar results were obtained when a specific P2Y12 receptor antagonist (AR-C69093; 10 μM) was employed or P2Y12 receptors were knocked down using shRNA viral plasmids.

Conclusion: These results demonstrate that UTP and S-UTP are potent P2Y12 receptor antagonists and inhibit agonist-induced platelet aggregation as well as thrombin-induced endothelial hyperpermeability. Moreover, ADP mediates endothelial barrier protective effect via activation of P2Y1 receptors and this effect can be potentiated by inhibition of P2Y12 receptors.

5978 | BENCH
Gremlin-1 is released by platelets and its expression level correlates with the degree of platelet activation in patients with coronary artery disease

Background: Gremlin-1 is a member of the DAN-protein family, a subdivision of the cysteine knot superfamily. Through its interaction with Slit proteins Gremlin-1 regulates monocyte chemotaxis. Furthermore Gremlin-1 is an endogenous inhibitor of MIF and modulates vascular inflammation and atherosclerosis. Platelets play a central role in atherogenesis and have been shown to be a major source of Gremlin-1.

Methods: Weanamized 222 patients with CAD undergoing PCI. Using Western blot analysis and FACS we showed that Gremlin-1 is highly expressed by resting and activated human platelets. Platelet aggregation was assessed using Multiplate Analyzer®.

Results: We found that expression of Gremlin-1 on platelets’ surface was independent from platelet count (mean platelet count: 250, platelet-bound Gremlin-1: 14,866±7,0 vs. 17,7±7,5, p=0,987). Platelets activated with ADP showed a higher expression of Gremlin-1 compared to resting thrombocytes (14,866±7,27 vs. 14,76±6,20, t-test for Equality of Means p=0,000). Platelets, which showed a high expression of P-selectin (cut-off 5,5), appeared to express also higher amounts of Gremlin-1 on their surface (14,9±6,2 vs. 10,4±2,6; p<0,039). Diabetes mellitus, the presence of an acute coronary syndrome and an impaired left ventricular function also correlated with a significantly higher expression of Gremlin-1 in platelets (diabetes: 15,4±4,8 vs. 14,6±6,4; p<0,018; ACS: 16,1±8,2 vs. 13,7±6,1; p=0,036; impaired left ventricular function: 14,8±3,8 vs 13,8±5,8; p=0,035) compared to controls. The amount of platelet-bound Gremlin-1 did not significantly vary depending on the degree of platelet aggregation (r=0,49, p=0,571). The platelet-bound expression of GREM1 was not influenced by a therapy with P2Y12-inhibitors (14,95±6,8 vs 14,6±10,1; p=0,16), aspirin (14,2±6,3 vs 15,4±7,9; p=0,08) or oral anticoagulation (14,8±7,3 vs 15,3±7,6; p=0,43).

Conclusion: Gremlin-1 is carried and released by platelets. Its expression level depends on the degree of platelet activation, suggesting platelets as an unrecognized source of Gremlin-1 in acute and chronic cardiovascular diseases. Gremlin-1 might therefore be used as a marker for thrombocyte activation in patients with stable CAD or ACS independent from anti-platelet treatment or platelet count.

5979 | BENCH
Secretion of the proinflammatory signaling lipid sphingosine-1-phosphate (S1P) in platelets depends on the multidrug-resistance protein (MRP)-4 and is inhibited by statins

Purpose: Activated platelets secrete the immunomodulatory lipid mediator sphingosine-1-phosphate (S1P). Numerous biological functions such as inflammation, cell migration and survival are regulated by S1P. The underlying release mechanism may involve ATP-dependent transport. A potentially involved transport protein is the multidrug-resistance protein (MRP)-4 (ABCC4), which is highly expressed in platelets. Several statins are substrates for MRPs and affect platelet function. Therefore, we investigated the contribution of MRP4 to the secretion of S1P from activated platelets and a possible interference by statins.

Methods: Transport of S1P was investigated in isolated inside-out membrane vesicles of ST-9 insect cells transfected with human MRP4 and in human platelets. S1P was determined by mass spectrometry, MRP4 by Western blotting. Localization studies of platelet MRP4 and S1P were performed by confocal microscopy.

Results: Transport studies with fluorescein-labeled S1P indicated a significant ATP-dependent uptake into MRP4-enriched membrane vesicles compared to basal transport rates into vesicles from mock-transfected ST-9 cells. In addition, ATP-dependent transport of S1P was determined in membrane vesicles prepared from human platelets. The expression of MRP4 in platelets was confirmed by Western blotting. Detection of fluorescein-labeled S1P together with staining of MRP4 by a specific antibody in confocal fluorescence microscopy revealed a parallel co-localization of S1P and MRP4 in human platelets. Incubation of MRP4-expressing vesicles from ST-9 cells with flavositain or rosuvastatin (1 - 100 μM) resulted in a significant reduction of S1P transport, suggesting competition with this transport pathway. Furthermore, both statins also inhibited S1P release from human platelet activated with the thromboxane receptor agonist U46619 (10 μM) or with thrombin receptor activating peptide (100 μM).

Conclusions: Secretion of S1P from activated platelets depends on MRP4 and statins can interfere with this transport process. Potentially, this mechanism may contribute to the well-known pleiotropic anti-inflammatory effects of statins.

5980 | BENCH
Rivaroxaban, a direct factor Xa inhibitor, attenuates neo-intima formation following direct injury in mice through the inhibition of proliferative activation of vascular smooth muscle cells
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Background: Activated factor X (FXa) is a key player in the coagulation cascade responsible for thrombin generation, although accumulating evidence suggests it also has various biological functions in many cell types, contributing to the pathogenesis of neointima formation after vascular injury. In this study, we assessed the hypothesis that rivaroxaban, a direct FXa inhibitor, attenuates neo-intima formation after vascular injury in mice through the inhibition of proliferative activation of vascular smooth muscle cells (VSMCs).

Methods and results: C57BL/6 mice were subjected to wire-mediated vascular injury. Rivaroxaban (5 mg/kg/day) or vehicle (control) was administered orally for 4 weeks after injury. The cross sections of the injured arteries at four weeks were stained with elastic van Gieson (EVG) to evaluate neointima formation. There were no differences in body weight gain, blood pressure, plasma glucose levels and plasma lipid levels between the groups. Rivaroxaban significantly reduced neo-intima area (30452±2531 μm² vs. 19582±2531 μm²; P<0.05) and intima/media ratio (4.37±0.50 vs. 2.60±0.50; P<0.05) compared with control. There was no difference in cross sectional area of media between the groups (9460±1729 μm² vs 10214±1729 μm²; P=0.76). In vitro experiments using rat VSMCs demonstrated that FXa stimulation increased mRNA expression of Kruppel-like transcription factor (KLF-5), which is known as one of the key molecule correlogate VSMC proliferation.

Conclusion: Rivaroxaban attenuates progression of neointima formation in a mouse model of vascular injury. Our analyses suggest that FXa contributes to proliferative activation of VSMCs at least partially, participating in the progression of neointima formation after vascular injury.
5891 | BENCH

High density lipoprotein from patients with coronary heart disease loses anti-thrombotic effects on endothelial cells: impact on arterial thrombosis formation

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Background: Primary prevention studies demonstrated an inverse relation between HDL levels and the incidence of cardiovascular events. However, recent evidence suggests that HDL is impaired under certain conditions. HDL from coronary artery disease patients does not support platelet aggregation, while HDL from patients with stable coronary heart disease (CHD) or acute coronary syndrome (ACS) is normal.

Methods: HDL was isolated from healthy subjects or patients with stable CHD or ACS by sequential ultracentrifugation. Analysis of endothelial tissue factor (TF), tissue factor pathway inhibitor (TFPI), plasminogen activator inhibitor type 1 (PAI-1) and tissue plasminogen activator (IPA) expression was performed by Western blot analysis or ELISA.

Results: HDL from patients with stable coronary heart disease (CHD) or acute coronary syndrome (ACS) was found to be less effective.

5892 | BENCH

Influence of reconstituted HDL (rHDL) on activation of platelet G-protein coupled receptors (GPCR) in coronary artery disease

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Background: Thienopyridines such as clopidogrel are irreversible P2Y12-receptor inhibitors. They are used for prevention of ischemic events in atherosclerotic diseases like coronary artery disease (CAD). Though, there are various hints for impaired response to Clopidogrel due to various causes. The activity of the G-protein coupled P2Y12 receptor is dependent on a special membrane structure, so called lipid rafts. Amongst others, these rafts are modulated by HDL (high density lipoprotein).

We investigated whether P2Y12-receptor inhibitor response is modulated by endogenous HDL-levels in patients with CAD and if modulation of response can be achieved by substitution of reconstituted HDL (rHDL).

Methods: HDL was measured in CAD patients with S-T-elevation myocardial infarction and regarded in respect of PRI levels (platelet reactivity index = indicator for quality of response to P2Y12-receptor inhibitors). Moreover, reconstituted HDL was generated and in vitro experiments were performed including flow cytometry, aggregation, hemostatic and platelet bioptting.

Results: In CAD patients we found an inverse association of clopidogrel responsiveness with HDL (T<−2.1, p=0.040; PRI for HDL below median 62.6±4.0%; PRI for HDL above median 53.1±4.8%, p=0.05) indicating an influence of endogenous HDL-levels on P2Y12-receptor activity. Furthermore, PRI was detected by flow cytometry before and after in vitro incubation of whole blood with rHDL. A significantly reduction of PRI levels was observed after addition of 100μg/ml rHDL (p<0.05). Light transmission aggregometry showed a significantly reduced area under the curve (AUC) following ADP stimulation after incubation of platelet rich plasma (PRP) with different concentrations of HDL (p<0.05 for 100μg/ml rHDL). Moreover, a significant reduction in AKT-pathway signal transduction was observed after incubation of samples with HDL and subsequent stimulation with ADP. Finally, no aggregation was observed when washed platelets from patients suffering from coronary artery disease were generated.

Conclusion: The platelet membrane structure composition is important for receptor function. Substitution of rHDL seems to be beneficial for platelet integrity. Particularly in coronary artery disease, this could be of special interest in the face of minor response to P2Y12 receptor inhibitors.

PERIPHERAL ARTERY DISEASE: HIGHER BURDEN, MORE SOLUTIONS

6011 | BEDSIDE

Effect of statin treatment after endovascular therapy for femoropopliteal lesion

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Background: Statin treatment decreases cardiovascular events by reducing LDL cholesterol and inflammation. However, long term effects for peripheral artery disease (PAD) are little known. The purpose of this study is to survey statin treatment may affect PAD patients with femoropopliteal artery disease after endovascular therapy (EVT).

Methods: A multicenter retrospective analysis of femoropopliteal intervention between January 2004 and December 2011, 3469 limbs from 2740 patients were reviewed. The primary endpoint was defined as a composite of death / myocardial infarction (MI) stroke, and secondary endpoint was primary patency (defined as treated vessel without restenosis).

Results: Mean follow-up period was 22.2 months. 1021 patients (37.2%) were treated with statin. Freedom from MACE at 5 years was 81.2% in statin group vs. 78.4% in no statin group, p=0.001. Furthermore, primary patency rate at 5 years was 51.7% and 51.2%, p=0.398, respectively. After adjusting all variables, statin treatment significantly improved MACE (hazard ratio (HR): 0.800, 95% confidential interval (CI): 0.643-0.995, p=0.045). And there was no sig-
significant difference about failure of primary patency [hazard ratio (HR) 0.956, 95% confidential interval (CI) 0.822 - 1.113, p=0.564].

Conclusions: Statin treatment for PAD patients with femoropopliteal artery lesions is effective for reducing the cardiovascular events. However, there is no significant effect for vessel patency after EVT.

6012 | BEDSIDE
Below-the-ankle artery run-off; A predictor of technical success and mortality for critical limb ischemia
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Aims: Endovascular therapy for critical limb ischemia (CLI) still continues to develop for limb salvage and to improve the prognosis. However, it is unclear whether diseased level affects limb prognosis and mortality.

The purpose of this study is to survey how the existence of the below-the-ankle (BA) artery run-off affects for CLI patients after isolated below-the-knee (BK) interventions.

Methods: A multicenter retrospective analysis of BK intervention done for CLI between March 2004 and October 2010, 790 limbs from 689 patients with tissue loss CLI due to isolated BK lesions were studied. They were divided for two groups. One was with BA (1 or 2 run-off) group, and the other was without BA (0 run-off) group. The main endpoint was freedom from amputation, and secondary endpoint was survival rate.

Results: Mean follow-up period was 19.0±17.7 months. There was a significant difference between two groups with BA run-off group (7.9% in BA run-off group and 18.4% in without BA run-off group, p<0.001). By multivariate analysis, without BA run-off was a significant predictor of technical failure [hazard ration (HR) 2.35, 95% confidential interval (CI) 1.44-3.81, p<0.05]. In addition, technical failure was a significant predictor of major amputation [HR 2.61, 95% CI 1.44-3.81, p<0.05]. However, there was no significant difference for survival rate about technical success and failure (p=0.485). Without BA run-off was a predictor for mortality [HR 1.44, 95% CI 1.08-1.91, p=0.05].

Conclusions: The existence of the BA artery run-off is an important predictor for endovascular technical aspect and mortality. Technical success improves limb prognosis. However, Impact for survival rate is not technical success but the existence of BA run-off for CLI patients.

6013 | BEDSIDE
Comparison of treatment modalities for femoropopliteal lesion in claudicants
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Aim: Although endovascular therapy (EVT) has advanced, outcome of treatment for femoropopliteal artery disease is still not enough. There is still limited information regarding differences between EVT and Bypass surgery for femoropopliteal disease. The purpose of this study is to evaluate long-term outcomes of EVT (with or without stent) and bypass surgery (vein or PTFE graft) in claudicants with femoropopliteal disease.

Methods: Data from the RECALISE (REtrospектив Comparative ANALysis of the revascularization method for Infracrural arterial diseaseSE, surgical resection and Endovascular treatment) registry, retrospective, multicenter registry in our country (n=1308), was analyzed. In 589 claudicants with femoropopliteal lesion, bypass surgery (n=91) was performed with vein (n=32) or PTFE (n=59) graft, balloon angioplasty (n=203) or stent placement (n=295) was used in case of EVT (n=498). We evaluated each group by Kaplan-Meier methods and compared by the log rank test.

Results: 1 and 5 years primary patencies were 82% and 74% in bypass group; 68% and 51% in EVT group. According to log rank test, primary patency rates of bypass group with PTFE or vein graft were significantly higher than EVT group with stent.

Conclusions: In conclusion, bypass surgery is feasible treatment for the claudicant with femoropopliteal disease. Stent placement is better solution in case of EVT for femoropopliteal lesion.

6014 | BEDSIDE
Patients with rutherford classification IV have different characteristics and outcome, compared with V and VI
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Background: Endovascular treatment (EVT) has been progressing as the first-line treatment for critical limb ischemia (CLI). Patients with resting leg pain without ulcer or gangrene (Rutherford classification IV: R-4) are classified CLI, but they might have different characteristics compared with Rutherford classification V and VI (R-5/6). Our study aims were to estimate the clinical differences between R-4 and R-5/6 and also to find risk factors for EVT outcomes in R-4.

Methods: Based on the data obtained from a multi-center retrospective study, 1332 limbs (R-4: 331 limbs, R-5/6: 1001 limbs), those were undergone EVT as the primary treatment for isolated infra-popliteal disease at 14 hospitals in Japan between March 2004 and December 2012, were analyzed.

Results: For patients’ backgrounds, there were significant differences between R-4 and R-5/6 groups, in age (74 vs. 71 years, p<0.0001), body mass index (22.3 vs. 21.6, p<0.001), ambulatory status (76.1% vs. 54.6%, p<0.0001), dyslipidemia (38.1% vs. 30.6%, p=0.0034), diabetes mellitus (61.3% vs. 75.3%, p<0.0001), end stage of renal disease (54.4% vs. 66.0%, p=0.0016), and heart failure history (17.1% vs. 31.3%, p>0.0004). For lesions’ characteristics, Transatlantic Inter-Society Consensus (TASC) proportion (AB/CD: 21/310 vs. 28/973, p<0.0001) and a presence of below the ankle disease (45.8% vs. 67.3%, p<0.0001) had significant differences. Angiographic and clinical EVT success rate in R-4 group was significantly higher (97.6% vs. 90.4%, p=0.0001) and both freedom rate from major adverse limb event (MALE: 10.0% vs. 20.1%, p<0.0004) and amputation free survival rate (40.6% vs. 57.7%, p<0.0001) were also better in R-4 group during the mean follow up period (658 days).

Conclusion: From the present results, patients classified R-4 should be recognized to have quite different backgrounds from R-5/6. And once initial EVT obtained clinical success, they could keep free from MALE in such subset of CLI.

6015 | BEDSIDE
Endovascular therapy of steno-occlusive subclavian and innominate artery disease: safety and efficacy in a large cohort at a single center institution with over 20 years experience
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Background: Revascularization of atherosclerotic lesions of the subclavian or innominate artery can be accomplished either by surgical or endovascular therapy. In the recent past, endovascular procedures became increasingly favored over surgical procedures due to their minimally invasive character and low rate of complications especially in patients with significant cardiovascular comorbidities. Therefore, the main aim of this study was to determine the safety and outcome
of endovascular therapy for steno-occlusive subclavian or innominate artery disease at a large single-center institution over a long time period of more than two decades.

Patients and methods: We retrospectively analyzed all endovascular procedures of stenosis or occlusion of the subclavian or innominate artery at both sites of our institution between January 1990 and October 2013.

Results: During the observation period, a total of 130 procedures were attempted in 127 mostly symptomatic patients with stenosis (n=108; 83%) or occlusion (n=22; 17%) of the subclavian (n=119; 92%) and innominate (n=11; 8%) artery. The overall technical success rate was 97.7% (n=127/130). Accounting for the type of lesion, the success rate for stenosis was 100% (n=108/108) and for total occlusion 86% (n=19/22). The periprocedural complication rate was low and included stroke, transient ischemic attacks, and access site complications of 0.8%, 1.5%, and 3.8%, respectively.

During a mean follow up of 28 months (range 1-207 months) the rate of restenosis (>70%) was 12%. Apart from recurrence of symptoms, which was a significant predictor of restenosis (p=0.008), no further significant lesion or procedural risk factors for the development of restenosis could be identified.

Conclusions: Data from this large cohort of typical clinical patients demonstrate that stenosis and occlusion of the subclavian and innominate artery can be treated safely and successfully by endovascular therapy with excellent long-term patency.

ACUTE HEART FAILURE: UPDATE 2014

2064 | BEDSIDE

Does diagnostic position of Acute Heart Failure (AHF) have relationship to mortality? - a report from Euro Heart Failure survey-1

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Introduction: Heart failure is a common problem in elderly population that is almost always associated with other serious co-morbid conditions. Majority of previous publications reporting deaths and discharges with heart failure focused on patients with heart failure as a primary discharge diagnosis, which is likely only to be a minority of cases. Failure to quantify the size of the problem is likely to lead to an under-estimate of the health economic impact of heart failure and under-provision of resources for its care.

Methods: EHFS1 screened consecutive deaths and discharges during 2000-2001 primarily from medical wards over a 6 week period in 115 hospitals from 24 countries, to ascertain patients with known or suspected HF. Information on presenting symptoms and signs were gathered. Mortality was assessed during hospital admission and then 3 months after discharge.

Results: Of all 10,701 patients admitted with suspected HF, Heart failure was considered to be the primary reason for admission in 4,234 (40%), secondary reason for admission if complicated or prolonged stay in further 1,772 (17%), and in 4,695 (43%) it was uncertain that HF is actively contributing in index admission. Patients admitted with secondary heart failure were older 74 years versus 72 in primary HF and 73 in uncertain group. 71% from primary HF, 52% from secondary HF and 58% from uncertain group were on loop diuretic. 58% from Primary HF, 51% from secondary HF and 41% from uncertain group had hypertension and 3.8% from secondary HF, 28% (9%) from primary HF and 183 (4%) from uncertain group were died during index hospital admission. According to cox regression analysis Hazard ratio of death in secondary HF group was 3.26 (P<0.001, CI 2.7-3.93) and Primary HF 1.72 (P<0.001, CI 1.43-2.08) compare to uncertain group during index admission. Total death after 12 weeks of discharge were again higher in secondary HF, 389 (22%), 558 (13%) in primary and 412 (9%) in uncertain group. Conclusion: HF as a secondary diagnosis carries a high mortality. Suspected but unconfirmed HF is not benign and probably reflects a mixture of patients with a heterogeneous prognosis, including those with inadequately investigated HF, patients with other serious medical problems and inappropriate loop diuretic use.

2065 | BEDSIDE

Sex differences in new-onset heart failure patients with reduced and preserved ejection fraction

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Background: Heart failure (HF) poses a unique medical burden of high morbidity and mortality. Elevated resting heart rate is associated with worse outcomes in chronic HF but little is known about its prognostic impact in acute setting.

Methods and results: We examined the association of heart rate with in-hospital mortality in a cohort of 778 patients admitted for acute HF between January 2010 and December 2012. None of the patients had significant arrhythmias, required invasive ventilation, or presented with acute coronary syndrome or primary valvular disease. Heart rates were obtained 24-36 hours after admission. Forty patients died during the hospital stay. The patients were older (78.9 vs. 72±12 years; p=0.0021), had higher heart rate (92±22 vs. 78±18 bpm; p=0.0001), NT pro-BNP (p=0.0005), creatinine (18±18 vs. 14±4 mg/dL; p=0.023), were often diabetics (p=0.026) and had lower systolic and diastolic blood pressures (p<0.05). With multivariable analysis, age (p<0.006), heart rate (p<0.0001), and creatinine (p=0.024) emerged as independent predictors of in-hospital mortality. The mortality rate was higher in patients with a heart rate >80 bpm (11% vs. 3%; p<0.01).

Conclusions: Compared to men, women have a lower risk of developing HFrEF and a higher risk of developing HFrEF, the latter manifesting at higher age, and being associated with atrial fibrillation.
6027 | BEDSIDE
Mechanical circulatory support with the Impella 5.0 and intra-aortic balloon pump for cardiogenic shock in acute myocardial infarction. The IMPELLA-STIC study

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Background: Cardiogenic shock is associated with high mortality in patients with acute myocardial infarction (AMI). Adding a left ventricular assist device (LVAD) to an intra-aortic balloon pump (IABP) may help to bridge patients to recovery from left ventricular failure.

Objectives: This multicentric study aimed to test whether the LVAD Impella LPS.0 associated with an IABP provides superior hemodynamic support compared with IABP alone.

Methods: This was a prospective, randomized study. The primary end point was the change in cardiac power index (CPI) from baseline to 12 hours after implantation. Secondary end points included lactic acidosis change from baseline to 12 hours after support.

Results: Fifteen patients with cardiogenic shock were randomized and 13 were available for analysis. In 13 patients the allocated device (n=6 IABP, n=7 Impella LPS.0+IABP) could be safely placed. No patient died before the implantation. Baseline characteristics were similar in both groups. The CPI 12 hours of support was increased but not significantly in patients with Impella LPS.0+IABP compared with patients with IABP (LPS.0+IABP: 19.4 ± 8.8, IABP: 13.7 ± 5.7, p=0.143). Of 13 patients the allocated device (n=6 IABP, n=7 Impella LP 5.0) with IABP alone.

Conclusion: Use of the Impella L 5.0 and IABP provided no superior hemodynamic support compared to intra-aortic balloon pump alone.

6028 | BEDSIDE
Nesiritide in heart failure: post ASCEND-HF and ROSE-AHF meta-analyses and systematic review

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Background: The use of nesiritide for the treatment of acute decompensated heart failure (ADHF) patients has been controversial due to questions raised on its comparative high cost and side effects. Earlier meta-analyses on nesiritide produced contradictory results. We aim to investigate the clinical outcomes including mortality, haemodynamic and renal effects of nesiritide treatment on patients with ADHF.

Method: We searched multiple databases, without language restrictions, to identify pertinent studies published from January 1998 to March 2013. We selected randomized, controlled trials that compared nesiritide with standard treatment, control or placebo to treat patients with ADHF that provided mortality data.

Results: This meta-analysis has included eleven trials and a total number of 9242 patients with results published between 1996 and 2013. Specifically, it has added data from the four most recent relevant studies including ASCEND-HF and ROSE-AHF studies. There were no significant differences found on 30 day all-cause mortality and readmission, odds ratio (OR): 0.96 (95% CI: 0.77, 1.19) and 0.95 (95% CI: 0.66, 1.36) respectively. The OR for hypotension was significantly higher (95% CI: 0.66, 1.36) respectively. The OR for hypotension was significantly higher in the nesiritide group OR: 2.54 (95% CI: 1.62, 4.00). We also found a small but significant rise in the risk of worsening renal function for the nesiritide group OR: 1.30 (95% CI: 1.04, 1.62).

Conclusion: Use of nesiritide for treatment of ADHF did not improve clinical outcomes but increased risk of worsening renal function. Nesiritide has no role in the management of acute heart failure.

6029 | SPOTLIGHT
Global trends in hospitalization and mortality in acute heart failure: economic burden and the need for innovation in disease management and healthcare policy

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Background: In Europe there are over one million venous thromboembolism (VTE) events annually. However, for this major health problem, there is a paucity of data on the current real-life case-mix and in management.

Methods: The PREFER in VTE Registry enrolled the first patient in January 2013. Enrollment is ongoing until March 2014. Centres in France, Germany, Switzerland, Austria, Italy, Spain and UK (33% office-based/67% hospital-based) are participating. We collected patient characteristics, pulmonary embolism (PE)/deep vein thrombosis (DVT) presentation at time of diagnosis, and management information at baseline and after 1, 3, 6 and 12 months after baseline. Here, we report a snapshot of the available baseline data.

Results: 1843 evaluable VTE patients (mean age 61.6 ± 17.7 years) participated in the pre-specified analysis of VTE and 37.2% suffered from PE with previous VTE making up 18.2% of the cohort. Risk factors included cancer, varicose veins, prolonged immobilization, major surgery/thrombosis. Common cardiovascular comorbidities were comparable within both groups. Bleeding events in the three months prior to diagnosis were recorded in 4.4%, 25.9% were major, 51.9% were clinically relevant non-major. Gastrointestinal and intracerebral bleeds made up 32.1% and 14.8% of all bleeds, respectively (Table).
Cost-effectiveness of apixaban compared to other anticoagulants for the acute (6-month) treatment of venous thromboembolism

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Purpose: The AMPLIFY trial compared apixaban to low-molecular-weight heparin (LMWH) followed by warfarin for acute treatment and prevention of venous thromboembolism (VTE) over a six-month period. Two other novel oral anticoagulants (NOACs), dabigatran (initiated after parenteral anticoagulant therapy) and rivaroxaban, have also been studied for this indication. This analysis evaluated the cost-effectiveness of apixaban compared to other NOACs and LMWH/warfarin from the perspective of the UK National Health Service.

Methods: A Markov model was developed to evaluate the lifetime clinical and economic impact of six-month treatment of patients following a VTE event with apixaban versus other NOACs and LMWH/warfarin. A network meta-analysis was conducted comparing apixaban to other NOACs and LMWH/warfarin for the following end-points: recurrent VTE and related deaths, major bleeds, clinically relevant non-major bleeds, myocardial infarction, and ischemic stroke. Outcomes were time since diagnosis, quality-adjusted life years gained (QALYs), and costs estimated in 2012 GBP. Cost and health outcomes were discounted at 3.5% per year.

Results: Six-month treatment with apixaban following a VTE event was predicted to increase life expectancy and QALYs versus dabigatran, rivaroxaban, and LMWH/warfarin over a lifetime horizon. Apixaban was associated with cost savings versus dabigatran and rivaroxaban, dominating these treatments in cost-effectiveness analysis. Apixaban was a cost-effective alternative to LMWH/warfarin at an ICER of approximately £7,000/QALY. One-way sensitivity analysis indicated that model conclusions were robust over a wide range of inputs. Probabilistic analysis demonstrated that apixaban had the highest probability of being the most cost-effective treatment at willingness-to-pay threshold of £9,000 per QALY.

Conclusions: Six months of apixaban for acute treatment and prevention of VTEs appears to be a dominant alternative to other NOACs and a cost-effective alternative to current standard of care comprising LMWH/warfarin.

Cost-effectiveness of apixaban

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Δ Costs</th>
<th>Δ QALYs</th>
<th>ICER (cost/QALY) for apixaban vs. comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>£66</td>
<td>0.020</td>
<td>Dominant</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>£5</td>
<td>0.005</td>
<td>Dominant</td>
</tr>
<tr>
<td>LMWH/warfarin</td>
<td>£156</td>
<td>0.022</td>
<td>£7,136/QALY</td>
</tr>
</tbody>
</table>

VTE and VTE-related death

Dabigatran 0.77 (0.61, 0.98)** 0.76 (0.63, 0.90)** (23%) 0.66 (0.50, 0.84)** 0.29 (0.19, 0.46)** (27%) 0.78 (0.63, 0.98)** 0.50 (0.36, 0.67)** (28%) 1.60 (1.24, 2.04)** 1.26 (0.93, 1.71)** (20%)

Rivaroxaban 0.69 (0.55, 0.86)** 0.67 (0.53, 0.85)** (38%) 0.57 (0.43, 0.75)** 0.36 (0.26, 0.51)** (50%) 0.63 (0.50, 0.81)** 0.47 (0.35, 0.64)** (52%) 1.35 (1.09, 1.68)** 1.13 (0.87, 1.45)** (24%)

Apixaban 0.67 (0.53, 0.83)** 0.66 (0.52, 0.83)** (39%) 0.54 (0.40, 0.71)** 0.33 (0.23, 0.49)** (50%) 0.61 (0.48, 0.80)** 0.44 (0.32, 0.60)** (51%) 1.31 (1.06, 1.66)** 1.09 (0.84, 1.42)** (22%)

Conclusion: Statin use after diagnosis of incident VTE was associated with a decreased risk of recurrent VTE. Our study suggests the need for a trial to assess the efficacy and safety of statins in the long-term management of VTE.
Use of midodrine for patients with reflex syncope, single-centre results in 178 patients A. Anwar, Y. Saeed, A.P. Fitzpatrick. Manchester Royal Infirmary, Manchester, United Kingdom

Background: Reflex syncope is the most common cause of transient loss of consciousness, T-LOC. Occasionally practical manoeuvres may help symptoms, but many patients need something more to sustain normal life. We report the use of open-label midodrine, an α1-agonist, in the treatment of this common problem.

Objectives: To examine the effect of midodrine in patients with reflex syncope in routine clinical practice in an arrhythmia clinic and Rapid Access Blackouts Triage Centre.

Patients: We treated 178 patients. 140 female (78%), 38 male, (22%) patients with midodrine. Mean age was 48±18, (range 16-90. 72 patients were under 30. All patients had had episodes of T-LOC, for a duration of 49±55 months at first appointment. Thirty nine patients had previously been misdiagnosed with epilepsy.

Data Collection and Analysis: All patients had to have the drug prescribed and dispensed from the base-hospital, because midodrine is not licensed in the UK. For similar reasons, all had regular and frequent follow-up offered, which documented treatment adherence, compliance and number and frequency of syncopes. Patients typically started on 2.5mg tds, and were titrated upwards until symptoms resolved or side-effects prevented a further increase. All patients had a 12-lead ECG.

Results: Follow up data were available for 167 patients (93%), and 11 were lost to follow-up. 156 patients had a normal ECG. 118 patients (68%) showed improvement in symptoms, (sympathetic reduction from 19±18 to 0±23) per 6 months and of these 51 (28%) patients had complete resolution of symptoms. 41 (23%) patients had been on sodium tablets, and 37 (21%) had been on fluordrocortisone without improvement. 16 (9%) patients were able to stop treatment when symptoms resolved completely after 52±42 months of treatment. 13 (7%) patients could only tolerate a minimum dose of midodrine, (2.5mg tds), 17 (9%) had to stop midodrine because of side effects. 15 (8%) patients had no response at all. Conclusion: In

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Purpose: The optimal medical therapy of patients with vasovagal syncope (VVS) remains controversial. Since “stress” is commonly associated with recurrent syncope episodes and serotonine reuptake inhibitors (SSRIs), such as fluoxetine, ex- hibiting a “stress”-like nervous system response, we aimed at examining whether fluoxetine exerts beneficial effects relative to placebo in their ability to prevent VVS in the subset of pts with psychosocial distress.

Methods: We assessed 105 pts with typical history of recent VVS (at least 2 episodes during the preceding 6 months), without any other comorbidity, mean age 48±5 years, 36 males/24 females, all with a typical history of VVS and a diagnosis of a psychiatric, positive head-up tilt test (HUT). Their psychological, stress-related profile was assessed by the Anxiety Sensitivity Index (ASI) questionnaire, a simple, 16-item, self-questionnaire, assessing fear of anxiety-related sensations. At the day of the HUT test, fluoxetine 20mg/day or placebo were randomly assigned to the patient in a 2:1 way to receive either 10-40 mg fluoxetine daily (n=40) or placebo (n=20), and were followed for 1 year. Log-rank test was used to compare the time to occurrence of syncope between the 2 groups. Only syncope episodes occurring after the first month of treatment were included in the analysis.

Results: Following a 12-month follow-up period, a significant difference was observed between pts receiving fluoxetine and those with placebo treatment, regarding the distribution of syncope-free time during the study period (log rank test p<0.05). A significant difference was also observed between the 2 groups regarding the total number of patients who experienced syncope during follow-up: 5/40 (12.5%) of pts with fluoxetine vs 9/20 (45%) pts with placebo, p<0.05.

Conclusion: Fluoxetine is superior to placebo in VVS associated with anxiety and may be a first-line pharmacological treatment in this difficult-to-treat subgroup of patients with VVS.
6065 | BENCH 
Prognostic value of very prolonged asystole during head-up tilt test
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Purpose: To evaluate the frequency and prognosis of a cardioinhibitory response with a very prolonged asystole (>30 seconds) during head-up (HUT) test.

Methods and results: Dual-centre retrospective study, including a total of 2210 consecutive HUT tests (with pharmacological sensitization with isosorbide dinitrate) performed in 2194 patients with syncope of unknown etiology, between January/2003 and October/2013. Cardioinhibitory response with asystole was observed in 145 (6.6%) of these tests [44.1% women, mean age 39±20 years old, 168 (7.6%) in the non-pharmacological phase], with a median duration of asystole of 10 [6-19] seconds. Very prolonged asystole (>30 seconds) was documented in 10 patients (50%) in one patient, floridocortisone was started, but discontinued after 10 months on the patient’s own initiative (no symptomatic improvement); tilt training was conducted in 1 patient and none received a pacemaker. Three patients (30%) had syncope recurrences (median number of syncope 1.67±1.16), but with no significant trauma, and no patient died.

Conclusion: In our study, very prolonged asystole was rare (0.5%) and prognosis, in terms of syncopal recurrence and mortality, was benign despite a non-aggressive management.

6066 | BESIDE 
A long-term follow-up of patients with prolonged asystole >15 secs on head-up tilt testing
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Purpose: Head up tilt testing (HUT) is often used for the diagnosis of vasovagal syncope (VVS), and can provoke a cardioinhibitory response. VVS is a significant cause of syncope and is usually considered benign having little or no effect on mortality and quality of life. We sought to characterise the long-term outcomes of patients with prolonged asystole (>15s) on HUT. We describe the longest duration follow-up of patients with prolonged asystole on HUT.

Methods: In 2012, we conducted a retrospective study on patients found to have prolonged asystole (>15s) on HUT identified from 5,133 patients who were investigated between 1999-2012 at our institution. Patients were mailed questionnaires or telephoned directly to ascertain outcomes. Where contact was not initially possible, the patients’ general practitioners were contacted directly to ask for up-to-date contact details. Statistical analysis was performed using unpaired two-tailed Student’s t-test.

Results: A total of 26 (62% male) patients with a mean age of 45±18 years and a mean duration of asystole on HUT of 26±7s (range 17-45s) were successfully followed-up from a total of 77 patients identified. The follow-up duration was 99±39 months. Six of the 26 patients had undergone permanent pacemaker (PPM) implantation. Of the remaining 20 patients, 16 reported improved symptoms spontaneously. Ten patients sustained injury prior to HUT while only 3 patients sustained injury after HUT. There were no major injuries or deaths after HUT. The 6 patients that had undergone PPM implantation had an mean age of 68±13 (67% male), with 5 of these patients being over 60 at the time of follow up. 4 patients had no further syncope after PPM implantation, with 2 having an improvement in symptoms still suffering from vasovagal syncope. 51 patients could not be contacted by mail, telephone, or had moved without giving new contact details to their previous general practitioner. The high rate of patients lost of follow up was because patients were referred to our tertiary centre from a wide area and were not necessarily seen after HUT. These patients represented the younger cohort with a mean age of 35±16, they were therefore more likely to move place of residence. The mean duration of asystole in these patients was not different (26.5±8.5s, P = ns).

Conclusion: Prolonged asystole (>15s) on HUT does not necessarily predict adverse outcomes with most patients improving spontaneously over a long-term period. Pacemaker insertion does not abolish syncopal symptoms in all patients.

6067 | BESIDE 
A permanent pacemaker is often not the correct treatment for unexplained syncope and symptoms versus ECG correlation is crucial for correct decision-making
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Introduction: Syncope is traditionally associated with bradyarrhythmias, such as asystole and sinus arrest/ asystole, and in those patients a permanent pacemaker may be an appropriate treatment. However, syncope may also occur with tachyarrhythmias, that need other specific treatment, or in the absence of any arrhythmia.

Methods: The observational multicentre PICTURE registry provided an opportunity to assess the mechanism of unexplained syncope by means of an implantable loop recorder (ILR), that provided symptoms–ECG correlation by means of automatic or patient activated ECG capture, with both modes programmable at the investigator’s discretion. A total of 570 patients received an ILR (Reveal) and were followed until recurrence or for at least one year. A device-captured ECG was available in 175 of the 218 patients with a recurrence of syncope, while there was no capture in 43 patients. Bradyarrhythmias included asystole >3s, bradycardia <40 bpm and AV block; tachyarrhythmias included both ventricular and supraventricular tachycardias.

Results: In the 175 patients, syncope was associated with bradyarrhythmias in 95 (54%) patients, tachyarrhythmias in 50 (29%) patients, both brady- and tachyarrhythmias in 12 (7%) and no arrhythmia was found in 33 (19%) patients. A permanent pacemaker was implanted in 86%, 29%, 67% and 0%, respectively: an ICD in 4%, 18%, 25% and 0%; catheter ablation was performed in 1%, 14%, 8% and 0%; drug therapy given in 4%, 28%, 17% and 15%; education/counseling provided in 2%, 6%, 0% and 24%, and no treatment was prescribed in 6%, 22%, 11% and 55%. Brady- and tachyarrhythmias were diagnosed with patient activation in 15% and 26%, respectively; auto-activation in 45% and 34%, and with both modes in 40% and 40%.

Conclusion: While almost all patients with bradyarrhythmias were eventually implanted with a permanent pacemaker, as many as 42% had an arrhythmia mechanism that required other treatment, if any. If a pacemaker had been implanted based on symptoms alone, a large proportion of patients would have received inappropriate treatment. The ILR provided proof of the underlying mechanism of syncope which made specific treatment possible, whether pharmacological and/or non-pharmacological.

Poster Session 7
PUBLIC HEALTH AND HEALTH POLICY

P6069 | PUBLIC HEALTH AND HEALTH POLICY
Impact of premature myocardial infarction in the family: cardiovascular disease and medication use before and after a premature myocardial infarction in a first-degree relative
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Purpose: A premature myocardial infarction (MI), <55 years in men, <65 years in women) in the family is a dramatic event that may prompt first-degree relatives to seek medical advice about their own disease risk. However, the health profile of this group is unknown. In a cohort of MI-free persons with premature MI in a first-degree relative, we assessed the incidence of cardiovascular disease indicators before and after the sentinel MI.

Methods: Using national registers, we identified index persons with a premature MI in the period 1977-2012. We then identified a cohort of first-degree relatives alive and MI-free at the time of the index person’s MI (IP-MI). We estimated cohort incidence rates (expressed per 1,000 person-years) of ischemic heart disease (IH) and stroke and prevalence of treatment for hypertension and dyslipidemia before and after the IP-MI, as evaluated by the Index person’s MI.

Results: We identified 132,682 persons with a premature MI in a first-degree relative. Rates of incident IH in the year before the IP-MI were 0.55 and 0.80 for 35-50 year-old men and women, respectively, 4.26 and 3.71 for 50-65 year-olds, and 7.00 and 6.52 for those >65 years. Corresponding stroke rates were 0.63 and 0.96 for 35-50 year-olds, 3.41 and 2.84 for 50-65 year-olds, and 5.73 and 5.53 for those >65 years. In the year after the IP-MI, IH and stroke rates increased 2-fold to 2.9. Thereafter, IH rates, and stroke rates for all those >65 years, gradually dropped to pre-IP-MI rates; stroke rates in the oldest age group remained elevated -5 years later (men, p=0.003, women, p=0.02). Mean age at MI was 52 and 63 years for cohort men and women, respectively. For persons >50 years, rates of MI were highest 1 year after the IP-MI and then dropped by >65% in subsequent years (p<0.003); MI rates in younger persons were stable over time. Before the IP-MI, 6.5% of men and 12.8% of women were using anti-hypertensive medication, while 3.0% and 4.2% were using lipid-lowering medication. Initiation of lipid-lowering medication use increased by almost 50% in the year after the IP-MI (p<0.001 for both sexes), while the prevalence of initiation of
anti-hypertensives rose 20% for men (p=0.002) and remained stable for women (p=0.32).

Conclusions: Our results suggest an intensification of healthcare seeking behaviors immediately after a premature MI in the family; this increased awareness, however, is not sustained long-term. In line with ESC guidelines, a more intensive and systematic clinical focus on screening and follow-up of these first-degree relatives is warranted.

P6070 | BEDSIDE
Comparing hospital performance in treatment and short-term outcome of patients with acute myocardial infarction
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Background: Judging hospitals according to their quality of care is one approach to improve hospital performance. The statistics behind these interhospital comparisons are frequently rather simple and misleading. Our study was aimed at showing that it is feasible to compare the quality of care between departments of cardiology in different hospitals addressing the problems of random variation and differences in patients' mix.

Methods: The BE is an ongoing prospective acute myocardial infarction registry. Our analysis was a cross-sectional interhospital comparison of 3571 patients with ST-segment elevation myocardial infarction (STEMI) from 18 hospitals (2010-12), and a longitudinal interhospital comparison for 6312 STEMI patients from 16 hospitals (2007/08, 2009/10, 2011/12). Hospital mortalities were compared by fitting a two-level random effects model with patient characteristics as covariates to the data. The resulting mortalities are Empirical Bayes (EB) estimates adjusted for differences in patient populations between hospitals and with missing data imputed.

Results: In the cross-sectional as well as in the longitudinal comparison there were large interhospital differences in crude hospital mortality rates. After Bayesian shrinkage and adjustment for the differences in patient mix, the range in hospital mortality was reduced in the cross-sectional as well as in the longitudinal comparison with no significant differences between hospitals. Adjusted mortality rates were 8.9% in 2007/08, 8.7% in 2009/10, and 8.5% in 2011/12 (p=0.009).

Conclusion: Our analysis demonstrates that the naïve comparison of hospitals by crude means may be unfair and misleading. A statistical analysis that takes population differences and random effects into account may result in different conclusions and may show stable results for average-size hospitals, if data are pooled over 3 years.

P6071 | BEDSIDE
Association of poor adherence to statins and anti-hypertensive drug regimens with the incidence of cardiovascular events
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Purpose: Nonadherence to treatment hinders the successful management of cardiovascular diseases such as hypertension and hypercholesterolemia. Although studies have suggested that poor adherence would result in a higher incidence of cardiovascular (CV) events, medication adherence differs under different healthcare and social environments and the effects of poor adherence on CV events might differ among populations. Here, we investigated the association between adherence to antihypertensive and/or statin therapy and the incidence of CV events in a general clinical, which is characterized by a fast-aging society, higher incidence of stroke than coronary arterial disease due to hypertension, and relatively high medication adherence.

Methods: We performed a retrospective case-control study using a medical record database that contains medical and prescription data of patients in nationwide hospitals. Among patients treated with both antihypertensive and statin therapy, those who experienced CV events (resulting in death or hospitalization for myocardial infarction [MI], stroke, or other CV events) were compared to those who did not. In total, 73 MI, 533 stroke, 17 MI+stroke, and 231 arterial embolism events were included in this study.

Results: The overall age-standardized cumulative prevalence of non-rheumatic MI was 7.8% in 2006, 7.6% in 2008, 7.7% in 2010, and 8.0% in 2012, respectively. Similar results were obtained with adherence to antihypertensive therapy alone and to statin therapy alone. Comparison between patients with stroke and those with cardiovascular events revealed that poor adherence was significantly associated with the incidence of stroke.

Conclusions: Poor adherence to antihypertensive or statin therapy is significantly associated with the incidence of CV events, where medication adherence rates are relatively higher and major CV event types differ from those seen in Western countries.

P6072 | BEDSIDE
Analysis of drugs stored at home by elderly patients with chronic heart failure
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Background: Evidence-based pharmacotherapy improves morbidity and mortality in patients with chronic heart failure (CHF). Medication management and adherence are important components for the effectiveness and safety of the treatment. This study investigated and characterized the drugs stored at home in elderly patients with CHF.

Methods and results: One-hundred-and-one patients with stable CHF age ≥65 years were visited at home and a standardized interview and a thorough assessment of the complete medication were performed. Mean age of the patients was 77.7 years, 53% male, mean NYHA functional class of 2.75 and a Minnesota-Living-with-Heart-Failure score of 59.4 points, indicating poor quality of life. The mean number of different drug packs per patient was 13.1 (range 4-33, mean costs per patient 403€). Cardiovascular drugs accounted for 32% of the packs accounting for 30% of the total costs. On average, 2.4 packs contained medication that was not taken by the patient (18% of the medication, range 0-10, mean costs 61€). Fifty-six percent of the drugs were prescribed by general practitioners, 23% in the hospital, and 7% by medical specialists and 14% were over-the-counter drugs. Sixty-three packages (0.05%) of the drugs at home were expired.

Conclusion: On average, elderly patients with CHF have to manage 13 different drug packs at home. New strategies are needed to support medication management at home.

P6073 | BEDSIDE
Changes in the etiology of valvular heart disease
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Background: The aim of this study is to assess changes in the causes of valvular heart diseases between 2006 and 2011 in our country.

Methods: Data were collected from the National Health Insurance Service from 2006 through 2011. These data consisted of primary diagnoses related to valvular heart disease diagnosed regardless of other conditions. Valvular heart disease included non-rheumatic mitral valve disorders, non-rheumatic aortic valve disorders, rheumatic mitral valve disorders, and rheumatic aortic valve disorders.

Results: Overall, the age-standardized cumulative prevalence of non-rheumatic valvular heart disease was 7.0 per 100,000 persons in 2006 and 110.3 in 2011. It increased from 42.2 in 2006 to 65.2 in 2011 in women and from 28.4 in 2006 to 45.1 in 2011 in men. In particular, it showed greater increase in the group aged greater than 65 years showed greater increase compared to those in the 20-44 year-old group or the 45-64 year-old group in both genders. The age-standardized cumulative prevalence of rheumatic valve diseases did not change dramatically between 2006 and 2011 year.

Conclusions: The overall age-standardized cumulative prevalence of non-rheumatic mitral valve disorders increased between 2006 and 2011, especially in those older than 65 years. These changes should be considered in future designs of cardiovascular healthcare services in rapidly aging countries.
P6074 | SPOTLIGHT
Adherence and uptake of guideline-advocated preventive care in the Australian cohort of the SNAPSHOT Acute Coronary Syndrome Registry

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Purpose: To identify adherence to and uptake of guideline-advocated preventive care during the 18 months after admission for acute coronary syndrome (ACS). Also, to summarise access to medical professionals and secondary prevention programs.

Methods: All patients hospitalised in Australia with ACS were identified between 14-27 May 2012. The Australian death registry, telephone and survey 18 months after discharge was used to determine hospital readmissions, adherence to medications, access to medical professionals and secondary prevention uptake. The EQOD was collected to assess quality of life.

Results: In total, we followed-up 1485 ACS patients, across 251 hospitals, who survived their index admission. The mean age was 68 ±13 years, median GRACE risk score was 126 (IQR: 104-149), two-thirds were male, 257 (17%) had a discharge diagnosis of ST elevation myocardial infarction, 612 (41%) non-ST elevation myocardial infarction and 616 (42%) unstable angina. During follow-up, 135 (9%) died, 102 (11.2%) experienced a heart attack or stroke, 87 (6.5%) had recurrent angina and 188 (20.6%) underwent coronary revascularisation. Mean number of visits to a family doctor was 11 ±9 (range 0-40) and to a cardiologist was 2 ±2 (range 0-20). Of those who survived, 43% withdrew or were uncontactable resulting in 911 survivors completing the follow-up survey. At the time of discharge, 65% of participants were prescribed ≥4 cardio-protective medicines but at 18 months only 273 (30%) were taking ≥4 medicines, including 610 (62%) taking an aspirin and 591 (65%) taking a cholesterol-lowering agent. At follow-up, of the 21% who were smokers at baseline 8% had quit with most (44%) doing so spontaneously, one-third (34%) using nicotine replacement therapy and one-quarter using prescription medication. A total of 342 (37%) participants reported having attended cardiac rehabilitation with two-thirds completing the program. Further, 529 (58%) participated in a community exercise program or were regular walkers, 40 (4%) received telephone coaching/counselling and 13 (1.4%) participated in a community exercise program or were regular walkers.

Conclusions: Whilst considerable secondary prevention is evident throughout 18 months post ACS, new events and procedures are commonplace and the taking of medicines and management of risk factors can be improved. The systematic delivery of secondary prevention offers one mechanizm to a better outcome for all ACS survivors.

P6075 | BEDSIDE
Trends in acute myocardial infarction incidence and mortality: a long term follow-up of a primary prevention program in Sweden

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Background: In 1988 a cardiovasorl prevention program, combining an individual and population based strategy, was launched in primary health care in Sollentuna municipality (Sollentuna).

Aims: To study trends in incidence and mortality of acute myocardial infarction (AMI) and all-cause mortality during two decades after implementation of a cardiovascular prevention program within Sollentuna municipality in Stockholm County, Sweden.

Methods: AMI incidence and AMI- and all-cause mortality were obtained for the population of Stockholm County minus Sollentuna municipality (Stockholm) and Sollentuna during the study period using national registries. Incidence and mortality were calculated by calendar years and gender using the mean population as denominator. Differences between the groups were studied as the interaction effect in a multiple analysis of variance with year and group as independent variables. The average population was 1 795 504 in Stockholm and 56 589 in Sollentuna during 1997-2010.

Results: During the period 370 295 deaths (48% men) and 135 958 AMI cases (58% men) were observed in Stockholm and 8504 deaths (50% men) and 3 207 AMI cases (55% men) in Sollentuna. AMI death was registered in 30 365 cases (55% men) in Stockholm and 1 011 (58% men) in Sollentuna. The AMI incidence declined more in women from Sollentuna compared to women from Stockholm (on average -22% vs. -7%; p for difference in slope <0.05) (Fig. 1).

Conclusion: The decreased acute myocardial infarction incidence and mortality, and all-cause mortality may indicate a positive effect of cardiovascular prevention and treatment in general. Acute myocardial infarction incidence declined significantly more in women from Sollentuna compared to women from Stockholm.

P6076 | BEDSIDE
Poor illness perception of symptoms in patients with acute coronary syndrome: a need to improve

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Introduction: The time between onset of symptoms and repetition is a critical determinant of prognosis in patients with acute coronary syndrome. Cardiac symptom's interpretation may influence timing of hospital admission. We decide to explore illness perception and its predictors among patients with acute coronary syndrome.

Methods: We conducted a cross-sectional study of all consecutive patients admitted at Cardiology department with acute coronary syndrome (ACS) between January 2011 to September 2012. Data was obtained from personal patient registries and telephonic interview asking patients about their perception of the symptoms beginning. The question for all was: “Did you consider the possibility of heart infarction diagnosis when you started chest pain?” Patients without constrictive chest pain and those who had initial symptoms in hospital were excluded. Results: One hundred and eighty patients with ACS (mean age 63.99±18 years old) were included (12.3% with unstable angina, 38.5% with ST-segment elevation myocardial infarction, 42.8% with no ST-segment elevation and 6.4% with undetermined ECG location). The majority (62.6%) of patients didn’t have perception of ACS, until the doctor information. Among those who had perception, 82.6% were men, 58% had previous ischemic coronary disease diagnosis. Patients with arterial hypertension and dyslipidaemia had superior illness perception (p<0.05). Only 27.5% of patients with ST-segment elevation myocardial infarction had perception of cardiac disease. No association was found between ACS perception and age, academic degree and residence (rural vs urban). Among patients with ACS, only 29% decided to seek a hospital within the first thirty minutes of symptoms. Of those, the illness perception was present in 42%.

Conclusions: The illness perception of patient with acute coronary syndrome needs to be improved, independently of socio-demographic factors. An educational program for the general population, focusing in the alert signs for ACS may be necessary to improve hospital admission time and treatment in this setting.
AOK and BMIR data are not comparable for coding of risk factors or secondary diagnoses not important for reimbursement, i.e. smoking (CC: 0.394). AOK data have only a limited capacity to summarize patients history, i.e. previous AMI (CC: 0.004). AOK data cannot differentiate between “present on admission” and “during hospital stay”, which leads to more patients being diagnosed with i.e. CHF in the AOK data set compared to the BMIR (CC: 0.012).

Conclusion: The AOK data set can give an overview of existing structures, processes (i.e. PCI), and hospital mortality. The BMIR can provide additional data on risk factors, secondary diagnoses and patients’ history necessary for adjusting for hospital mortality.

P6078 | SPOTLIGHT

Teachers' knowledge and attitudes related to rheumatic heart disease

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Purpose: Rheumatic heart disease (RHD) is a major public health problem in Africa affecting 1-5% of school-aged children. Community and school involvement is increasingly recognized to be an essential component of national strategies to control RHD, but very little is known about teachers' knowledge and attitudes about the disease. As part of a public-private partnership to combat RHD in Zambia, school-based screening of up to 10,000 school children will be conducted in Lusaka for the first time using portable echocardiography. In preparation, we sought to investigate teachers' knowledge of RHD, explore their willingness to participate in RHD screening programs, and assess their general interest in participating in RHD advocacy efforts.

Methods: A workshop was conducted for primary and secondary school teachers and their students in June 2016. The teachers were taught about RHD and its association with various clinical and experimental materials produced by the World Health Organization and the World Heart Federation, and included a focus group session and written attitude survey. Participants also completed an 8-item multiple-choice questionnaire before and after the course to evaluate basic knowledge about RHD. Mean test scores were compared using paired Wilcoxon signed rank sum testing (SOFA software, version 1.3.4).

Results: Fifty-three teachers from more than 45 schools participated. Most were female and all but 3 had been teachers for at least 5 years. Approximately half of the teachers also served as their school’s health officer. Only 55% had ever heard of RHD before the workshop, and 24% reported that they had known a student with RHD. Forty-nine percent of teachers were unaware that RHD is caused by bacterial infection of the throat and few (less than 25%) knew that children with RHD require regular antibiotics to prevent progression of their heart disease. Pre-work knowledge scores improved from 3.88 (SD 0.9) to 5.98 (SD 1.2; p < 0.001). In the focus group discussion, teachers were overwhelmingly eager to help facilitate RHD screening programs at their schools. They also expressed interest in learning more about how to prevent and treat RHD in order to help keep their students healthy.

Conclusion: Teachers' baseline awareness of RHD is poor and few report first-hand exposure to students with RHD despite the high prevalence of the disease in Africa. Notwithstanding, teachers were eager to learn about RHD and demonstrated significant knowledge and a desire to play a role in RHD-related school-based screening programs. Teachers appear poised to be vital partners in school-based screening programs and may also play important roles in long-term efforts to control RHD.

P6079 | BEDSIDE

Electrocardiographic abnormalities associated with increased risk of development and progression of chronic kidney disease

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Introduction: There is a close relationship between cardiovascular disease and chronic kidney disease (CKD). Although we have identified that atrial fibrillation is associated with increased risk of renal dysfunction, the association of common electrocardiographic (ECG) abnormalities with renal function is unknown.

Methods: This prospective observational cohort study was based upon an annual health check-up program in Japan. We studied the effects of ECG abnormalities on development and progression of CKD in 227,342 subjects (72,908 men; age, 61.0±11.7 years).

Results: (1) ECG risk factors for CKD development. During a follow up of 5.9±2.3 years, 14,507 subjects (6%) without baseline CKD newly developed proteinuria. The multivariate models revealed that PR prolongation (HR, 1.25; 95% CI, 1.10–1.53), left ventricular hypertrophy (HR, 1.36; 95% CI, 1.14–1.62), ST-segment abnormality (HR 1.20; 95% CI, 1.07–1.35), and premature beats (HR 1.45; 95% CI, 1.24–1.70) were associated with development of renal dysfunction and proteinuria.

(2) ECG risk factors for CKD progression. Among 4,240 subjects with eGFR ≥60 mL/min/1.73m², 513 (12%) subjects lost eGFR (≥10 mL/min/1.73m²) during a follow-up. In the multivariate models, left ventricular hypertrophy (HR 1.92; 95% CI, 1.15–3.20) and premature beats (HR 1.63; 95% CI, 1.04–2.54) were associated with progression of CKD.

Conclusion: Various ECG abnormalities increased the risk of development and progression of CKD.
**P6083 | BEDSIDE**

**Disease duration and cardiovascular perspective in type 1 diabetes mellitus**

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**Purpose:** Innovative simultaneous assessment of micro- and macrovascular abnormalities in type 1 diabetes mellitus (DM) may be essential to understand the increased cardiovascular mortality. We sought to assess cardiac microvascular abnormalities, endothelial dysfunction, atherosclerosis, and the relationship with disease duration (DD).

**Methods:** One hundred and twenty asymptomatic type I DM patients with DD varying from 5 to 52 years were included. All patients underwent Doppler of the carotid arteries and a CT-scan at two different levels for coronary calcium score (CACS, Agatston score, GE 64-slice) and abdominal visceral fat measurement. A complete 2D, Doppler and tissue-Doppler imaging rest echocardiography was performed. Fasting and postabsorptive myocardial perfusion echocardiography (Philips ie33 using echocoantil Sonovue) to assess contractile and perfusion abnormalities at baseline and peak stress. Fasting blood samples were taken for extensive laboratory analysis.

**Results:** Fifty eight percent (70/120) were men with a mean age of 46.7±13.3 years, BMI 25.9±4.2 kg/m², HbA1c 7.6±0.92% and DD of 25.3±10.3 years. At baseline 57% had diastolic dysfunction with a LVEF of 69%±7% and systolic blood pressure (SBP) 127±10/76±17 mmHg. Atherosclerotic plaques in bilateral bifurcations of the common carotid and carotid arteries and a CT-scan at two different levels for coronary calcium score (CACS, Agatston score, GE 64-slice) and abdominal visceral fat measurement. A complete 2D, Doppler and tissue-Doppler imaging rest echocardiography was performed. Fasting and postabsorptive myocardial perfusion echocardiography (Philips ie33 using echocoantil Sonovue) to assess contractile and perfusion abnormalities at baseline and peak stress. Fasting blood samples were taken for extensive laboratory analysis.

**Conclusions:** Our data shows progressive cardiovascular abnormalities with increasing DD regardless of glycemia control in type I DM. After correction for age and CACS, DD remains significantly associated with extent of inducible myocardial PD and functional reserve.

**P6084 | BEDSIDE**

**Screening for diabetes in chronic systolic heart failure: How do the new HbA1c criteria perform compared to oral glucose tolerance testing?**

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**Purpose:** To compare the prevalence and long-term prognostic impact of newly detected diabetes diagnosed either by Hemoglobin-A1c (HbA1c) or by oral glucose tolerance testing (OGTT) in chronic systolic heart failure (CHF) patients.

**Methods:** We assessed the glycemic status in 254 outpatients (age 69.1±11 years, 67% male) with CHF, a left ventricular ejection fraction (LVEF)<45%, and without known diabetes. Newly detected diabetes was defined as an HbA1c level ≥6.5% or by OGTT if either fasting or post-load glucose concentrations were ≥7.0 mmol/L and ≥11.1 mmol/L, respectively. Information on age, sex, ischemic heart disease, hypertension, current smoking, type 2 diabetes, body mass index (BMI), albuminuria, hypertension, type 2 diabetes, body mass index (BMI), albuminuria, 24-hour blood pressure monitoring, oral antihypertensive drugs, and left atrial size were obtained. Diabetes was defined by HbA1c level ≥6.5% or by OGTT if either fasting or post-load glucose concentrations were ≥7.0 mmol/L and ≥11.1 mmol/L, respectively. Information on age, sex, ischemic heart disease, hypertension, current smoking, type 2 diabetes, body mass index (BMI), albuminuria, hypertension, type 2 diabetes, body mass index (BMI), albuminuria, 24-hour blood pressure monitoring, oral antihypertensive drugs, and left atrial size were obtained.

**Results:** Of 254 patients newly detected diabetes was diagnosed by HbA1c in 35 (14%) whereas the proportion diagnosed by OGTT was 51 (20%). Sixty-nine (27%) had newly detected diabetes by either criteria, but only 17 (7%) by both criteria. Newly diagnosed diabetes was associated with increased all-cause mortality compared to patients without diabetes when detected by HbA1c (adjusted HR: 2.4, 95% CI 1.2-4.9, P=0.02) and trend-wise when detected by OGTT (adjusted HR: 1.8, 95% CI 0.9-3.3, P=0.08).

**Conclusions:** HbA1c and OGTT detect different populations with diabetes among CHF patients. Thus, these methods can be considered complementary in the assessment of risk related to glucose metabolism, since newly detected diabetes is frequent by either criterion and seems associated with an approximate 2-fold increase in long-term mortality.

**P6085 | BEDSIDE**

**Effects of obesity and weight loss on diastolic function, functional capacity, chronotropism and blood pressure in apparently healthy individuals**

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**Purpose:** Effects of obesity on cardiovascular system in healthy individuals have not been sufficiently studied in a multimodal, integrated way.

**Methods:** 359 apparently healthy patients, 40.8% obese, 42.5±7.4 years old (24-65), 84.7% men, were studied by echocardiogram, exercise test on treadmill, and routine blood test. Obese patients were offered a program of diet, exercise, and monthly control, with 24-hour blood pressure monitoring, echocardiogram, blood sample and exercise test at inclusion and after 6 months.

**Results:** Obese patients exhibited a worse diastolic function (E/A 1.25±0.3 vs 1.48±0.4 m/s, E’ by tissue-doppler 13.4±3.8 vs 16.9±11.2 cm/s, p=0.017), achieved a worse functional capacity (11.6±2.2 vs 14.8±2.4 MET) with a higher maximal SBP (173±14 vs 168±12 mmHg), showed a higher basal heart rate (79±13 vs 70±14 bpm), blood pressure (SBP/DBP 127±10/81±6 vs 120±10/76±17 mmHg), and a worse chronotropic response (heart rate reserve 91 vs 101 bpm).

22.9% of obese patients completed a 6-month program based on diet and exercise achieving weight loss (BMI 29.7±3.8 vs 35.7±3.4), improvement in diastolic function (E’ by DTI 16.1±4.3 vs 10.9±3.5 cm/s, p=0.021), functional capacity (14.5±2.6 vs 11.8±2.2 METs on exercise test), risk profile (2.5±1.5 vs 4.2±3.3%) by DORICA score; p=0.039, analytic parameters (Glycemia 88.9±9 vs 95.3±17; p=0.037, Insuline 9.8±5.7 vs 13.8±7.9 mU/ml; p=0.01, Total Cholesterol 186±42 vs 203±38 mg/dl; p=0.05, LDLc 116.8±36 vs 130±30 mg/dl; p=0.006), and a reduction in 24-h-BP-monitoring: mean SBP 117.2±4.8 vs 128±2.2 mmHg (p=0.002, mean DBP 73.8±7.2 vs 79.9±9.3; p<0.001 for all except when referred).

Obesity decreases diastolic function, functional capacity and chronotropic response, increases blood pressure and heart rate. Weight loss and exercise improve these items, risk score, analytic parameters, and blood pressure measured by 24-h-BP-monitoring.

**P6086 | BEDSIDE**

**Carotid plaque burden is related to impaired glucose metabolism among patients with acute coronary syndromes**

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**Background:** Type 2 diabetes (DM2) and impaired glucose tolerance (IGT) are established risk factors for atherosclerosis. The aim of this study was to evaluate the atherosclerotic plaque burden in the carotid arteries of patients with acute coronary syndromes and relate it to the presence of newly diagnosed DM2, IGT, or normal glucose metabolism (NGM).

**Methods:** Ninety-eight ACS patients (male 77%, age 63 years) with no previous diagnosis of DM2 were consecutively included in the study. Measurements of glucose metabolism were made before hospital discharge and repeated 3 months later. Atherosclerotic plaques in bilateral bifurcations of the common carotid and internal carotid arteries were evaluated with ultrasound examination and patients classified as having none, minimal, moderate or severe atherosclerotic plaques. Carotid artery plaques were independently assessed by 2 reviewers with NGM, IGT and DM2, respectively. The prevalence of moderate or severe carotid plaques was 47%, 56% and 91% in patients with NGM, IGT and DM2, respectively. Carotid artery plaque burden was significantly related to impaired
glucose metabolism (p=0.006) between patients diagnosed with NGM, IGT, or DM2.

Conclusion: Carotid atherosclerotic plaque is found in nearly all patients with ACS. The severity of plaque burden is directly related to impaired glucose metabolism. Newly diagnosed DM2 among ACS patients indicates a high likelihood of moderate or severe carotid plaque burden.

P6087 | BEDSIDE
Increased left ventricular mass reduces left ventricular diastolic function more in healthy subjects with elevated fasting glucose levels: a cross-sectional study
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Purpose: The ratio of the peak early mitral inflow velocity (E) to early diastolic mitral annulus velocity (e’) provides a good approximation of left ventricular filling pressure with increasing values corresponding to increasing filling pressure. The objective of this study was to examine whether worsening of glucometabolic status is associated with increasing values of E/e’ ratio independently of higher left ventricular mass index (LVMI) in middle-aged or older apparently healthy subjects.

Methods: We examined cross-sectional associations between the E/e’ ratio (using the average e’ obtained from the septal and lateral parts of the mitral annulus), LVMI, and fasting plasma glucose (FPG) categorized as normal fasting glucose (NFG: FPG ≤ 6.0mmol/L), impaired fasting glucose (IFG: 6.1-6.9mmol/L) and diabetes mellitus (DM: FPG ≥ 7.0mmol/L). In 498 men and 214 women aged 56-79 years without overt cardiovascular disease who received no cardiovascular, antidiabetic or lipid lowering drugs and had a preserved left ventricular ejection fraction (>50%). Correlations were assessed using Pearson product moment correlation, and the associations were further evaluated using multiple linear regression analysis.

Results: In separate age and sex-adjusted models, FPG category was significantly associated with both LVMI (beta=2.04 [95% confidence interval (CI), 0.07-4.00]; p=0.04) and E/e’ ratio and LVMI were likewise significantly correlated (r=0.22; p<0.001), and the strength of the correlation increased with worsening glucometabolic status (NFG: r=0.08; p=0.01; IFG: r=0.29; p=0.001; DM: r=0.36; p<0.001) due to a significant interaction between LVMI and FPG category (p<0.002). After adjusting for traditional cardiovascular risk factors, E/e’ ratio remained significantly associated with LVMI (beta=0.25 [95% CI, 0.15-0.35]; p<0.001), independently of age (beta=0.22 [95% CI, 0.19-0.26]; p<0.001), sex (beta=1.58 [95% CI, 1.08-2.08]; p<0.001), systolic blood pressure (beta=0.010 [95% CI, 0.002-0.022]; p=0.02), and HDL cholesterol (beta=-0.085 [95% CI, 1.37 to -0.32]; p=0.002).

Conclusion: E/e’ ratio was positively associated with LVMI independently of traditional cardiovascular risk factors, and the strength of the association increased with worsening glucometabolic status, possibly due to myocarcial glycosylation.

P6088 | BEDSIDE
Cardiovascular events and mortality in immigrants and long-term residents with diabetes: are all immigrants healthier?
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Purpose: Contrast-induced nephropathy (CIN) is the third most common cause of acute renal failure. It is also associated with increased morbidity and mortality rates, prolonged hospitalization and potential need for dialysis. Screening patients who are vulnerable to development of CIN is essential to reduce this complication. We aimed to investigate the effect of metabolic syndrome (MetS) on the development of CIN in patients who underwent non-urgent percutaneous coronary intervention (PCI).

Methods: A total of 599 patients who underwent PCI were divided into two groups: Three hundred and thirteen MetS patients and 286 age and gender adjusted controls were enrolled. Serum creatinine levels were measured before and 48 h after angiography. CIN was defined as an increase in serum creatinine of ≥ 0.25 mg/dl above the baseline value 48 hours after angiography.

Results: Baseline clinical and demographic characteristics were similar between groups (table). Serum creatinine levels were increased in both groups (from 0.96 ± 0.46 to 1.15 ± 0.65 mg/dl in MetS, p=0.03 and from 0.98 ± 0.27 to 1.05 ± 0.50 mg/dl in control, p=0.07). However significantly higher levels of serum creatinine were observed among patients with MetS than control patients 48 h after PCI (1.15 ± 0.65 vs 1.05 ± 0.50 respectively, p=0.04). CIN occurred in 9.3% (29 of 313) of the MetS group and 4.9% (14 of 286) of the control group (p=0.04).

Conclusion: CIN is associated with higher incidence of CIN in patients who undergo PCI. We recommend to check the MetS status in all patients before PCI.

P6089 | BEDSIDE
Metabolic syndrome is a risk factor for contrast-imduced nephropathy among percutaneous coronary intervention patients
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Purpose: Contrast-induced nephropathy (CIN) is the third most common cause of acute renal failure. It is also associated with increased morbidity and mortality rates, prolonged hospitalization and potential need for dialysis. Screening patients who are vulnerable to development of CIN is essential to reduce this complication. We aimed to investigate the effect of metabolic syndrome (MetS) on the development of CIN in patients who underwent non-urgent percutaneous coronary intervention (PCI).

Results: Baseline clinical and demographic characteristics were similar between groups (table). Serum creatinine levels were increased in both groups (from 0.96 ± 0.46 to 1.15 ± 0.65 mg/dl in MetS, p=0.03 and from 0.98 ± 0.27 to 1.05 ± 0.50 mg/dl in control, p=0.07). However significantly higher levels of serum creatinine were observed among patients with MetS than control patients 48 h after PCI (1.15 ± 0.65 vs 1.05 ± 0.50 respectively, p=0.04). CIN occurred in 9.3% (29 of 313) of the MetS group and 4.9% (14 of 286) of the control group (p=0.04).

Conclusion: CIN is associated with higher incidence of CIN in patients who undergo PCI. We recommend to check the MetS status in all patients before PCI.

P6090 | BEDSIDE
Epicardial adipose tissue is related to left ventricular viability in patients with chronically occluded left anterior descending coronary artery

Purpose: Mechanisms underlying the reported lower mortality in obese patients with coronary artery disease (“obesity paradox”) remains unclear. Epicardial adipose tissue (EAT), especially in obesity, is metabolically active, capable of secreting various vasoactive cytokines and located in direct proximity to coronary vascular bed. It can be hypothesized that EAT impacts collateral circulation development. This study sought to determine relationships between EAT and myocardial viability in relation to BMI in patients with chronically occluded left descending coronary artery (LAD).

Methods: 24 consecutive patients with chronically occluded LAD as assessed by angiography or computed tomography and myocardial viability assessed with cardiac MRI between 2008 and 2013 were retrospectively included. Viability was assessed on late gadolinium enhancement MRI images and expressed as the percentage of the myocardial mass.
centage of viable segments in 17-segment model of left ventricular myocardium. EAT quantity was obtained in standardized fashion from MRI images by manually tracing EAT area in 4 chamber view and expressed in cm². Traditional cardiovascular risk factors were collected by telephone and medical records review.

Results: The studied cohort included 62 patients (mean age 63.2±10.9yrs, 11.3% females, BMI ≥ 25, n=80.0±16.7, r=0.57, p=0.006). This correlation remained significant after adjustment for age, sex, BMI, and traditional cardiovascular risk factors (p=0.049). There was no correlation between EAT area and myocardial viability in the entire cohort (r=0.14, p=0.28). There was a significant correlation between EAT and myocardial viability in patients with BMI in the 3rd tertile (BMI ≥ 25, n=46, r=0.57, p=0.006). The correlation remained significant after adjustment for age, sex, BMI, and traditional cardiovascular risk factors (p=0.049). There was no correlation between EAT area and viability in the 1st (BMI < 25, n=30, r=-0.04, p=0.84) tertiles. BMI determined presence of the relationship between EAT and viability in interaction analysis (p=0.03).

Conclusions: Greater amount of epicardial adipose tissue is related to greater myocardial viability in the settings of chronically occluded LAD in patients with higher BMI.

P6091 | BEDSIDE
Association of sleep apnea related nocturnal hypoxia with oxidized lipids in patients treated in a weight loss program
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Purpose: Central obesity and sleep apnea (SA) are both associated with a higher risk of cardiovascular disease and mortality. Moreover oxidized LDL (oxLDL) is known to play an important role in pathogenesis of atherothrombosis. The aim of the study is to investigate whether central obesity and SA-related hypoxia are associated with increased plasma oxLDL.

Methods: Sixty-four obese participants (mean age 42±11yrs, 44% male and mean body mass index 41.6±kg/m²) of a structured 1-year weight-loss program were studied. All participants were examined with a home-based 2-channel-screening device for SA (measuring nasal flow and oximetry). An apnea-hypopnea index (AHI) of ≥15/h indicates moderate to severe SA. Waist-to-hip ratio was used as a surrogate for the degree of central obesity.

Results: Moderate SA was present in 28% of participants of the program. Increased waist to hip ratio and reduced mean SaO2 were significantly related (Betascore=β [0.33, 0.381, 1.04], p=0.036; β=0.24, [0.08, 0.56], p=0.140, respectively). There were significant correlations between waist-to-hip ratio (β=75.755 [25.647, 125.864], p=0.004), LDL (β=0.45 [0.29, 0.60], p=0.001) and mean SaO2 (β=4.51 [-6.77, -2.25], p=0.001) with oxLDL. In the multiple regression analysis SaO2mean (β=3.28 [-5.24, -1.32], p=0.002) and LDL (β=0.37 [0.22, 0.52], p=0.001) remained significantly associated with oxLDL, whereas the waist-to-hip ratio was not (β=-22.174 [72.735, 65.084], p=0.304).

Conclusion: SA is common in obese patients with weight loss programs. SA-related nocturnal hypoxia is an independent risk factor of an increased plasma oxLDL. Whether treatment of SA may lower plasma oxLDL merits further investigation.

P6092 | BEDSIDE
Influence of weight on echocardiographic parameters
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Purpose: Influence of body size on echocardiographic parameters has led to the need to index them by the body surface area and to establish a normal reference values for clinical practice according to body size, age and gender. Whether the presence of overweight (Body mass index ≥ 25) influence echocardiographic parameters has not been previously addressed. We aim to report the influence of Body mass index (BMI) on echocardiographic parameters in a contemporary cohort of healthy patients.

Methods: NORRE study is a multi-centre study involving accredited echocardiography laboratories of the European Association of Cardiovascular Imaging (EACVI) studying echocardiographic parameters according to recommended echocardiographic approaches in a large cohort of healthy population (n=726; 43% were women; 20% patients with different types of prior CV disease: coronary artery HR 0.94 [95% CI 0.59, 1.49] (based on 75 events); cerebrovascular HR 0.89 [95% CI 0.46, 1.71] (37 events); peripheral vascular HR 0.37 [95% CI 0.15, 0.88] (27 events); and CHF HR 1.04 [95% CI 0.39, 2.83] (20 events). In patients with prior CV disease, DAPA showed a favourable point estimate for MACE irrespective of the number of different types of prior CV disease (0 to 4 for: coronary, cerebrovascular, peripheral vascular or CHF). Hypothycaemia as a putative risk factor did not appear to have an effect; the HR was favourable regardless of whether or not hypothycaemia was experienced.

Conclusions: Consistent results for MACE were observed in patients with various degrees of CV risk. The results suggest that DAPA is not associated with increased risk of CV events and raise the hypothesis of benefit, which will be tested prospectively in the ongoing DECLARE study.

P6095 | BEDSIDE
Metformine and Contrast-Induced Nephropathy in Diabetic patients treated with Primary Percutaneous Coronary Intervention for ST segment elevation myocardial infarction (STEMI) study
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Background: Contrast-induced nephropathy (CIN) is a frequent complication in patients undergoing percutaneous coronary intervention (PCI), associated with increased mortality. The impact of metformin, which has potential interactions with renal function, on CIN remains to be investigated.

Methods: Our study was designed to investigate the association between chronic metformin treatment and the development of CIN after primary PCI for ST segment elevation myocardial infarction (STEMI).

Results: 372 patients with diabetes mellitus (DM) treated with PCI ≥24h in 2 coronary care units (Paris-Bichat and Dijon Hospital, France) were included. Serum creatinine (Cr) was measured before and 48h after PCI. CIN was defined as an increase in Cr of 44 μmol/L (0.5 mg/dl) or 25% over baseline after PCI. Since PCI was urgent, metformin could not be withheld prior to PCI but was usually stopped after PCI.

Conclusion: Overweight (BMI ≥ 25) does not influence the size of left and right ventricle, and also not the LA size. Differences in RA volume and RV end-diastolic area in men might be related to the monoocyte measurement of these parameters and to the higher weight in this subgroup of patients.

METABOLISM AND HEART

P6094 | BEDSIDE
Cardiovascular safety of dapagliflozin in type 2 diabetes mellitus (T2DM) patients with various degrees of cardiovascular risk
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Purpose: Patients with T2DM are at increased risk of cardiovascular (CV) disease. Dapagliflozin (DAPA), an SGLT2 inhibitor, lowers blood glucose by increasing urinary glucose excretion and also reduces weight and blood pressure. In a pre-specified meta-analysis of DAPA vs control (CTRL; placebo or active) the incidence rates per 100 years of exposure for the primary composite end point of CV death, myocardial infarction (MI), stroke or hospitalisation for unstable angina were 1.62 for DAPA vs 2.06 for CTRL. HR 0.79 [95 CI 0.58, 1.07]. We further characterise the effects in subgroups of patients with various degrees of CV disease.

Results: DAPA showed a favourable point estimate for MACE regardless of the number of risk factors for CV disease beyond ≥2 to ≥6: history of CV disease, hypertension, dyslipidemia, smoking, family history, advanced age, or renal impairment. The results for MACE were similar in patients with and without prior CV disease (HR 0.80 [95% CI 0.53, 1.22] and HR 0.65 [95% CI 0.34, 1.24], respectively). A favourable or neutral estimated HR for MACE was observed in patients with different types of prior CV disease: coronary artery HR 0.94 [95% CI 0.59, 1.49] (based on 75 events); cerebrovascular HR 0.89 [95% CI 0.46, 1.71] (37 events); peripheral vascular HR 0.37 [95% CI 0.15, 0.88] (27 events); and CHF HR 1.04 [95% CI 0.39, 2.83] (20 events). In patients with prior CV disease, DAPA showed a favourable point estimate for MACE irrespective of the number of different types of prior CV disease (0 to 4 for: coronary, cerebrovascular, peripheral vascular or CHF). Hypothycaemia as a putative risk factor did not appear to have an effect; the HR was favourable regardless of whether or not hypothycaemia was experienced.

Conclusions: Consistent results for MACE were observed in patients with various degrees of CV risk. The results suggest that DAPA is not associated with increased risk of CV events and raise the hypothesis of benefit, which will be tested prospectively in the ongoing DECLARE study.

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of CIN taking into account classical risk factors showed no impact of chronic metformin therapy, even in stratified analysis in patients with chronic kidney disease. Hospital mortality was similar between groups (7 vs 6%, respectively, p=0.69). Moreover, no case of lactic acidosis was reported during the hospital stay. **Conclusion:** In this multicentre study reflecting current clinical practice, metformin treatment prior to primary PCI had no significant impact on CIN. Larger studies are needed to confirm these findings.

P6096 | BEDSIDE

**Genetic susceptibility of type 2 diabetes in our population**

S. Gomes1, M.I. Mendonca1, A.M. Pereira1, A.C. Sousa1, H. Cafe1, R. Rodrigues1, G. Guerra2, M. Rodrigues1, D. Pereira1, R. Palma Dos Reis3.

The prevalence of type 2 Diabetes Mellitus (T2D) has increased sharply around the world and the actual estimation suggests that this trend will continue to rise in the future. Eight genetic variants associated with T2D by GWAS were genotyped in the population of Sapienza University of Rome, Department of Cardiov. & Respiratory Sciences, Nephrology & Geriatrics, and incidence: 10-year (2002-2012) follow-up of the ATTICA study

**Methods:** A case-control study was performed with 1405 participants: 621 diabetes patients selected according to the IDF criteria and 784 controls, adjusted for age and gender. Eight genetic variants associated with T2D by GWAS were genotyped. Quantitative data were assessed by Student's t-test and Mann-Whitney, while qualitative data were assessed by chi-square test. The power of association was expressed by OR and 95% CI. A p-value <0.05 was considered significant.

A logistic regression determined which variants were associated with T2D. A ROC curve estimated the AUC and Hosmer-Lemeshow test estimated the model calibration.

**Results:** The genetic variants that showed statistical significance as risk factors of T2D were: ADIPOQ GG (OR=1.72; p=0.025) and TCF7L2 TT (OR=1.48; p=0.011). After logistic regression, the ADIPOQ GG and TCF7L2 TT showed an increased risk of T2D (OR 1.81; p=0.027 and 1.59; p=0.010, respectively) as well as BMI, hypertension, smoking, dyslipidemia and sedentary life. The AUC indicated a good accuracy of the model (72%) and the Hosmer-Lemeshow test determined its goodness of fit (p=0.011). After logistic regression, the ADIPOQ GG and TCF7L2 TT showed an increased risk of T2D (OR 1.81; p=0.027 and 1.59; p=0.010, respectively) as well as BMI, hypertension, smoking, dyslipidemia and sedentary life. The AUC indicated a good accuracy of the model (72%) and the Hosmer-Lemeshow test determined its goodness of fit (p=0.011).

**Conclusion:** In our population, ADIPOQ GG and TCF7L2 TT were found to affect the susceptibility to T2D. Individuals carrying these variants should be advised to adopt a healthy lifestyle in order to alter the genetic predisposition, especially in younger age groups.

P6097 | BEDSIDE

**Long term effects of therapy with DPP-4 Inhibitors on fitness, cardiovascular function and mortality: a cohort study in elderly population**

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**Purpose:** The impact of DPP-4 Inhibitors on long-term major clinical outcomes in type 2 diabetes remains unknown. We examined cardiac fitness, incidence of heart failure, major cardiovascular events and cardiovascular mortality associated with all available DPP-4 Inhibitors compared with usual therapy with metformin in elderly subjects.

**Methods:** Elder patients (range 65-90 yrs), in therapy with DPP-4 Inhibitors, metformin or combined therapy between 2007 and 2013, were followed for up to 6 years (median 4.9 years). Fitness was assessed with use of some tests, such as Short Physical Performance Battery (SPPB) and 6 Minutes Walking Test (6MW), using ANDA test. Diagnosis of Heart failure, according to ESC Guidelines 2012, was evaluated using Chi square test and relative risk. The composite of myocardial infarction (MI), stroke, and cardiovascular mortality associated with individual DPP-4 Inh was investigated in patients by multivariable Cox proportional-hazard analyses including propensity analyses.

**Results:** A total of 1374 subjects were included. Compared with metformin, results for the composite endpoint in patients in therapy with sitagliptin (hazard ratios and 95% confidence intervals): 1.05 (0.91-1.18), saxagliptin: 1.09 (0.93-1.23) and vidagliptin: 1.02 (0.90-1.28), were not statistically different from metformin. Incidence of Heart Failure was significantly lower in patients in therapy with DPP-4 Inhibitors [Sitagliptin RR 0.71 (0.51-0.96); Saxagliptin RR 0.76 (0.35-0.91); Vildagliptin RR 0.72 (0.35-0.95)]. Besides, elderly subjects treated with DPP-4 Inhibitors showed a significant difference in fitness compared to metformin group [Sitagliptin p value 0.02 (0.001-0.91); Saxagliptin 0.04 (0.01-0.97); Vildagliptin 0.03 (0.01-0.93)].

**Conclusions:** Monotherapy with the most used DPP-4 Inhibitors, including sitagliptin, vildagliptin and saxagliptin, seems to be associated with lower risk of heart failure and improvement in fitness. No differences were found in major cardiovascular events and cardiovascular mortality compared with metformin and combined therapy.

P6098 | BEDSIDE

**Physical activity moderates the effect of lipid levels on diabetes incidence: 10-year (2002-2012) follow-up of the ATTICA study**

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**Objective:** The association between lipid levels and diabetes incidence: 10-year (2002-2012) follow-up of the ATTICA study

**Methods:** During 2001-2, 1514 men and 1528 women (18-years) without any clinical evidence of cardiovascular disease (CVD) at the baseline examination, were included. Athens greater area, Athens Hospital, Athens, Greece. Physical activity levels were assessed using the IPAQ questionnaire, in two categories: active or sedentary.

**Results:** The 10-year incidence of diabetes was 11.6 per 100 men and 11.2 per 100 women. Data analysis revealed that high total cholesterol (≥200mg) was found to increase 47% the 10-year risk of diabetes (95%CI 1.04, 2.09). Similarly, TC/HDL ratio increased diabetes incidence (Relative Risk 1.47, 95%CI 1.04, 2.09). However, after splitting the sample based on physical activity status, hypercholesterolemia and TC/HDL ratio were associated with diabetes incidence, only among sedentary participants (Relative Risk 1.62, 95%CI 1.04, 2.54 and 1.24, 95%CI 1.05, 2.45, respectively), whereas for physically active participants the results were not significant.

**Conclusions:** This work underlines the deleterious effect of high lipid levels on the development of diabetes mellitus; however, this association was found to be modified by physical activity level, as only physically inactive participants were affected.

P6099 | BEDSIDE

**Outcome of sulfonylurea and insulin vs. incretin-based treatment in type 2 diabetes patients uncontrolled on prior metformin mono-therapy: results of DiaRegis**

A.K. Gitt1, P. Bramlage2, S. Schneider3, C. Binz4, M. Krekler4, D. Tschoepe5

**Objective:** Outcome of sulfonylurea and insulin vs. incretin-based treatment in type 2 diabetes patients uncontrolled on prior metformin mono-therapy: results of DiaRegis Study Group. 1Herzcentrum Ludwigshafen + Institut f. Herzkirzforschung Ludwigshafen, Ludwigshafen, 2Institute for Cardiovascular Pharmacology & Epidemiology, Mahlow, 3Institut f. Herzkirzforschung Ludwigshafen, Ludwigshafen am Rhein, 4BMS, Munich, 5Heart and Diabetes Center NRW, Bad Oeynhausen, Germany.

**Background:** Metformin is the first line treatment of type-2 diabetes (T2D). The impact of different treatment escalation strategies for metformin mono-therapy-failure on glucose control and morbidity has not been investigated in the real life setting.

**Methods:** DiaRegis is a multicenter registry of 3,810 patients with T2D. For the analysis we selected patients who were on metformin mono-therapy at baseline, and in whom either incretin-based drugs (Incretin), Sulfonylureas (SU), or Insulin were added. **Results:** At baseline, 2,064 patients received metformin mono-therapy. Incretin (DPP-4 or GLP-1 A) was added in 38.0% of patients (n=783), SU in 15.7% (moderate or high dose in 12/10-CD-10 criteria (fasting blood glucose-12mg/dl or the use of antidiabetic medication)). Glucose, total cholesterol (TC), oxidized LDL cholesterol, HDL-cholesterol and triglycerides were recorded, using fasting blood samples. The LDL/HDL and TC/HDL cholesterol ratios were calculated as well. Participants were classified based on their physical activity level, using IPAQ questionnaire, in two categories: active or sedentary.

**Conclusion:** The 10-year incidence of diabetes was 11.6 per 100 men and 11.2 per 100 women. Data analysis revealed that high total cholesterol (≥200mg) was found to increase 47% the 10-year risk of diabetes (95%CI 1.04, 2.09). Similarly, TC/HDL ratio increased diabetes incidence (Relative Risk 1.47, 95%CI 1.04, 2.09). However, after splitting the sample based on physical activity status, hypercholesterolemia and TC/HDL ratio were associated with diabetes incidence, only among sedentary patients (Relative Risk 1.62, 95%CI 1.04, 2.54 and 1.24, 95%CI 1.05, 2.45, respectively), whereas for physically active participants the results were not significant.

**Conclusions:** This work underlines the deleterious effect of high lipid levels on the development of diabetes mellitus; however, this association was found to be modified by physical activity level, as only physically inactive participants were affected.
Results: At baseline, patients in the hyperuricemia group showed a higher prevalence of male gender, hypertension and dyslipidemia. The hyperuricemia group had higher levels of basal insulin, HOMA-IR, triglyceride and lower levels of HDL-C. Development of new-onset DM was higher in the hyperuricemia group (13.5% vs. 7.9%, p<0.001). After PSM, baseline characteristics were well balanced (C-statistic=0.731). After adjustment with cox-regression analysis, hyperuricemia remained to be a independent predictor of new-onset DM (OR 1.72, 95% CI 1.01-2.94, p=0.045, figure).

Conclusions: Hyperuricemia was shown to be an independent predictor of new-onset DM. Therefore it may be suggested that uric acid levels should be included in the prediction of DM and patients with hyperuricemia may benefit from measures to reduce the uric acid.

P6102 | BEDSIDE Leptin serum levels are independently determined by obesity and by the presence of the metabolic syndrome
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Purpose: Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are not obese. The single and joint associations of the adipokine leptin with obesity and the MetS have not yet been investigated and are addressed in the present study.

Methods: We measured leptin in four groups of patients: subjects who were non-obese and did not have the MetS (n=196), non-obese patients with the MetS (n=149), obese subjects who did not have the MetS (n=13) and obese patients with the MetS (n=77). Obesity was defined as a BMI ≥30 kg/m²; presence of the MetS was defined according to the current harmonized consensus definition.

Results: Compared to serum leptin in non-obese subjects who did not have the MetS (3.1±1.5 μg/dl), leptin was significantly higher in non-obese subjects with the MetS (9.29±7.73 μg/ml; p<0.001), as well as in obese subjects without (11.15±5.97 μg/ml; p=0.016) or obese patients with the MetS (15.92±11.61 μg/ml; p<0.001), in whom leptin trended (p=0.127) to be higher than in obese patients without the MetS and was significantly (p<0.001) higher than in non-obese patients with the MetS. Analysis of covariance showed that both obesity and the MetS significantly and independently predicted serum leptin, with obesity being the stronger predictor (F=17.016; p<0.001) than presence of the MetS.

Conclusions: Obesity and presence of the MetS are independent determinants of serum leptin, but obesity explains a larger amount of serum leptin variation than the presence of the MetS.

P6103 | BEDSIDE Indexes of obesity and cardiac remodeling: is body mass index enough?
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Purpose: Body Mass Index (BMI) has been widely employed as a reliable anthropic index of overweight and obesity. However, evidence in favour of a pivotal role of abdominal obesity in cardiovascular disease has emerged. Waist to height ratio (WHHR), a new index which takes into account fat distribution, has been proposed as an alternative tool for patients’ risk stratification. Little information, however, is available about the respective power of BMI and WHHR to discriminate patients with echocardiographic parameters indicative of unfavourable cardiac remodeling.

Methods: We evaluated 813 consecutive adult asymptomatic patients, referred for risk factors evaluation and treatment. All patients underwent a complete echocardiographic evaluation; patients with ejection fraction <50% or valve disease >5% were excluded. Receiver Operating Characteristic (ROC) curves were employed in order to evaluate the power of BMI and WHHR to discriminate patients with cardiac remodeling. The dichotomisation of echocardiographic parameters was made according to American Society of Echocardiography cut-off values.

Results: The study population consisted of 813 patients (males 44.2%, mean age 57.9±12.2 years; females 55.8%, mean age 58.0±13.5 years). The prevalence of obesity and hypertension was respectively 59.5% and 77.7%. WHHR showed
higher areas under the curve (AUC) in identifying left atrial dilatation, left ventricular hypertrophy, relative wall thickness >0.42 and diastolic dysfunction, while BMI had a higher AUC in identifying left ventricular dilatation.

Conclusions: In a population with high prevalence of obesity and hypertension, WHR seems to provide additional information to BMI and should therefore be incorporated in the routine clinical evaluation of these patients.

THE COST OF HEART DISEASE: ECONOMIC AND PSYCHOSOCIAL

P6105 | BEDSIDE
Comparison of costs between transradial and transfemoral percutaneous coronary intervention: data from one large single center in China
C. Jin, Fu Wai Hospital, National Center for Cardiovascular Diseases, Beijing, China, People’s Republic of

Purpose: To evaluate the costs and complications of transradial percutaneous coronary intervention (TRI) and transfemoral percutaneous coronary intervention (TFI) from one large single center in China.

Methods: The study was a retrospective inpatient cohort analysis using medical data of patients undergoing percutaneous coronary intervention (PCI) in 2010 in our hospital. The primary outcome was the cost of PCI during hospitalization. Cost was obtained from our hospital’s cost accounting system. Independent costs of TRI and transfemoral intervention (TFI) were identified using propensity-scoring matching methods. The secondary outcome included in-hospital mortality and the length of stay.

Results: In 6068 PCI procedures performed from 1 January to 31 December in 2010 in our hospital, except for those patients with chronic thrombotic obstruction (CTO), cardiac stroke and no expense invoice, 5539 cases were analyzed. 4888 (82.2%) cases were in TRI access and the others were in TFI approach (n=651, 11.8%). There were 508 TRI cases matched with 508 TFI cases. The total costs of TRI were lower than TFI group (V58971.5±25189 vs. V68558.5±29114). T1. TRI access was associated with a cost saving of V95875 (95% confidence interval [CI]: V6236 to V12399; p<0.001), of which V4834 (95% CI: V2189 to V7479; p<0.001) were procedural savings and V4753 (95% CI: V3187 to V6319; p<0.001) were post-procedural savings. Compared to TFI group, the lengths of stay in TRI group was shorter (3.3-day vs. 4.2-day; p<0.001), and the rate of bleeding events was lower (0.8% vs. 2.6%; p=0.024). However, there were no significant differences in the inhospital mortality (TRI vs. TFI 0.0% vs. 0.0%, myocardial infarction (TRI vs. TFI 2.0% vs. 2.2%; p=0.825), stroke (TRI vs. TFI 0.0% vs. 0.6%; p=0.249) and revascularization (TRI vs. TFI 0.2% vs. 0.6%; p=0.624) between the groups.

Conclusions: Compared to TFI approach, TRI was associated with lower total hospitalization costs, lower incidence of bleeding events and shorter length of hospital stay.

P6106 | SPOTLIGHT
The prevalence of acute myocardial infarction during Greek financial crisis in the Cardiology Department of a greek central Hospital
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Introduction and purpose: Cardiovascular morbidity and mortality tend to increase during periods of crisis, such as war, social depression or natural disasters. The financial crisis that Greece is experiencing during the last years bears major social implications, such as unemployment and poor quality of life. The purpose of the present study was to investigate the prevalence of acute myocardial infarction (AMI) during the period of financial crisis.

Methods: Two separate time periods were studied retrospectively regarding the prevalence of AMI in the Cardiology Department of a greek central Hospital. The period from 1.1.2003 until 31.12.2007 was considered the “pre-crisis period”, while the period 1.1.2008 until 31.8.2012 was defined as “crisis period”. Results: The results are shown in Table 1.

Conclusions: The results show an increase in the number of admissions due to AMI in both sexes during the “crisis period” compared to the “pre-crisis period”. This increase was statistically significant in women (P<0.001) but not in men. The prevalence of AMI was increased in patients younger than 45 years old during the “crisis period”, but the increase was statistically significant only for women (P<0.01). The prevalence of AMI was also increased in males without social insurance (P<0.04).

P6107 | SPOTLIGHT
Cost impact of left atrial appendage occlusion to prevent stroke in patients with nonvalvular atrial fibrillation
S. Panikker1, J. Jarman1, J. Lord1, J.P. Foran1, S. Haldar1, D.G. Jones1, T. Salukhe1, J.R. Clague1, V. Markides1, T. Wong1. 1 Royal Brompton Hospital, Heart Rhythm Centre, NIHR Cardiovascular Research Unit, London, United Kingdom; 2 Brunel University, Health Economics Research Group, London, United Kingdom

Purpose: Recent evidence supports left atrial appendage (LAA) occlusion as a cost-effective alternative to warfarin. However these findings, based on clinical trial populations, may not be generalisable to clinical practice. The cost-impact of a real world experience of LAA occlusion compared with warfarin, dabigatran, rivaroxaban, apixaban and no therapy in patients with nonvalvular atrial fibrillation (AF) is unknown.

Methods: Cost minimisation analysis using a cost impact model was used to systematically assess the costs of Watchman device implantation over a 10 year time horizon to determine the costs of LAA occlusion in relation to all other treatment strategies in patients with nonvalvular AF at risk of stroke, with and without contraindications to anticoagulation. Complications and subsequent stroke rates were determined from an experience of 85 implants in 84 patients (Age 70.8±9.7, CHA2DS2-VASc 4.6±1.7, HAS-BLED 3.9±1.2). Watchman implantation and complication costs were obtained from UK NHS 2014 tariffs, while those for stroke and bleeding were sourced from peer-reviewed literature. Overall cost-impact of Watchman device implantation was quantified as time to achievement cost parity with other strategies and with the other strategies.

Results: Cost parity was achieved between 3.5 (vs Rivaroxaban) to 5.4 (vs Apixaban) years. Cost saving over 10 years ranged between 42.8% against PROTECT...
Sexual activity after cardiac diagnosis often declines, although little is known about changes over time. This study examined predictive factors for change in sexual activity before and after cardiac diagnosis.

Methods: Cardiac patients (N=192), through self-report survey, reported frequency of sexual activity before their cardiac problem and the past 2 months. Participants were categorized into 3 groups: sex as frequently as before (n=68), sex less often (n=93), and no sex prior to diagnosis nor presently (n=31, control group). The survey included demographic questions and a Sexual Concerns Inventory (SCI, rated “never” to “frequently”, 3 subscales), with 2 items on ED combined for patient/male partner’s ED, for 11 total items (R=0-33). Statistical analysis: chi-square, ANOVA, logistic regression.

Participants were more likely to have sex as frequently as before (n=68), smokers (59%; 31% never smokers) were less likely to have sex as frequently as before diagnosis (Table). Regarding atypical symptoms such as tiredness, dyspnea, cold sweat was more common in patients without diabetes, pain in shoulders (57% vs. 42%, p<0.01), and cold sweat (55% vs. 44%, p<0.05). Other symptoms were not statistically different between patients with and without diabetes. Predictors of change in sexual activity were age, education, employment status, SCI score, and SCI score adjusted for diabetes.

Conclusion: Only half of the STEMI patients utilise the ambulance service when falling ill. Every fifth patient contacts advisement nurses by phone as their first medical contact, jeopardising a rapid reperfusion.

P6110 | BEDSIDE
Factors predictive of change in sexual activity after cardiac diagnosis

E.E. Steinke, T.J. Hill, V. Mosack. Wichita State University, Wichita, United States of America

Purpose: Sexual activity after cardiac diagnosis often declines, although little is known about changes over time. This study examined predictive factors for change in sexual activity before and after cardiac diagnosis.

Methods: Cardiac patients (N=192), through self-report survey, reported frequency of sexual activity before their cardiac problem and the past 2 months. Participants were categorized into 3 groups: sex as frequently as before (n=68), sex less often (n=93), and no sex prior to diagnosis nor presently (n=31, control group). The survey included demographic questions and a Sexual Concerns Inventory (SCI, rated “never” to “frequently”, 3 subscales), with 2 items on ED combined for patient/male partner’s ED, for 11 total items (R=0-33). Statistical analysis: chi-square, ANOVA, logistic regression.

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Conclusion: Only half of the STEMI patients utilise the ambulance service when falling ill. Every fifth patient contacts advisement nurses by phone as their first medical contact, jeopardising a rapid reperfusion.
P6112 | BEDSIDE
Sexual dimorphism in marital and socioeconomic differences regarding the risk factors, symptomatology and management of patients with coronary artery disease in Poland - the results of RECENT trial S. Tubek 1, M. Stepkowska 1, A. Szczeruzewska 1, M. Storek 2, A. Rzasa 2, M. Matyszczak 2, P. Pociupany 3, W. Banasik 4, P. Ponikowski 3, E.A. Jankowska 4.

Background: In Western Europe there are proven relationships between socioeconomic status (SES), risk factors, prevalence of treatment and outcomes among patients with coronary artery disease (CAD). All of this data from Poland is scant.

Methods: We analyzed the data of 2593 patients with stable CAD from RECENT study. SES is influenced by many factors, education, constitutes a most commonly used SES measure in epidemiological studies, hence was applied in this analysis. As regards the reported level of educational attainment, patients were divided into three groups (primary educated, secondary educated and highly educated). According to MS, patients were split up into two groups - participants declaring marriage formed married population (MP), while all the others were incorporated into single population (SP).

Results: When groups according to MS were analyzed no differences in prevalence of risk factors and applied treatment between sexes were found. Married subjects were more often: smoke (p<0.01) and give a history of hyperlipidemia (p<0.01) or myocardial infarction (p<0.01). On the other hand invasive (PCI p<0.01; CABG p<0.01) as well as evidence-based pharmacological treatment (p<0.01) is applied more often in that group in single individuals. The control of CAD symptoms is associated with sex - the usage of long lasting nitrates (p=0.05) and CCS class (p<0.01) is higher in single women, but not in men.

Considering SES, there is stronger relationship in the prevalence of risk factors in female than in male subjects. Low educated in women is associated with overweight (p<0.01), higher systolic (p=0.04) and diastolic (p=0.03) diastolic blood pressure and worse heart rate control (p=0.01). However, smoking is more frequent in highly educated women (p<0.01), than in those with lower education. Invasive treatment (RECI PCI p=0.03; CABG p<0.01) and statins (p<0.01) are implemented more often in subjects holding higher education, regardless of sex. SES is a good predictor of symptoms control - highly educated patients of both sexes are in lower CCS class (p<0.01) and report chest pain (p<0.01) as well as usage of anginal medications more frequently than the others.

Conclusion: MS and SES differentiate Polish CAD patients in terms of risk factors, applied treatment and symptoms control. Hence those characteristics should be considered as indicators of patients being in need of an intensiﬁed medical attention.

P6113 | BEDSIDE

Background: The impact of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) in patients with smoking history is not clear. Smoking history is known to have an adverse effect on clinical outcomes of coronary artery disease. We evaluated the 12 month clinical outcomes between PCI and optimal medical therapy (OMT) for CTO lesions in patients with smoking history.

Methods: A total of 321 consecutive CTO patients with smoking history were divided into 2 groups according to treatment strategy; PCI group (n=145) and OMT group (n=176). Twelve-month clinical outcomes were retrospectively compared between the two groups.

Results: At baseline, patients in the OMT group had a lower left ventricular ejection fraction, and higher prevalence of elderly, cerebrovascular accident, peripheral vascular disease, congestive heart failure, left main disease, multivessel disease, right coronary artery CTO lesion, and left main disease. At 12 months were similar between the 2 groups except lower mortality in the PCI group at univariate analysis. After baseline adjustment by multivariate analysis, 12-month mortality remained lower in the PCI group (OR 0.112, 95% CI 0.014-0.910, p=0.041) despite of increased target lesion revascularization (TLR) in the PCI group (table).

Conclusions: In our study, PCI seems to be a favorable choice of therapy for CTO lesions in patients with smoking history in terms of reducing 12-month mortality. Long-term follow up with a larger study population will be necessary for further clarification.

LONG-TERM FOLLOW-UP IN CARDIOVASCULAR DISEASE
P6115 | BEDSIDE
The previous coronary heart disease mortality rates decrease stopped in the older age strata in the Czech Republic J. Bruthans 1, M. Zvolenská 2, V. Lanska 3, M. O’Flaherty 3.

Background: In Western Europe there are proven relationships between socioeconomic status (SES) and coronary heart disease (CHD) risk factors, prevalence of treatment and outcomes among patients with coronary artery disease (CAD). All of this data from Poland is scant.

Methods: Our analysis comprised the whole adult population of the Czech Republic aged 35-84 years, using mortality data from the Czech Bureau of Statistics. Differences in the mortality rates, all cause and cause specific CHD mortality, resulted from age specific and period specific trends in CHD mortality in the Czech Republic.

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Conclusions: Our analysis comprised the whole adult population of the Czech Republic aged 35-84 years, using mortality data from the Czech Bureau of Statistics. Differences in the mortality rates, all cause and cause specific CHD mortality, resulted from age specific and period specific trends in CHD mortality in the Czech Republic.

P6116 | BENCH

Background: Cardiovascular risk factors (smoking, overweight, hypertension and lipid disorders) are the major causes of morbidity and mortality in Russia. Control of the risk factors from adolescence may reduce cardiovascular events in adulthood. During the 1990s Russian population has been exposed to major political, economic and social changes.

Objectives: The aim of the study was to assess trends in cardiovascular risk factors and their associations among siberian adolescents during the last 25 years.


Results: Smoking, overweight, hypertension and lipid disorders are the major causes of morbidity and mortality in Russia. Control of the risk factors from adolescence may reduce cardiovascular events in adulthood. During the 1990s Russian population has been exposed to major political, economic and social changes.

Conclusions: The aim of the study was to assess trends in cardiovascular risk factors and their associations among siberian adolescents during the last 25 years.

Long-term follow-up in cardiovascular disease

cholesterolemia during this time has fallen by more than 5 times. 25-year trends of HT were shown double decreasing during the reform period and stabilization in the post-reform time. Prevalence of HT was 5-fold increased in boys and 3-fold increased in girls from lowest BMI to highest.

Conclusion: Data from Novosibirsk indicate a downward trend in prevalence of smoking, obesity, hypertension and higher age (Relative Risk (RR) = 1.07, 95%CI: 1.00-1.16), are the most significant risk factors. Multi-adjusted analysis revealed that increased age (Relative Risk (RR) per year increase = 1.05, 95%CI: 1.03-1.07) and gender (Relative Risk (RR) female vs male = 1.15, 95%CI: 1.08-1.23) were the most important protective factors. Incidence of fatal or non-fatal CVD (coronary heart disease, acute myocardial infarction, non-ST-elevation acute myocardial infarction, ST-elevation acute myocardial infarction, and other coronary events) among 50-year-old men and women from the course of 10 years was the most important protective factor.

P6117 | BEDSIDE
Ten year cardiovascular disease and all-cause mortality: the Attica study
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Aims: The 10-year incidence of cardiovascular disease (CVD) and all-cause mortality, as well as its determinants, in a sample of men and women from Greece, was evaluated.

Methods: From May 2001 to December 2002, 1514 men and 1528 women (<18 y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011-12, the 10-year follow-up was performed in 2583 patients (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria.

Results: The 10-year incidence was 14.3% in men and 9% in women (p<0.001). Multiple logistic regression indicated that increased age (Relative Risk (RR) = 1.07, 95%CI: 1.05-1.09), male gender (Relative Risk (RR) = 1.34, 95%CI: 1.27-1.42) and diabetes (Relative Risk (RR) = 1.56, 95%CI: 1.23-1.99) were the most significant risk factors. The prevalence of diabetes was 10 times higher in men than in women. Men also had higher prevalence of hypertension, hypercholesterolemia and smoking. The most important protective factor was exercise (Relative Risk (RR) = 0.80, 95%CI: 0.70-0.91).

Conclusion: Incidence of CVD increased in Greece in the past 10 years, as compared with previous reports, despite the various prevention strategies and public health actions; adherence to the traditional diet still seems to be an effective, non-pharmacological mean for the reduction of disease burden.

P6118 | BEDSIDE
One-year outcomes in Asian patients with ST-segment elevation myocardial infarction, non-ST-elevation acute myocardial infarction and unstable angina: Observations from the EPICOR Asia study
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Aim: To examine caregiver burden over time during 24 months follow-up in partners to patients with heart failure.

Background: Due to aging populations in many countries worldwide and the fact that medical treatment for both acute myocardial infarction and heart failure have improved, patients with heart failure become older and live at longer home.

Conclusion: NSTE-ACS demonstrates more adverse outcomes than STEMI. Studies are warranted to identify better long-term management strategies in these patients.

P6119 | BEDSIDE
Secondary prevention in Jordan is underdeveloped and requires urgent improvement to meet the guidelines
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Purpose: CHD is a major health problem in Jordan and the leading cause of death is known about the current provision and perceptions of Jordanian health care professionals’ towards secondary prevention (SP) strategies. This study is designed to evaluate risk factors, explore the current provision of secondary prevention and health professionals’ perceptions of SP for patients treated for established CHD in Jordan.

Method: A mixed methods repeated measures research design was used. 180 patients were recruited from 3 intervention hospitals after: acute myocardial infarction (AMI) treated medically; Percutaneous Coronary Intervention (PCI); and coronary artery bypass graft (CABG); then followed up 6 months later. The European guidelines on CHD prevention 2012 were used to compare against recommended targets. Semi-structured interviews with a purposive sample of 20 doctors and nurses from the 3 hospitals explored their perceptions of SP strategies.

Results: Of the 180 patients at discharge, 77% were obese or overweight, 59% were smokers, 59% had low levels of physical activity, 51% had elevated LDL, 44% were hypertensive and 36% were diabetic. Of the 169 patients at follow up 75% were obese or overweight, 47% continued to smoke, 41% had low levels of physical activity and 25% had not controlled blood pressure. Recording of risk factor measurement at follow up was insufficient to evaluate achievement of therapeutic targets. Recording of risk factor history and current status was incomplete. No patients had psychological risk factors or dietary assessment. There was no cardiac rehabilitation, smoking cessation or secondary prevention available post discharge. The majority received brief physician advice about medications (72%) and smoking (49%). The use of prophylactic drug therapies was as follows: Aspirin 92%, lipid lowering drug 88%, beta-blockers 78%, ACE inhibitors 52% and statins 88%.

Interviews confirmed that while health professionals expressed the importance of education, they also indicated that they found it difficult to establish CHD in Jordan. These findings confirm that despite extremely high prevalence of risk factors in this population, the provision of secondary prevention is poor and obstacles to its development are widespread. SP of CHD in Jordan requires urgent improvement and the contribution of nurses’ to prevention should be enhanced to provide an effective, convenient and culturally sensitive SP services.
Method: A randomized study design with patient-partner dyads affected by heart failure with a follow-up assessment after 24 months. The intervention included a nurse-led psycho-educational 3-session program.

Result: 155 dyads were included and 96 partners concluded the 24 months assessment. The intervention did not show any significant differences in any dimension in caregiver burden among the partner dyads after 24 months. After 24 months follow up the total caregiver burden had increased significantly in both groups compared to baseline (36 vs 38, p < 0.05).

Partners in both the intervention and control group reported decreased physical health status as assessed by the assessment and the 24-month follow-up. However, those in the intervention group had a significantly greater decrease in both PCS (B = -4.13, t(90) = -2.43, p < 0.05), and physical functioning (B = -6.76, t(93) = -2.21, p < 0.05).

There was no significant difference between the groups in the number of admissions in hospital or number of days in hospital during the follow up period. Admission within 24 months occurred in 13% of the partners (n=9) in the intervention group and in 24% (n=19) in the control group.

Conclusion: This study is the first long-term follow up of caregiver burden in partners to patients with HF describing an increase in several aspects of this burden over time. To identify caregivers that experience high caregiver burden and target those with support and interventions can lead to a significant improvement in caregiver wellbeing.

P6121 | BEDSIDE

Carotid artery intima-media thickness and ideal cardiovascular health. The Paris Prospective Study III

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Purpose: Carotid intima-media thickness (cIMT), a structural component of the arterial remodeling, has been repeatedly associated with the onset of cardiovascular (CV) disease and is widely sued as a surrogate marker of CV disease. In 2010, the American Heart Association’s 2020 Strategic Goals defined a new concept of ideal CV health composed of 7 modifiable health metrics in order to prevent CV disease. We hypothesized that ideal CV health status would be associated with thinner cIMT.

Methods: We included 5126 men and women aged 50-75 years who enrolled in the Paris Prospective Study III (PPPS) from 2008 to 2011 and who were free of overt CV disease and treatment. The CV health status was defined as poor (0 or 1 health metric present), intermediate (2, 3 or 4) and ideal (5, 6 or 7). cIMT was measured in the right common carotid artery in an area free of carotid plaques using carotid echo tracking, a highly accurate method with 20 micrometers precision. The likelihood of a thinner cIMT (sex specific first quartile) associated with CV health status was evaluated by logistic regression analysis.

Results: Mean age was 58.9 years and 60.6% were men. The median cIMT was 0.73 ± 0.44 in men and 0.68 ± 0.31 in women. Mean CHADS2 score was 1.0 ± 1.4. Among the young, the incidence of stroke was considerably high in patients with vascular intervention; the proportion of patients within target PT-INR range was 28.9% in patients with vascular intervention (P < 0.0001) with adjusted HR of 1.6 [1.24-2.32], and 2.01 [1.39-3.48], respectively.

Conclusions: In modern practice and in real life conditions, the higher risk of CAD patients with a history of vascular intervention is well taken into account, with more intense secondary prevention and similar risk factor control than patients without such history. Despite this, however, these patients remain at higher risk and thus it should be discussed more aggressive targets for secondary prevention in patients with polyvascular disease.

P6123 | BEDSIDE

Clinical characteristics of young atrial fibrillation patients: From one-year follow-up of the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) is a common arrhythmic disorder among the elderly, and is increasing significantly as the population ages (reportedly 0.6% total population in Japan). Stroke is a devastating complication of AF, and advancing age is a well-known risk factor for stroke. However, clinical characteristics of young AF patients have not been well described.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Kyoto, Japan. Fushimi-ku is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. At present, we have enrolled 3,821 patients (1.4% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,968 patients as of December 2013.

Results: Young AF patients (< 65 year of age; n=517, 17.4% of total) were less likely to have major co-morbidities compared with others (n=2,449); congestive heart failure (young vs. others: 17.6% vs. 28.9%; p < 0.01); hypertension (50.7% vs. 63.5%; p < 0.01); diabetes mellitus (21.1% vs. 24.1%; p < 0.05) and previous stroke (10.3% vs. 21.2%; p < 0.01). Therefore, CHADS2 score was lower in the young (1.12 vs. 1.05 vs. 2.25 ± 1.31; p < 0.01), and they received much lower anticoagulation therapy (42.8% vs. 52.8%; p < 0.01). Moreover, guideline adherence in PT-INR control for patients taking warfarin (the Japanese guideline recommends 1.6-2.5 for patients <70 years of age, and 2.0-3.0 for those <70) was much lower in young AF patients; the proportion of patients within target PT-INR range was 29.1% in the young and 58.9% in the others.

During one-year follow-up, the incidence of stroke was 1.5% (n=8) in the young, and 2.8% (n=68) in the others. Of 8 young stroke patients, 5 had not received anticoagulation therapy (4 patients were CHADS2 score 0 or 1, 1 patient was 2). Among the young, the incidence of stroke was considerably high in patients with CHADS2 score ≥3 (3/58, 5.2%), compared with those with CHADS2 score 0-2 (5/459, 1.1%).

The incidence of major bleeding in the young patients was low (4/517, 0.8%) compared with that in the others (42/2,449, 1.7%; p = 0.01).

Conclusion: Young AF patients have smaller risk profiles for stroke, and the incidence of stroke was low indeed, but it cannot be neglected especially for those with high CHADS2 score. A better risk stratification scheme, and better management is definitely needed for young AF patients.

P6124 | BEDSIDE

A comparison of cardiac event rates in patients with or without multiple myeloma in the US

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Background: Multiple myeloma (MM) patients have age-, disease-, and treatment-related risk factors for cardiac events; it is unknown if this risk is greater than in non-MM patients.

Methods: Two cohorts were identified in the 2006–2011 MarketScan database: 1) MM patients treated with corticosteroids and ≥3 drugs (bortezomib, IMiDs, and alkylating agents or anthracyclines), where the index date (ID) was the date criteria of exposure to the 3 drugs was met; and 2) age and sex matched NO-MM patients (5:1); the distribution of No-MM patients’ IDs matched MM patients. Baseline was 6 months prior to the ID. Patients were followed from ID to study end. Baseline variables included age, sex, geographic area, and comorbidities. Incidence was calculated for patients without the event(s) at baseline. Hazard ratios (HR) and 95% confidence intervals (CI) were adjusted for baseline variables when univariate analyses showed a 10% difference.
MECHANISMS OF THE PROGRESSION ON HYPERTENSION

P6127 | BENCH
Long-term exercise alleviates hypertension and improves vascular redox state via upregulating Glrx-1 in spontaneously hypertensive rats
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Aim: Glutaredoxin-1 (Glxr-1), a redox-regulator of thioredoxin superfamily, plays an important role in the redox signaling of cardiovascular diseases. Our previous studies showed that exercise training in young spontaneously hypertensive rats (SHRs) can delay the development of hypertension. The objective of the present study was to investigate the role of Glrx-1 in exercise-generated anti-hypertensive effects in SHRs.

Methods: Eight-week-old male SHR were divided into sedentary (SHR-Sed) and exercise-trained (SHR-Exe) which were subjected to a single bout of aerobic treadmill running at 20 m/min, 1 h/d for 16 weeks. Age-matched Wistar-Kyoto rats were used as normotensive control groups (WKY-Sed and WKY-Exe). Blood pressure was determined by tail-cuff method and mesenteric artery function was assessed with DMT myograph system. Vascular total reactive oxygen species (ROS) were determined by DHE staining, mesenteric vascular GSH, GSSG and NO production were measured spectrophotometrically.

Results: SHR subjected to 16-wk treadmill training exhibited significantly lowered systolic blood pressure (P<0.01) and enhanced vasorelaxation of mesenteric artery (P<0.01) to ACh as compared with their sedentary counterparts, whereas exercise did not affect blood pressure and vasorelaxation of mesenteric artery in WKY rats. Long-term exercise increased vascular Akt and eNOS phosphorylation and NO production in both SHR and WKY rats. Although mesenteric vascular Glx-1 levels were similar in sedentary SHR and WKY, exercise training significantly increased vascular Glrx-1 expression in SHR (2.05±0.24-fold, P<0.01) but not in WKY rats. Moreover, exercise training increased GSH/GSSG ratio (SHR-Exe 12.35±0.53 vs. SHR-Sed 7.03±0.21, P<0.01), together with reduced ROS levels in SHR.

Conclusion: These results demonstrate that long-term exercise improves vascular redox state and mesenteric vascular function via up-regulating vascular Glrx-1.

P6129 | BEDSIDE
Correlation between dysfunction of different hemostatic links and microalbuminuria in patients with arterial hypertension
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Aim: To establish the relationship between activity of different hemostatic links and presence of microalbuminuria in patients with arterial hypertension.

Material and methods: 60 patients with arterial hypertension (grade 2) were included in the study. 1st group included 22 patients with microalbuminuria, 2nd group included 38 patients without microalbuminuria. Among patients prevailed age group 50-59 years (40%).Venous blood samples were drawn from the cubital vein after an overnight fasting and were examined for: 1) platelet hemostasis 2) coagulation...
activity: Activated Partial Thromboplastin Time (aPTT), Thrombin Time (TT), Soluble Fibrin-Monomer Complexes (SFMC) 3(fibrinolytic activity; XII-a dependent fibrinolysis; 4)anticoagulant activity: Antithrombin III, Protein C.

Results: By level spontaneous aggregation and platelet aggregation with ADP was not observed statistically significant differences between the two study groups. However, the analysis of platelet aggregation with epinephrine attracted attention more pronounced changes in the group with MAU. So, the degree of aggregate with epinephrine in the group with MAU was 2.6 times higher than in the group without MAU (p < 0.05). It was noted also change the speed of platelet aggregation in patients with MAU was higher at 2.54 times (p < 0.05). 1st group of patients exhibited acceleration of aPTT (14,4% shorter in comparison to aPTT of the 2nd group (p = 0,041), acceleration of TT (11,5% shorter in comparison to TT of the 2nd group (p = 0,04)). It was found that by conter- part of SFMC observed a statistically significant difference between the groups with the presence and absence of MAU. So in patients with MAU level of SFM-Cincresased in 1.56 times relative to the comparison group. In patients with MAU inhibition of XII-a dependent fibrinolysis was 1.45 times higher than in the group without MAU. Noteworthy that the content of natural anticoagulants - antithrombin III and protein C was significantly lower in both groups of patients.

Conclusions: Microalbuminuria in patients with arterial hypertension is associated with activation of thrombin and fibrin formation, and reduction of anticoagulation potential, which proves significance of microalbuminuria in development of thrombotic complications in this group of patients.

P6130 | BEDSIDE
Clinical characteristics of patients with resistant hypertension in Greece: Data from a multi-center national registry

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Purpose: Resistant hypertension is related with adverse cardiovascular prognosis, whereas there are scarce data regarding its clinical characteristics in Greece. The aim of this national registry was to identify and analyze cases of resistant hypertension in Greece.

Methods: For this purpose we studied 340 patients with resistant hypertension (office blood pressure (BP) ≥140 and/or 90 mmHg despite the use of >3 antihypertensive drugs at maximum tolerated doses including one diuretic) who par- ticipated in the Greek multi-center HERHODOTOS registry. From all participants data were collected regarding office and home BP, renal function, current antihypertensive treatment and clinical comorbidities.

Results: Resistant hypertensive patients (mean age: 68, 183 males, office BP: 158/87±11 mmHg, heart rate 70±19 bpm under 4.4±0.6 drugs) exhibited high body mass index (30.9±3.8 kg/m²) and 30% were smokers. In the whole population, home BP was 148/84±18/10 mmHg while creatinine values were 1.0±0.3 mg/dl. Severe resistant hypertension (office systolic BP: ≥160 mmHg) was present in 39.2%. Regarding clinical comorbidities, 12% of the registered patients suffered from sleep apnea, 36% had diabetes mellitus and 54% exhibited dyslipidemia. The prevalence of coronary heart disease was 28%, while stroke and heart failure were present in 6% and 8% of the patients respectively. Chronic kidney disease was found in 11% of the resistant hypertensives, while 4% suffered from peripheral arterial disease and 16% from arterial fibrillation.

Conclusions: The present registry shows that in a Greek population of resistant hypertensive patients, a high prevalence of severe resistant hypertension, coronary heart disease and arterial fibrillation. Our findings improve understanding of the clinical phenotype of resistant hypertension in Greece and could contribute in better clinical management of these high risk patients.

P6131 | SPOTLIGHT
Prediction of total mortality in patients with hypertension

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Objective: To model the high risk group of total mortality in patients with hyper- tension (HT) living in an urban area.

Design and methods: We conducted a 10-year prospective cohort study of 1070 patients with hypertension living. The participants were examined in 1999 (1st survey) and 2008 (2nd survey). The research included standard questions, questionnaires for detection of cardiovascular risk factors, blood pressure measurement, electrocardiography, echocardiography and cholesterol data. The total mortality data for the period of 10 years were analyzed. The logistic regression model was used to show the relation between essential risk factors in patients with HT and total mortality.

Results: In 10 years, we had 336 cases of death. Comparative analyses did re- veal significant difference in total mortality between men and women during a ten-year period (35.1% vs. 27.8% respectively, p < 0.01). Multifactor model of signif- icant risk factors of total mortality included a high (>29.0 kg/m²) index of body mass (p < 0.001), high (SVI + RV5 + V6 > 35 mm) hypertrophy of the left ventricle according to ECG signs (p < 0.001), non-optimal (<4.9 mmol/l or >6.2 mmol/l) glu- cose level (p < 0.001), myocardial infarction in the history case (p < 0.001), alcohol abuse (p < 0.01), a high (>3.8 mmol/l) level of cholesterol of low density lipoprotein (p < 0.01), diabetes mellitus (p < 0.01), a high (>100 μmol/l) creatinine level (p < 0.01), moderate (28 mm < SVI + RV5 + V6 < 34 mm) hypertrophy of the left ventricle based on ECG signs (p < 0.01), absence of higher education (p < 0.05), a high (≥150 mmHg) systolic blood pressure (p < 0.05), stroke in the history case (p < 0.05), high (≥85 beat/min) frequency of heart rate (p < 0.05), hypertrophy of the left ventricle based on echocardiographic signs (p < 0.1), smoking (p < 0.1). The proposed multifactor model permits to separate a group of non-significant, low and high risk of total mortality.

Conclusion: Using risk factor population norms, the multifactor model predicting the relative risk total mortality in hypertensive patients was suggested.

P6132 | BEDSIDE
Influence of climatic factors on recourse of patients with arterial hypertension in emergency department

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Purpose: To determine the relationship between climatic factors and the recourse of patients with arterial hypertension (AH) in the emergency department.

Methods: 1477 cases of appeals in the emergency department of Perm city hos- pital were registered in 2012 year. Fluctuations and averages of climatic factors (temperature, barometric pressure, relative humidity, wind speed) were de- termined every day during this year. Cross- tables, indexes Pearson Chi-square and Cramer’s V were used to assess the results. Data are presented as mean ± standard deviation.

Results: The largest numbers of cases of AH was in spring (391) and in winter (383). Maximum number of appeals was in March (148) and in January (147). Among the 1477 patients admitted to the emergency department were 25% men and 75% women. It was found that the number of appeals (p < 0.05), stroke in the history aged from 70 to 80 years. Average age of men with AH was 58.1±15.5 years and women with AH was 65.1±13 years. The peak of hypertensive patients in the emergency department was registered at 11.00-12.00 a.m. and at 9.00-10.00 p.m. Average systolic blood pressure was 182±23 mm Hg and average diastolic blood pressure was 98±12 mm Hg. There was a significant relationship between the number of calls and temperature fluctuations (Cramer’s V=0.32; p<0.001). Significant relationships with barometric pressure fluctuations (Cramer’s V=0.24; p<0.001), variation of humidity (Cramer’s V=0.24; p<0.001) and mean wind speed (Cramer’s V=0.27; p<0.001) were determined too. There were no relation- ships between recourse numbers and the average temperature, average pressure, average humidity and wind velocity fluctuations. But it was found that the number of appeals increase when the relative humidity level was more than 71%.

Conclusions: Moderate forces relationship was marked between instability of weather conditions and recourse of patients with AH to the hospital. Particularly this relationship was noted for such values of climatic factors as temperature fluctuations, pressure fluctuations, fluctuations in humidity and average wind speed. Perhaps relationship will be stronger if we consider the combination of several factors simultaneously.
with MHT (mean age 48.2 ± 12.9 years, female 44.8%), and 83 patients with SHT (mean age 49.5 ± 13.9 years, female 44.6%) were included. In echocardiographic findings, subjects with NT and WCHT had similar, and also subjects with MHT and SHT had similar. MHT had significant higher relative wall thickness (RWT) (p = 0.047, p = 0.002), and LV mass (p = 0.012, p = 0.012) than NT and WCHT. WCHT had lower RWT (adjusted lifetime risk to age 95) and LV mass than SHT. There were no significant differences in LV ejection fraction and left atrial diameter.

Conclusion: MHT had significant cardiac damage than NT and WCHT. This result showed ABPM is more predictive of target organ damage to clinical BP, and patients with MHT should be carefully follow up about the elevated cardiovascular risk.

# P6134 | BEDSIDE

Blood pressure and incidence of twelve cardiovascular diseases; lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people

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Background: The associations of blood pressure (BP) with the different manifestations of incident cardiovascular disease (CVD) in a contemporary population have not been compared.

Methods: Using electronic health records from 1997 to 2010, we assembled a cohort of 1.25 million initially CVD-free participants aged >30 years, a fifth of whom received BP-lowering treatments. We studied the heterogeneity in the age-specific associations of clinic BP with twelve acute and chronic cardiovascular disease outcomes among a contemporary population.

Results: After baseline examination, they were followed up for the median of 1,106 days (45%). Hypertension. Median SUA concentration (mg/dl) at baseline in each group were 325.3 ± 115.7 mg/dl in the 2nd SUA group, 371.2 ± 118.6 mg/dl in the 3rd SUA group showed higher (p < 0.05) than that in the 1st SUA group. 2. Hypertension (BP > 140/90 mmHg or BP treatments), had a lifetime risk of total CVD at age 30 of 63.3% (62.9–63.8) (vs. 46.1% [45.5–46.8] for those without) and de- creeed across the tertiles for baseline levels of oxidative stress in male (69.8, 78.6, and 82.1 per 1000 person-year in the first, second, and third tertiles, re- spectively, p < 0.05), but not female subjects. The hazard ratios of incident hyper- tension (first quartile as a reference) in male subjects was 0.951 (95% confidence interval 0.661-1.369) and 1.440 (1.010-2.054) in the second and third tertiles, re- spectively, after adjustment for possible factors. Multivariable Cox hazard analysis, where d-ROM was taken as a continuous variable, indicated a significant corre- lation between d-ROM levels at baseline and future incidence of hypertension in male (hazard ratio 1.004; 95% confidence interval 1.001-1.006), but not in female subjects.

Conclusions: In male general population, increased oxidative stress evaluated by d-ROM levels was significantly associated with the future development of hyper- tension. Oxidative stress may be involved in the process of developing hyper- tension.

# P6137 | BEDSIDE

Increased oxidative stress predicts future development of hypertension in male general population

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Purpose: Oxidative stress is considered to be associated with several cardiovascular disorders including the process of atherosclerosis. The present study tested the hypothesis that increased oxidative stress predicts future development of hypertension, one of the major risk factors of cardiovascular diseases, in the general population.

Methods: Serum levels of derivative reactive oxygen metabolites (d-ROM), a marker of oxidative stress, were measured in non-smoking normotensive 2,106 subjects who visited our hospital for a physical check-up (male:38.2%, 55.2±10.9 year-old). Their blood and urine were sampled early in the morning after overnight fasting and serum d-ROM was measured using colorimetric assay (Diaclon, Italy). After baseline examination, they were followed up for the median of 1,106 days with the endpoint being the development of hypertension. Hypertension was defined as systolic blood pressure >140mmHg, diastolic blood pressure >90mmHg, or the use of antihypertensive medications. The exclusion criteria were: ischemic heart disease, valvular heart disease, congestive heart failure, atrial fibrillation, inflammatory disease, and malignant disease.

Results: During the follow-up, hypertension developed in 419 subjects (66.7 per 1000 person-year), with the incidence being more frequent in male than female subjects (83.2 vs. 56.8 per 1000 person-year). Incident hypertension was increased across the tertiles for baseline levels of oxidative stress in male (69.8, 78.6, and 82.1 per 1000 person-year in the first, second, and third tertiles, respectively, p < 0.05), but not female subjects. The hazard ratios of incident hyper- tension (first quartile as a reference) in male subjects was 0.951 (95% confidence interval 0.661-1.369) and 1.440 (1.010-2.054) in the second and third tertiles, re- spectively, after adjustment for possible factors. Multivariable Cox hazard analysis, where d-ROM was taken as a continuous variable, indicated a significant corre- lation between d-ROM levels at baseline and future incidence of hypertension in male (hazard ratio 1.004; 95% confidence interval 1.001-1.006), but not in female subjects.

Conclusions: In male general population, increased oxidative stress evaluated by d-ROM levels was significantly associated with the future development of hyper- tension. Oxidative stress may be involved in the process of developing hyper- tension.

# P6138 | BEDSIDE

Morning central blood pressure surge is lower than morning peripheral blood pressure surge in untreated hypertensives

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Morning blood pressure (BP) surge is considered to be an independent risk factor for cardiovascular diseases. On the other hand, there is increasing evidence that central systolic pressure (CSP) is stronger correlated with target organ damage and cardiovascular events than peripheral systolic pressure. Therefore, the aim of study was to evaluate the relationship between morning central and peripheral systolic pressure.

Methods: Fifty patients with newly diagnosed, never treated hypertension (age 40.4±11.5 years, 35 men) and 50 normotensive subjects (matched for age and sex) were included into the study. Applanation tonometry of the radial artery has
been used to derive 24-hour CSP (BPro, HealStat). Peripheral BP was measured using Spacelabs device. For analysis of the morning surge (MS) in BP, we determined the awake and asleep periods from the subjects’ diary cards. The sleep-through MS was the difference between the morning pressure (the average BP during the 2 hours after awakening) and the lowest nighttime BP (the average of the lowest pressure and the 2 readings immediately preceding and after the lowest value). The preawakening MS was the difference between the morning blood pressure and the preawakening BP (the average BP during the 2 hours before awakening).

Results: The 24-hour CSP was 129.5±10.6 mmHg in hypertensives and 110.5±12.4 mmHg in normotensives (p<0.05). The average daytime and nighttime CSP was 133.8±11.1 mmHg and 123.1±11.1 mmHg (p<0.05) in hypertensives whereas 114.3±13.7 mmHg and 104.8±11.7 (p<0.05) in normotensives, respectively. The corresponding peripheral systolic pressure was 141.5±7.6 mmHg vs. 124.7±9.4 mmHg (p<0.05) in hypertensives and 126.0±6.6 mmHg vs. 109.6±7.9 mmHg (p<0.05) in normotensives. The values of morning BP surge are presented in the table.

The mean values (±SD) of morning surge

- **Peripheral sleep-through MS**
  - Hypertensives (n=50), mmHg: 24.0±7.1 (8.8-37.7) 0.006 16.8±8.9 (0.0-37.1) 12.2±5.1 (7.1-19.0) 0.006
  - Normotensives (n=50), mmHg: 21.8±8.4, 17.5±3.2, 13.2 0.058 18.3±9.1, 15.2±4.1, 13.6±9.8, 0.008

- **Central sleep-through MS**
  - Hypertensives: p < 0.29 0.62 0.44 0.92
  - Normotensives: p < 0.05

- **Peripheral preawakening MS**
  - Hypertensives: p < 0.29 0.62 0.44 0.92
  - Normotensives: p < 0.05

- **Central preawakening MS**
  - Hypertensives: p < 0.29 0.62 0.44 0.92
  - Normotensives: p < 0.05

SD, standard deviation; BP, blood pressure; MS, morning surge.

Conclusion: Central sleep-through MS and preawakening MS are significantly lower than peripheral sleep-through MS and preawakening MS in hypertensives. In normotensives only central preawakening MS is lower than peripheral preawakening MS.

P6139 | BEDSIDE
Cirradiation of acute aortic dissection: significance of blood pressure dipping pattern

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Purpose: Acute aortic dissection (AAD) is a life threatening cardiovascular disease with high mortality. Hypertension has been known to be a risk factor of AAD. However, little is known about the association between the onset-time of AAD and circadian variation of blood pressure (BP). The purpose of this study was to clarify the characteristics of cirradiation of BP in AAD and its relation to the onset time of this disease.

Method: This study included type B spontaneous AAD patients who were referred to our institution and treated conservatively between January 2008 and June 2013. Patients with type A AAD, secondary to trauma, and type B AAD which was preceded surgical intervention were excluded.

Results: There were 115 patients with spontaneous type B AAD in the study period. Thirty-nine patients did not receive ABPM during admission. Eight patients were excluded because the onset-time could not be identified certainly. Finally, Sixty-eight patients with type B AAD were enrolled in this study. The distribution of cirradiation patterns in the study patients were as follows: extreme-dipper, 0% (none); dipper, 20.6% (n=14); non-dipper, 50% (n=34); rizer, 29.4% (n=20).

Non-dipper and rizer pattern were more frequently observed compared with other population studies reported previously. Moreover, no patient in dipper group had night-time onset while 31.5% of the patients in non-dipper group had it (p<0.01).

Figure 1. Cirradiation of aortic dissection.

Conclusions: Non-dipper pattern of BP was frequently seen in AAD patients. Absence of nocturnal BP fall may be a risk factor of AAD. Cirradiation pattern of BP may also affect the onset time of type B AAD.

P6140 | BEDSIDE
The prevalence and related risk factors of prehypertension in middle age and elderly population with impaired fasting glucose

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Both prehypertension and impaired fasting glucose (IFG) have been strongly associated with cardiovascular disease. But there have been few studies of the epidemiology and risk factors of prehypertension with IFG. By analyzing cross-sectional cohort data from total 824 individuals aged 45 or over (men 343, women 481) who live in our city, we evaluated the prevalence and risk factors of prehypertension with IFG among local residents. The prehypertension was defined as systolic blood pressure is from 120 to 139 mmHg, and/or diastolic blood pressure is from 80 to 89 mmHg. The IFG was defined as fasting serum glucose concentration is from 100 to 125 mg/dl. The prevalence of prehypertension with IFG was 7.8% (64 of total 824, men 24, women 40). The prevalence of normotension with normoglycemia was 10.4% (85 of total 824, men 27, women 58).

An univariate analysis showed body mass index, waist circumference, gamma-glutamyltransferase, total cholesterol, triglyceride, insulin, homeostasis model assessment of insulin resistance (HOMA-IR) were significantly higher in prehypertension with IFG group than normotension with normoglycemia group. Whereas systolic and diastolic BP were still significant.

Association between office blood pressure and self-reported apneas in epidemiology study


Objective: To evaluate association between anthropometric parameters, office blood pressure (BP) and self-reported sleep apneas in a randomized cohort from Russian epidemiologic study (ESSE-RF).

Design and methods: A randomized sample included 1600 St Petersburg citizens aged 25-65 years, 1597 subjects [men mean age 50 (21-68), males – 570 (35.7%)], and 920 (28.3%) were eligible for analysis. All participants underwent a survey, including questions on sleep duration; BP was measured according to European guidelines (35.7%)

Results: According to the survey data 939 subjects (338 males and 601 females) did not complain on sleep apneas, 83 participants (39 males and 44 females) complained on sleep apneas, and 575 subjects (193 males and 382 females) could not give any definite answer (27.6% vs. 27.6%)

Snorers were also more obese: body mass index (BMI) 25.3 (16-38.8) vs. 27.5 (15-65), and 27.9 (16.3-51.7) kg/m², respectively (F=126.5; p<0.001), and the median waist circumference (WC) was higher in both males [91 (62-123); 83.4 (44-126) and 89.5 (57-139) cm, respectively; F=19; p<0.001] Erythrocyte sedimentation rate was significantly higher in both males and females [91 (62-123); 83.4 (44-126) and 89.5 (57-139) cm, respectively; F=19; p<0.001] indicating android obesity. One-way analysis of variance showed higher office systolic BP [32.5 (90-180); 124 (85-225) and 130 (90-240) mmHg, respectively; F=12.6; p<0.001] and diastolic BP [82 (67-107); 78.5 (48-131) and 80 (51-150) mmHg, F=7.8; p<0.001] in snorers compared to non-snorers and participants who did not give a definite answer about snore. After adjustment for BMI and WC the differences in systolic (F=103.4; p<0.001) and diastolic BP (F=12.6; p<0.001) were still significant.

Conclusion: Epidemiologic data confirm that prevalence of sleep apneas increases with age. Subjects with self-reported sleep apneas are characterized by higher BMI, mostly due to the abdominal fat. Both systolic and diastolic BP is higher in respondents with self-reported sleep apneas independently of the major risk factors, including age, BMI and WC.
**P6142 | BEDSIDE**

Age-dependent blood pressure increase in different Brazilian race/ethnic groups

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Background: Arterial pressure (AP) depends on interaction between genetic and environmental factors. Population-based studies show higher AP levels in African ancestry population. There is controversy if this finding depends on genetic or on environmental/social factors. Age-related AP increase in different race/ethnic groups was investigated.

Methods: ELSA-Brasil is a cohort (35-74 y; N=15,105) to investigate determinants of chronic diseases. In baseline exams three AP readings were obtained (Onom 7655) in fasting conditions. Race/ethnicity (white, black, indigenous, asian or "brown") was self reported. "Browns" are mixed subjects with a recognized African ancestry. Linear regression was used to calculate age-related systolic and diastolic AP increments.

Results: Analysis included individuals of the three groups (white, black and brown) not in use of antihypertensive drugs. Significant (p<0.001) regression was observed in all groups for both genders. In men, systolic AP increase (mmHg) per decade was 3.0 in whites, 4.5 in blacks and 4.8 in browns (p<0.001). In women these values were respectively, 4.9, 6.4 and 6.6 mmHg/decade (p<0.001). Differences among groups remained significant after adjustment for age, body mass index (BMI) and socioeconomic variables (education, income and work activity).

Arterial pressure and race/ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>White</td>
<td>78.6±11</td>
<td>75.8±11</td>
</tr>
<tr>
<td>Brown</td>
<td>76.8±12</td>
<td>74.4±12</td>
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<tr>
<td>Black</td>
<td>73.9±12</td>
<td>72.7±12</td>
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</tbody>
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(adjusted hazard ratio 0.562 (95%CI 0.404-0.782) per 10 years, p<0.001), peak CPK (adjusted hazard ratio 0.772 (95%CI 0.688-0.890) per 100 U/L, p<0.001) and post-procedural gradient (adjusted hazard ratio 1.152 (95%CI 1.020-1.301) per 10 mmHg, p=0.023) were significant predictors.

Conclusions: Age, post-procedural gradient and peak CPK of 1st PTSMA were independent variables to predict repeat procedure. It is reasonable to perform PTSMA for older patients, and sufficient ablation of the culprit septal myocardium is desirable to achieve favorable results.

**P6145 | BEDSIDE**

Cardiovascular impact of acquired familial amyloid polyneuropathy after sequential liver transplantation

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Purpose: Sequential liver transplantation (SLT), in which the liver of a patient with familial amyloid polyneuropathy (FAP) is transplanted into another patient, is a strategy that has been used to overcome the paucity of available organs. However, the long-term consequences of SLT, concerning the manifestations of acquired FAP and, in particular, its cardiovascular (CV) repercussions, have been under-addressed. Our purpose was to evaluate patients with acquired FAP (AFAP) after SLT and to study the occurrence of CV changes.

Methods: We studied 37 liver recipients whose donor was a FAP patient (AFAP) and 664 subjects with an hereditary FAP-related transferrin mutation (H-FAP) and no liver transplantation (TRV). All subjects underwent a CV assessment.

Results: Concerning AFAP patients, a mean age at SLT of 53±7 years old and 70% were male. The median follow-up was 9 years (IQR 8-10) and, during that time, 54% of the recipients developed symptoms of AFAP. The mean interval of time between first AFAP and first symptoms of myocardial involvement was 7.4±3.3 years. However, given that among TRV carriers the beginning of symptoms was at 33 years old (IQR 28-32), with a minimum age of 20 years old, one would expect that the clinical manifestations of AFAP would appear only 2 decades after SLT. The first symptoms of AFAP were neurological in 85% of the cases, gastrointestinal in 7.5% and CV in 7.5%. During follow-up, 22% of the patients developed CV symptoms (mean interval of 7.5±7.0 years after SLT). In this group, 4 patients had pacemaker, placed pre-phylactically before liver re-transplantation: the % of pacings was identical to other patients with FAP and none was pace-dependent. During follow-up, none of the patients died; 2 patients were re-transplanted and 2 are on the waiting list. The prevalence of electrocardiographic changes, namely conduction disturbances, was not statistically different between AFAP and FAP, but the mean time of follow-up after the first clinical manifestations of AFAP was only 1 year (vs 5 years in FAP patients).

Conclusions: In our cohort, a significant proportion of SLT recipients developed symptoms in the first 8 years after transplantation - earlier than expected. Even though 1/3 of the SLT recipients reported CV symptoms, they didn’t have major CV changes, but the follow-up time since the first clinical manifestations of the disease was quite short. More studies are needed for an accurate evaluation of the incidence of clinical AFAP and for determining the natural history of patients after SLT, who seem to undergo a faster progression of the disease, comparing to hereditary FAP.

**P6146 | BEDSIDE**

Cardiovascular impact of acquired familial amyloid polyneuropathy

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Background: Percutaneous transluminal septal myocardial ablation (PTSMA) is a promising alternative to surgical myectomy, however, there are problems regarding the residual gradient and repeat septal reduction therapy. Therefore, we investigated the clinical characteristics and the morphological analysis of cardiac magnetic resonance (CMR) in the patients received to repeat PTSMA.

Methods: We performed PTSMA procedures for 157 patients from 1998 to 2013, and 70 patients received repeat procedure (Group R) because of residual gradient and repeat septal reduction therapy. Therefore, we investigated the clinical characteristics and the morphological analysis of CMR (n=101), with comparisons between the patients in Group R (n=30) and those without repeat PTSMA (Group S, n=71).

Results: Median age of both PTSMA procedures was 61±501 days, and 16 patients (53%) received 2nd procedure within 1 year. In comparisons with Group S, the patients in Group R were younger (54±16 vs 64±13 years, p<0.001), lower in peak CPK (869±366 vs 1271±541U/L, p<0.001), higher in post-procedural gradient (36±40 vs 24±32 mmHg, p<0.038) and similar in baseline gradient (91±83 mmHg, p=0.495), injected ethanol dosage (2.2±1.0 vs 2.6±1.3, p=0.158) and baseline NYHA functional class (2.7±0.3 vs 2.7±0.5, p=0.832). From CMR analysis, the left ventricular mass (187±56 vs 174±58g, p=0.372), the left atrial diameter (44±7 vs 42±7mm, p=0.401), the number of regional hypertrophied segment in the left ventricle (4.2±3.2 vs 3.7±2.6 segments, p=0.670) and the delayed enhancement (4.8±2.4 vs 6.8±1.7 g, p=0.787) were similar in both groups. In multiple logistic regression model for the baseline characteristics, age (adjusted hazard ratio 0.562 (95%CI 0.404-0.782) per 10 years, p<0.001), peak CPK (adjusted hazard ratio 0.772 (95%CI 0.688-0.890) per 100 U/L, p<0.001) and post-procedural gradient (adjusted hazard ratio 1.152 (95%CI 1.020-1.301) per 10 mmHg, p=0.023) were significant predictors.

Conclusions: Age, post-procedural gradient and peak CPK of 1st PTSMA were independent variables to predict repeat procedure. It is reasonable to perform PTSMA for older patients, and sufficient ablation of the culprit septal myocardium is desirable to achieve favorable results.
no LVT-AL group (figure). In multivariable analysis, even after adjusting for age, gender, NYHA functional class and LV ejection fraction, LVT-AL remains a significant marker of mortality (Hazard ratio = 1.9, 95%CI: 1.1-3.2, p = 0.02).

Conclusion: The presence of LVT-AL is a common finding in patients with AL and is associated with impaired both LV systolic and diastolic function, worse functional status and advanced stage of the disease. In addition, LVT-AL is a powerful marker of mortality. These results suggest that the assessment of LVT-AL may help to enhance risk stratification of AL patients.

P6147 | BENCH
Unequal abundance of mutated myosin among individual cardiomyocytes: the trigger for myocardial phenotype development in familial hypertrophic cardiomyopathy related to beta-myosin mutations?

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Familial Hypertrophic Cardiomyopathy (FHC) is the most common inherited disease of the heart. In most cases it is caused by mutations in sarcomeric protein. Abnormal structure of the beta-myosin heavy chain (B-MHC). It is generally assumed that pathological hypertrophy, myocyte disarray and other features result from functional changes induced by the respective mutation at the sarcomeric level. Yet, the underlying pathomechanisms are still unclear. Different mutations even in the same protein affect function of the sarcomere quite differently and a common trigger for development of the FHC-phenotype has not yet been identified.

In earlier work on muscle fibers we found large functional variation, and large variation in mutated B-MHC RNA expression among individual slow-fiber-myocytes. It is the soleus muscle of affected FHC-patients in which the B-cardiac MHC is the expressed MyHC isoform. We concluded that the observed functional variation results from variation in the expression of mutated B-MHC from fiber to fiber. On this basis we hypothesized that FHC-typical myocardial features arise from variation in the expression of mutated myosin from cardiomyocyte to cardiomyocyte. Functional alterations caused by the mutated myosin such as higher force generation that we previously found for several FHC-related B-MyHC-mutations would then lead to imbalanced force generation among neighboring cardiomyocytes, resulting in distortions and even disarray within the cellular network of FHC-patient's myocardium.

To test this hypothesis we quantified the relative abundance of mutated B-MHC-mRNA in individual cardiomyocytes isolated from cardiac samples of two FHC-patients with B-mutation mutation R723G. We found that the relative expression of B-MHC-MRNA with the R723G mutation varies from cell to cell from almost pure mutant to almost pure wildtype expression. Measurements of force generation and calcium sensitivity of individual myocytes with the R723G mutation also revealed a significantly larger functional variation compared to unmutated myocytes. Based on these data we propose that unequal expression of mutated B-MHC from cardiomyocyte to cardiomyocyte in FHC-patient's myocardium triggers functional imbalance, thus setting off altered cell signaling and morphology resulting in hypertrophy and myocyte disarray.

P6148 | BEDSIDE
Significance of ventricular wall thickening for assessing inflammatory activity in cardiac sarcoidosis

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Purpose: Conventional echocardiography has an established role in assessing the morphological and functional status in cardiac sarcoidosis (CS), but its usefulness to evaluate the inflammatory activity in CS has not been determined.

Methods and results: 67-Gallium (Ga) single-photon emission computed tomography with integrated computed tomography (SPECT/CT) demonstrated that abnormal Ga uptake in the myocardium was observed in 15/27 consecutive CS patients. Each left ventricle was divided into four segments for evaluation, and 32/60 inflammatory segments detected by SPECT/CT corresponded with some echocardiographic abnormalities, such as abnormal wall motion (AWM), wall thickening (WT), and wall thinning. SPECT/CT sensitivity was 91% and the specificity was 52%. AWM was the most frequent observation (42/60 segments), although its specificity for myocardial inflammation was not high (56%). However, WT was less frequent (16/60 segments, 8 cases), and 15 segments corresponded to abnormal Ga uptake (specificity: 96%; positive predictive value: 94%). After 1 year of prednisolone (PSL) therapy, ameliorated WT associated with improvement of wall motion in 4/5 cases (Figure) and disappearance of Ga uptake in all cases was observed.

Conclusions: Echocardiographic abnormalities of WT coinciding with AWM may be highly specific not only for detecting new inflammatory regions but also for predicting of the reversibility of cardiac function, which aids in assessing the myocardium during long-term follow-up in patients with CS.
ventricular cardiomyopathy (ARVC) remains challenging. Soluble ST2 (sST2), a member of the interleukin 1 cytokine family, can be induced in mechanically over-loaded cardiomyocytes and is elevated in patients with left ventricular (LV) heart failure. In ARVC patients, right ventricular (RV) function is predominantly affected. We wanted to explore if the plasma concentration of sST2 was associated with reduced myocardial function and arrhythmic events in patients with ARVC.

Methods: We included patients with ARVC and their mutation positive family members. sST2 was determined by ELISA in plasma collected at time of echocardiographic examination. Myocardial function was assessed by echocardiography including strain by speckle tracking technique. RV function was assessed by RV fractional area change (FAC) and by RV global strain (average longitudinal strain from 6 RV segments). LV function was assessed by ejection fraction (LVEF) and LV global strain (average longitudinal strain in 16 LV segments).

Results: We included 46 ARVC mutation positive subjects (age 41±15 years, 21 female), of whom 22 had previous ventricular arrhythmia and 24 had no arrhythmic events. sST2 was elevated in those with arrhythmias compared to those without (34±13 ng/mL vs. 26±7 ng/mL, p=0.009). sST2 correlated with RV function by RV global strain (R=0.51, p=0.001) and RVFAC (R=0.36, p=0.02) and with LV function by LVEF (R=−0.43, p=0.003) and LV global strain (R=−0.48, p=0.001). ROC analyses for sST2 showed C-statistics of 0.70; 95% CI 0.55-0.86. A sST2 level of 30 ng/mL identified ARVC patients with ventricular arrhythmias with a sensitivity of 50% and a specificity of 88%.

Conclusions: Soluble ST2 was elevated in ARVC patients with arrhythmic events and correlated well with RV and LV function. sST2 may be of additive value in risk stratification for ventricular arrhythmias in ARVC.

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**P6153 | BENCH**

**End-stage hypertrophic cardiomyopathy phenotype is an age-specific red flag for aetiological diagnosis**


**Purpose:** Left ventricular (LV) hypokinesia associated with hypertrophic cardiomyopathy (HCM) phenotype (end-stage evolution) includes a broad spectrum of disease subtypes and carries an ominous prognosis due to high rates of refractory heart failure and sudden arrhythmic death. The prevalence of the different aetiologies in adults and children is not known. Additionally, the age-distribution of the different disease subtypes of the end-stage HCM phenotype have not been evaluated.

**Methods:** A total of 103 patients with LV hypokinesia (ejection fraction ~50%) associated with HCM phenotype (0-89 years) were evaluated at our referral center between 1990 and 2013. Aetiological diagnosis was made on the basis of clinical/instrumental features with particular attention to the presence of multi-organ involvement, type of inheritance, molecular biology, specific metabolic exams, cardiac or skeletal muscle biopsy, magnetic resonance imaging and 99mTc-DPD scintigraphy.

**Results:** According to the age at diagnosis, 93 patients (90%) were adults and 10 (10%) children (of whom 6 infants). The prevalence of the different disease aetiologies was: 66% amyloidosis (18% transtiretin-related, 15% wild type and 33% amyloid light chain), 26% sarcomeric HCM, 4% glycogen store diseases, 3% mitochondrial diseases and 1% Anderson-Fabry disease. The distribution of the different aetiologies according to age decades is presented in the figure. A strong relation between age at diagnosis and disease subtype was present, indicating that the finding of the end-stage HCM phenotype can suggest a specific diagnosis according to the age at presentation.

**Conclusions:** LV hypokinesia associated with HCM phenotype (end-stage evolution) can be considered an age-specific red flag for the disease subtype.
P6154 | BEDSIDE
Serial apical deformation change is predictive of outcome in patients with cardiac amyloidosis
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Purpose: Apical sparing pattern with preserved longitudinal systolic strain (LSsys) at apical segments and significantly reduced LSsys at mid and basal segments is a typical finding in patients with cardiac amyloidosis (CA). Reduced mid-septal LSsys is associated with poor outcome in CA patients. The purpose of this prospective study was to explore the predictive value of monitoring regional LSsys on outcome in CA patients.

Methods: Standard echocardiography was performed in 38 biopsy proven CA patients (mean age 65±10 years; 55% male) at baseline and during echocardiographic follow-up (median 278 days). Global and segmental LSsys were off-line assessed by two-dimensional speckle tracking imaging in septal and lateral walls of left ventricle (LV) from apical 4-chamber view. All patients were clinically followed-up by clinical visit or telephone call (median 486 days). The primary endpoint was defined as all-cause death.

Results: Twenty out of 38 (53%) patients died during clinical follow-up. During follow-up, NYHA class was significantly increased in non-survivors while remained unchanged in survivors, LV wall thickness and right ventricular dimension were significantly increased in both non-survivors and survivors (all P<0.05), LV global and regional LSsys remained unchanged in survivors while septal and lateral LSsys at apical segments were significantly reduced in non-survivors: septal -18.6±6% vs. 15.1±7%, P<0.022; lateral: -16.7±7 vs. 12.6±8, P<0.006). Univariate Cox analysis showed that baseline NYHA class (HR 2.75, P<0.034), LV mass index (HR 2.97, P=0.042), mid-septal LSsys (HR 2.82, P=0.028) reduced resection of apical-LV (HR 3.34, P=0.016) and apical-lateral (HR 5.61, P=0.01) segments during follow-up were predictors of mortality. Apical-septal and apical-lateral LSsys remained independent mortality predictors after adjustment for age, gender, baseline NYHA class, LV mass index and LV ejection fraction. CA patients with apical-septal LSsys reduction <2.5% or apical-lateral LSsys reduction >3.0% during follow-up was associated with a 4-5 fold higher risk of death compared to those with apical-septal LSsys reduction <2.5% or apical-lateral LSsys reduction >3.0%.

Conclusion: Longitudinal systolic strain reduction at apical segments over the follow-up period is an independent predictor of survival in CA patients.

P6155 | BEDSIDE
Clinical and genetic predictors of major cardiac events in patients with Anderson-Fabry disease
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Purpose: To determine the incidence of major cardiac outcomes and to identify clinical and genetic predictors of adverse cardiac outcomes in patients with Anderson-Fabry disease (AFD).

Methods: An observational, longitudinal, retrospective evaluation of 207 consecutive patients was performed. Missense mutations in exon 1 (Ala20Pro), exon 5 (Ans215Ser) and exon 6 (Met296Val, Met296Ile, Gln279Glu and Arg301Gln) of α-Fabry Disease (AFD).

The incidence of the primary endpoint was 2.64 per 100 person-years (CI 1.78–3.0%) during follow-up was associated with a 4-5 fold higher risk of death compared to those with apical-septal LSsys reduction <2.5% or apical-lateral LSsys reduction >3.0%.

Conclusion: Longitudinal systolic strain reduction at apical segments over the follow-up period is an independent predictor of survival in CA patients.

Conclusions: AFD is associated with a high burden of cardiac morbidity and mortality. This is associated with increasing age, global severity of AFD and QRS duration. Outcomes are similar in patients with and without cardiac genetic variants.

P6151 | BEDSIDE
Prognostic value of changes in blood pressure profile in patients with familial amyloid polyneuropathy

Background: Changes in blood pressure (BP) profile including abnormality in the circadian variation are frequent in patients with familial amyloid polyneuropathy (FAP). V30M-TTR and are attributed to autonomic dysfunction. However these changes have never been well characterized and its prognostic value is unknown.

Purpose: To evaluate the influence of age and duration of symptoms on the BP profile and determine the impact of BP changes in the prognosis of patients with FAP.

Methods: V30M-TTR mutation carriers underwent annual cardiac evaluation which included ambulatory blood pressure monitoring (ABPM). Hypertension was defined as daytime BP ≥140/90 mmHg or nighttime BP ≥125/75 mm Hg. The non-dipper pattern was defined as a decrease in systolic BP at night <10% and the reverse dipper pattern as systolic BP highest night.

Results: 226 patients (45±14 years, 54.4% female) were enrolled. During a follow-up of a median of 50 months, 756 exams were performed. Hypertension was documented in 37.1% of the exams (N=279) increasing its occurrence with age (23.8% in patients aged <30 years vs. 67.3% in those aged ≥70 years; P<0.001) and with the duration of symptoms (37.1% in patients with symptom duration <2 years vs. 54.1% in those with evolution >9 years; P=0.006). The 24 hr systolic BP increased progressively with age (Pearson R 0.21, P<0.001) but not with the duration of symptoms. On the contrary, the 24 hr diastolic BP increased with duration of symptoms (Pearson R=0.13, P<0.004) but not with age. During follow-up, 36 patients (15.9%) died. Multivariate Cox regression analysis (backward conditional method) with adjustment for age, showed that the risk of death increased with nocturnal systolic loads (Hazard Ratio (HR)=1.03, 95% CI 1.02-1.05; P<0.001) and with nocturnal decline in systolic BP (HR: 1.07, 95% CI 1.03-1.12; P<0.001). On the other hand the risk decreased with the 24 hr systolic BP (HR: 0.94, 95% CI 0.91-0.97; P<0.001) and diastolic daytime loads (HR: 0.98, 95% CI 0.96 to 0.99; P=0.018). Among the patterns of circadian BP variation, the one with the greatest prognostic impact was the reverse dipper with more than twice the risk of death (HR: 2.62, 95% CI 1.54 to 4.45; P<0.001).

Conclusions: In patients with FAP, the changes in the BP profile are associated with the risk of death. The ABPM is an inexpensive diagnostic method that can help to identify patients with unfavorable prognosis.

P6158 | BEDSIDE
Electrocardiographic QRS fragmentation as a marker for myocardial scarring in hypertrophic cardiomyopathy
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Background: Fragmented QRS complexes (fQRS) on a 12-lead ECG reflect intraventricular conduction delay and have been demonstrated to be a marker for myocardial scarring in coronary artery disease. However, few data exist regarding the diagnostic value of fQRS for estimating myocardial scarring in patients with hypertrophic cardiomyopathy (HCM).

Objective: We assessed whether fQRS shows better correlation with myocardial scarring than pathological Q waves in patients with HCM.

Methods and results: Forty-eight patients with HCM who underwent 12-lead ECG and cardiac magnetic resonance with late gadolinium enhancement (LGE-CMR) were investigated. The overall sensitivity, specificity, and accuracy of pathological Q waves were 9%, 95%, and 60%, respectively, for detecting myocardial scarring in the corresponding LV segments, and those of fQRS were 43%, 73%, and 61%, respectively. The number of leads displaying fQRS correlated with the extent of myocardial scarring (r=0.40, p=0.0047), whereas there was no correlation between the number of leads with pathological Q waves and the extent of
myocardial scarring. The frequency of prior major cardiovascular events (MACE) increased according to the number of leads with fQRS (p < 0.019).

Conclusions: fQRS showed a substantially higher sensitivity compared with pathological Q waves for detecting myocardial scarring in HCM. Furthermore, the number of leads with fQRS was associated with both the extent of myocardial scarring and the frequency of prior MACE. Even with availability of CMR, the 12-lead ECG can be used as a screening modality for myocardial scarring in HCM because of its simplicity and cost-effectiveness.

P6160 | BEDSIDE
More impaired diastolic function of light chain amyloidosis contribute to poor prognosis compared with transthyretin amyloidosis: results from longitudinal study of biopsy-proven cardiac amyloidosis

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Background: Immunoglobulin light chain (AL) amyloidosis is associated with higher mortality than transthyretin (TTR) amyloidosis, however, few data exist regarding the relationship between difference of type of amyloidosis and cardiac mortality, especially in hemodynamic and echocardiographic parameters.

Methods: We reviewed 51 consecutive patients with biopsy-proven cardiac amyloidosis from 2013 to 2016. Of these, 27 were AL amyloidosis and 24 were TTR amyloidosis. Hemodynamic, echocardiographic and clinical parameters were assessed.

Results: There were no differences between AL and TTR in age (68.1 ± 7.0 vs 70.1 ± 9.0, p = 0.14). Frequency of male was lower in AL than in TTR (70 vs 92%, p = 0.05). Systolic blood pressure was higher in AL than in TTR (128.2 ± 16.9 vs. 111.1 ± 13.8, p = 0.007). In AL, 1-year average survival was significantly lower in AL than that of TTR (p = 0.005). Average survival time from diagnosis to death was 272.2 ± 113.3 days in AL, 1675.1 ± 745.4 days in TTR (p < 0.05). Survival rate at 1 year from diagnosis was significantly lower in AL than in TTR (23 vs. 53%, p = 0.05). In AL, 1-year nonsurvivors showed shorter deceleration time than those of survivors, however, not statistically significant (131.3 ± 30 vs. 177.1 ± 11 ms, p = 0.069).

Conclusions: AL amyloidosis shows more restrictive physiology compared with TTR amyloidosis which could cause impaired diastolic function and higher cardiac mortality. Furthermore, only in AL amyloidosis, more impaired diastolic function might account for poor prognosis.

P6161 | BENCH
Early detection of diastolic and systolic dysfunction with spectrum-tracking echocardiography in carriers of hypertrophic cardiomyopathies

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Purpose: Diastolic dysfunction has been described as the first abnormality in patients with sarcomeric mutations, prior to left ventricular hypertrophy (LVH). Previous studies have demonstrated that regional peak systolic longitudinal strain (ι1) and strain rate (SSR) are reduced in overt hypertrophic cardiomyopathy (HCM). The aim of this study was to assess early changes in diastolic and systolic function using spectrum tracking echocardiography in subjects with genotype positive hypertrophic cardiomyopathy.

Methods: In this single-center prospective cohort of G+LVH patients, 78 (43% male, age 41 ± 13 years) patients underwent ≥ 2 echocardiographic evaluations between 2006-2013. Structural characteristics, systolic function and diastolic function were assessed by two-dimensional, Doppler, regional longitudinal and SSR were measured from apical 4-, 2-, and 3-chamber views. One (1%) patient with undiagnosable diastolic function was excluded. The standard diagnostic criteria for HCM were used.

Results: During a mean follow-up of 4.7 ± 1.9 (range 1.2-8.1) y, 1 patient developed overt HCM (LVH of 15 mm, after 6.6 y). No cardiac events occurred. Twelve (15%) patients had diastolic dysfunction at baseline, and 12 (15%) other patients developed diastolic dysfunction during follow-up. Septal ι (from 20.8 ± 10% to 16.7% ± 11.7%, p = 0.014) and lateral ι (from 13.2 ± 11% to 11.7% ± 12%, p = 0.012) were lower in patients with diastolic dysfunction than those without diastolic dysfunction (10 ± 2 mm, p = 0.01 45±44 kg, p = 0.02). p = 0.001).

Conclusion: Preclinical HCM patients, who developed diastolic dysfunction, not only had increased LV wall thickness and LV mass, but also regional systolic dysfunction, demonstrated by ι and SSR analysis. This impairment of regional systolic function may underlie the development of asymmetric hypertrophy.

P6162 | BEDSIDE
Mechanisms of taxanes-induced cardiac dysfunction: a 4D echocardiographic and genetic study

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Background: Use of taxanes in breast cancer is often limited by the development of cardiac dysfunction, leading to increase of morbidity and mortality. Therefore, better understanding of mechanisms of cardiac dysfunction induced by taxanes is essential. Our aim was to evaluate whether increased oxidative stress and arterial stiffness has a determinant role in the development of taxanes-induced cardiac dysfunction, and if this is related to a specific genetic polymorphism.

Methods: We studied prospectively 45 women with breast cancer (43±8 years), without known cardiac disease, and LVFEF> 50%, scheduled to be treated with taxanes, at baseline, and after the completion of treatment (cumulative dose of 540±150 g/m2). 4D auto LV quantification echo was used to assess LV geometry, systolic function (EF), and diastolic function. 4D regional longitudinal (ιL), and circumferential strain (ιC), and area strain (AS) were assessed from apical 4-, 2-, and 3-chamber views. 4D stiffness index was assessed from 4D strain curves. Myocardial collagen content from a small myocardial biopsies was analyzed.

Results: After the completion of chemotherapy, there was a reduction of EF, radial and longitudinal deformation, and area strain, whereas circumferential deformation remained unchanged. These changes were associated with an augmentation of oxidative stress and an increase of the arterial stiffness index (Table). Changes in LV deformation (ιL and AS) were inversely related to changes in oxidative stress.

Changes from baseline to follow-up

| Taxes | EF (%) | RS (%) | ιL (%) | ιC (%) | AS (%) | CCI (mmol/mg) | 4D stiffness index
|-------|--------|--------|--------|--------|--------|----------------|------------------|
| Baseline | 62±4 | 62.7 ± 33.8 | 21.3 ± 18.6 | 17.4 ± 22.1 | 33.9 ± 4.3 | 0.336 ± 0.104 | 7.7 ± 3.3
| Final | 55 ± 3 | 50.10 ± 30.4 | 17.4 ± 20.4 | 31.4 ± 20.4 | 0.500 ± 0.100 | 10.2 ± 3.1 | p = 0.001 | 0.001 | 0.014 | 0.012 | 0.07 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001

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and arterial stiffness (r=−0.56 and r=−0.49, for LS; r=−0.63 and r=−0.54, for AS; all p<0.01). Furthermore, homozygote of genotype rs1056836 was directly related to the decrease of EF and LS (r=0.59 and r=0.64, p<0.05) after the completion of treatment. Troponin-I was not changed.

Conclusion: Increased oxidative stress and arterial stiffness, and not direct myocardial damage, may play an essential role in the development of taxane-induced cardiac dysfunction, probably associated with a specific genetic variation.

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P6163 | BEDSIDE
Does alcohol septal ablation for hypertrophic obstructive cardiomyopathy induce ventricular arrhythmias?
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Objective: The purpose of the present study was to determine the incidence of ventricular arrhythmias before and after ASA.

Background: In patients with hypertrophic obstructive cardiomyopathy (HOCM), gradient reduction by alcohol septal ablation (ASA) is an alternative treatment option to surgical myectomy. However, concerns exist about whether the induction of a myocardial scar during ASA may create a substrate for ventricular arrhythmias.

Methods: The study group consisted of 44 patients in whom ASA was performed for symptomatic, drug-refractory hypertrophic cardiomyopathy. Continuous rhythm monitoring was obtained by an implantable loop recorder (n=30) or a pacemaker (n=14). The occurrence of ventricular and supraventricular arrhythmias before and after ASA was noted.

Results: The ASA procedure was considered successful (resting gradient <30 mmHg, and provoked gradient <50 mmHg at 4 months echocardiographic assessment) in combination with NYHA Class functional status <2 in 30 (68%) patients. Rhythm monitoring before ASA was available in 28 patients. The mean duration of rhythm monitoring after ASA was 3.5±2.8 years. Sustained VT/VF within 30 days after ASA occurred in three patients (7%), including 2 cases of VF during the procedure, while no VT/VF was observed before ASA (p<0.10). No sustained VT/VF was observed >30 days after ASA. No deaths occurred during follow up.

Conclusions: We conclude that the obstruction relief and improved NYHA class functional status provided by ASA are not offset by a high incidence of late occurrence of ventricular tachycardia or ventricular fibrillation.

P6164 | BEDSIDE
A founder mutation of the myosin binding protein-C gene in hypertrophic cardiomyopathy and adverse outcomes with compound heterozygosity
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Purpose: Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, caused by sarcomeric genes mutations. Although most of founder mutation carriers that arose from a common ancestor exhibit favorable clinical phenotypes, there still remain small fractions of these carriers associated with increased cardiovascular events. However, few data exist regarding defining factors that modify phenotypes of these patients particularly in terms of multiple gene mutations. Therefore, we assessed genotype-phenotype correlations and investigated factors that contribute to phenotypic diversities of the founder mutation carriers.

Methods and results: We screened unrelated 488 probands with HCM for sarcomeric genes mutations. We identified a prevalent founder mutation (V762D) in the MYBPC3 in 33 subjects from 19 families. Among them, 28 carriers harbored isolated V762D mutation and exhibited a late onset of overt HCM than other MYBPC3 mutations carriers (62.8±3.0 years vs 50.1±2.6 years, p<0.05).

Conclusions: Mutation carriers with founder MYBPC3 V762D can develop unfavorable phenotypes of HCM when combined with other sarcomere gene mutations.

P6165 | BEDSIDE
Immunosuppressive therapy limits myocardial damage and contractile dysfunction in eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
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Background: Cardiac involvement remains the major mortality predictor in eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss). The recognition of efficacy of immunosuppression to limit cardiac involvement may extend indications for immunosuppressive therapy in EGPA.

Objective: To assess the impact of addition of non-steroid immunosuppression to glucocorticoid therapy on cardiac disease in EGPA.

Methods: 51 patients (36 females, 15 males, mean age 44.3±14.4 years) with EGPA in clinical remission were retrospectively studied and scheduled for cardiac magnetic resonance (CMR) at follow-up. CMR images were assessed off-line for the presence of left ventricular ejection fraction (LVEF) <50% and myocardial damage depicted by late gadolinium enhancement (LGE).

Results: At diagnosis 15 patients presented with heart failure and 13 had LVEF ≤50%. At 39.3±38.7 months of follow-up, 25 patients demonstrated heart failure exacerbation or had LVEF ≤50% in CMR. Comparing subjects in whom non-steroid immunosuppressants were (n=18) and were not (n=33) initiated at diagnosis, the latter more frequently had new onset or progression of heart failure (16% versus 12%[p=0.02]). The baseline and follow-up LVEF was either ≤50% or ≥50% in 58.3±14.1% and 58.8±14.2% (p=0.30) or 54.8±13.9% and 49.8±17.7% (p=0.02), when non-steroid immunosuppression was or was not introduced at diagnosis, respectively. Both the lack of introduction of non-steroid immunosuppression at diagnosis and non-steroid immunosuppression discontinuity index defined as ratio between the treatment period without non-steroid immunosuppression and disease duration provided incremental predictive value over clinical data for the presence of LVGL (odds ratio (OR)=23.55, 95% confidence interval (CI): 2.69-206.45, p=0.004; OR=1.03 per 1% genetic risk, 95%CI: 1.01-1.06, p<0.01) and LVEF<50% (OR=16.11, 95%CI: 5.83-41.1% per 1%, p<0.01; OR=1.03 per 1%, 95%CI: 1.00-1.06, p<0.03) at follow-up, respectively (p<0.05 for increase in chi-square and area under curve).

After adjustment for age, relapse rate, maximal blood eosinophilia, the extent of myocardial damage at follow-up expressed as LVGL volume was associated with duration of non-steroid immunosuppression and non-steroid immunosuppression discontinuity index.

Conclusions: Non-steroid immunosuppressive therapy limits the extent of myocardial damage and dysfunction and may prevent development of heart failure in EGPA.

P6166 | BEDSIDE
Postoperative course and long-term prognosis of two chambered right ventricle
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Background: Two chambered right ventricle (TCRV), which is divided into two chambers by abnormal muscle bundle, is a rare disease. Most patients with TCRV were diagnosed in childhood or adolescence. The stenosis of TCRV is progressive, and early surgical intervention is recommended for patients whose symptom and/or pressure overload of RV inflow is progressive. However, there are few data about the postoperative course of TCRV and the surgical indication for asymptomatic patients is difficult.

Methods: We retrospectively investigated 38 consecutive patients who were diagnosed as TCRV and underwent surgical intervention between 1981 and 2009. The median age of surgical intervention was 5 years old (2-10.75 years old), and there were 4 patients with surgical intervention in adulthood. There were no perioperative death and complications. Among 38 patients, 37 patients had dilated or complicated ventricular septal defect with TCRV. Clinical background, pre and postoperative data of cardiac catheter, transthoracic echocardiography, and postoperative outcome were evaluated. Moreover, we picked up 26 patients who were followed-up by TTE for more than two years after surgery.

Results: The median age of surgical intervention was 5 years old (2-10.75 years old), and there were 4 patients with surgical intervention in adulthood. There were no perioperative death and complications. Among 38 patients, 37 patients had dilated or complicated ventricular septal defect with TCRV. Clinical background, pre and postoperative data of cardiac catheter, transthoracic echocardiography, and postoperative outcome were evaluated. Moreover, we picked up 26 patients who were followed-up by TTE for more than two years after surgery.

Conclusions: Surgical outcome and long-term prognosis of TCRV were good. There was no recurrence during long-term follow-up. Therefore, we should take into consideration early surgical intervention even for asymptomatic patients with TCRV.

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Conflicting gender-related differences during long-term followup of patients with idiopathic Dilated Cardiomyopathy

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Background: Gender differences may affect disease presentation, clinical pathways, diagnostic yield and prognosis of patients with cardiovascular disease; few information about gender differences in idiopathic dilated cardiomyopathy (IDCM) are available.

We evaluated possible clinical, laboratory and prognostic divergences in women and men with IDCM.

Methods and results: From 1988 to 2012, 803 consecutive patients with IDCM recorded in the Heart Muscle Disease Registry of Trieste (Italy) were evaluated; 576 (72%) were male and 227 (28%) were female.

At first evaluation women were significantly older (48 vs. 45 years old, p=0.008); 576 (72%) were male and 227 (28%) were female. 62 (28%) of women and 134 (23%) of men presented with NYHA functional class III-IV (p=0.026).

Women showed more frequently a left bundle branch block at ECG (38% vs. 28%, p=0.01), smaller left ventricular end-diastolic indexed volume at echocardiography (65 vs. 93 ml/m², p<0.002) and more frequently moderate to severe mitral regurgitation at Doppler (43% vs. 33%, p=0.015). No difference among medical treatment and device implantation rate was found.

Interestingly, during a median 108 months follow-up period women showed less frequently a clinical and echocardiographic improvement, but a significantly lower ten-years total mortality/heart transplantation rate and cardiovascular mortality (20% vs. 32% (p=0.001), and 9% vs. 15% (p=0.024).

Conclusions: In our population of patients with IDCM, women present with a more advanced phase of the disease and a lower clinical-instrumental improvement on optimal medical therapy than men, notwithstanding that women have a better long-term prognosis.

Evidence for altered cortisol stress responses in patients with takotsubo cardiomyopathy?

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Purpose: In patients with takotsubo cardiomyopathy (TTC), a catecholamine increase can be observed after the stressful trigger event and psychotic disorders, vulnerable personality traits and chronic stress were suggested as predisposing factors. Alterations of cortisol awakening and stress response (CAR, CSR) are sensitive markers for the basal activity and responsivity of the hypothalamus-pituitary-adrenal axis (HPAA) in psychopathological conditions. Now, these markers were investigated in TTC patients for the first time.

Methods: 19 female TTC patients were compared to 20 women with histories of myocardial infarction (MI) and to 20 healthy controls, matched by age and index event date. Repeated salivary sampling indicated cortisol release; questionnaires assessed personality, life events, chronic stress and psychiatric symptoms. Blood-sampling was not performed, because venipuncture itself can lead to HPAA activation.

Results: The groups did not differ in their basal HPAA activity, psychiatric or personality profiles. TTC patients revealed a significantly blunted cortisol stress response in contrast to controls [covariate: pre-stress cortisol; F(1,36)=4.35, p=0.04, r=0.23]; MMP9 (ng/ml) 657 [404;1668] vs 440 [317;637] (p=0.03); hsCRP 3,6[1,0;6,7] vs 0,63 [0,8;2,0] (p=0,02); Anti-dsDNA (U/ml) 3,7[2,8;7,1] vs 0,0 [0,0;0,0] (p<0.001). Stressful life events occurred significantly more often in TTC vs MI [same covariate; F(1,36)=4.35, p=0.04, r=0.33], despite increased heart rates and nervousness. The contrast response in contrast to controls [covariate: pre-stress cortisol; F(1,36)=4.35, p=0.04, r=0.33] was observed in TTC patients for the first time.

Conclusions: Evidence for altered cortisol stress responses in patients with takotsubo cardiomyopathy (TTC) is available. From 1988 to 2012, 803 consecutive patients with IDCM recorded in the Heart Muscle Disease Registry of Trieste (Italy) were evaluated; 576 (72%) were male and 227 (28%) were female. At first evaluation women were significantly older (48 vs. 45 years old, p=0.008); 62 (28%) of women and 134 (23%) of men presented with NYHA functional class III-IV (p=0.026).

Women showed more frequently a left bundle branch block at ECG (38% vs. 28%, p=0.01), smaller left ventricular end-diastolic indexed volume at echocardiography (65 vs. 93 ml/m², p<0.002) and more frequently moderate to severe mitral regurgitation at Doppler (43% vs. 33%, p=0.015). No difference among medical treatment and device implantation rate was found.

Interestingly, during a median 108 months follow-up period women showed less frequently a clinical and echocardiographic improvement, but a significantly lower ten-years total mortality/heart transplantation rate and cardiovascular mortality (20% vs. 32% (p=0.001), and 9% vs. 15% (p=0.024).

Conclusions: In our population of patients with IDCM, women present with a more advanced phase of the disease and a lower clinical-instrumental improvement on optimal medical therapy than men, notwithstanding that women have a better long-term prognosis.

Evidence for altered cortisol stress responses in patients with takotsubo cardiomyopathy?
of hsTNP in pts with ICMP correlates with the severity of myocardial hypertrophy r=0.8 (p=0.01), severity of cardioresilosis r=0.7 (p=0.02), ESV r=0.7 (p=0.009), EDV r=0.6 (p=0.04), EF r=0.6 (p=0.06), NT-pro BNP r=0.7 (p=0.007), ECP r=0.9 (p=0.005). SVCAM in pts with ICMP correlates with the severity of myocardial hypertrophy r=0.6 (p=0.03).

Conclusions: Comparison of DCM with DCM without signs of active inflammation the patients with ICMP have actvation of inflammatory response, higher levels of TGFβ and metalloproteinases activity. In pts with ICMP hsTNP secretion involves in myocardial fibrosis and hypertrophy.

P6172 | BEDSIDE Intramyocardial fibrosis and muscle mass in hypertrophic cardiomyopathy: may cardiac CT and osteopontin contribute to diagnosis?

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Introduction: Ventricular fibillation in Hypertrophic Cardiomyopathy (HCM) is partially due to intramyocardial fibrosis (IF). For IF assessment usually pro-vicuous invasive technology by LGE-CMR and different serum-markers have been introduced. Convincing correlations have never been proven. By validating with LGE-CMR we tested leMDCT and a new fibrosis serum-marker, osteopontin, a secreted glycoprotein (OPN) in consecutive HCM patients with regard to IF and left-ventricular muscle mass (LV-MM).

Methods: We included 30 patients consecutively. For IF-assessment all individuals were conducted to LGE-CMR (1.5T, 32-channel coil,) and leMDCT (64-slice). In leMDCT data acquisition (Phase Sensitivity Inversion Recovery sequence) was performed 12 minutes after injection of Gadolinium Diethylenetri- amines penta-acetic acid (0.15 mmol/kgBW). LeMDCT scans were carried out 7 minutes after injection of 150 ml iodated dye (lomiprod, iodine 350 mg/ml). Besides healthy controls all patients were taken blood samples for assessment of OPN levels (Human Osteopontin Assay; IBL). Finally, OPN was correlated with LGE-CMR, leMDCT and standard 2D echo-data.

Results: Mean age of patients and healthy controls was 62.4± 17.7 years. LeMDCT detected IF in 19/30 patients (63.3%) validated by LGE-CMR. Tissue density of IF was 142± 51HU vs. 89.9± 19.3HU in remote myocardium; p<0.001. LV-MM and IF-mass was assessed by leMDCT with 151.3± 46.8gMM and 8.4± 5.2gIF vs. by LGE-CMR with 169.4± 62.9gMM and 10.2± 6.3gIF. Controls and HCM-patients presented an OPN level of 396.7± 964.6ng/mL vs. 284.7ng/mL (p=0.0001). Controls vs. HCM-patients showed a significant difference in mean value of 267.3ng/mL (2sided T-test; p<0.0001). Controls vs. HCM-patients showed a significant difference in mean value of 267.3ng/mL (2sided T-test; p<0.0001). IF quantified by leMDCT and LGE-CMR correlated with OPN: r=0.21 (p=0.37) and r=0.23 (p=0.03). Correlation of IF with left-ventricular (LV) muscle mass (MM) assessed by LGE-CMR and leMDCT in HCM patients was 0.46.8± 51.5HU ± 89.9± 19.3HU (p=0.001). Controls vs. HCM-patients showed no significant increase in the QTc interval on standing. We also observed significant differences when compared the mean increase in the QTc interval between both groups (p<0.0001 for leads DII and V5). No significant differences in the increase of the QTc interval on standing were observed between LQTS1 and LQTS2 patients.

Table 1. QTc in supine and in standing positions

<table>
<thead>
<tr>
<th>Lead</th>
<th>QTc supine (ms)</th>
<th>QTc standing (ms)</th>
<th>ΔQTc (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DII</td>
<td>147±34</td>
<td>190±37</td>
<td>43</td>
</tr>
<tr>
<td>V5</td>
<td>147±34</td>
<td>190±37</td>
<td>43</td>
</tr>
</tbody>
</table>

Conclusions: Prevalence of ABS was 0.9% in pts admitted for ACS. ABS and STEMI pts have no significant difference in long-term survival. ABS pts presented a decrease risk of cardiovascular death when compared to STEMI group pointing out a different pathophysiological mechanism.

P6174 | BEDSIDE The response of the QTc interval to standing as a new diagnostic tool for long QT syndrome

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Background: The QT interval duration depends on the heart rate (HR) and is related with the autonomic nervous system regulation. Patients with Long QT Syndrome (LQTS) due to mutation of the potassium channels have an abnormal response to abrupt changes in HR and to the sympathetic stimulation that occurs with the brisk standing.

Objective: The purpose of our study was to describe the QT interval changes provoked by standing in a group of patients with congenital LQTS, and compare the changes with a group of unaffected relatives.

Methods: We performed an ECG in the supine position and another immediately after getting up in 26 pts with LOTS and 26 unaffected relatives. We measured the corrected QT interval (QTc) (Bazett’s Formula) in supine position and immediately after standing in DII and V5 to assess whether there were differences in the QTc in both leads. We evaluated the increase in the QTc interval (ΔQTc = QTc in standing-QTc in supine).

Results: LOTS group consisted of 26 patients with genetic confirmation for LQTS (42±17 years, 50% males). Among LQTS patients, 6 (23%) had LQTS1, 17 (65%) had LQTS2, and 3 (12%) had LQTS7. In the control group the mean age was 40±15 years, and 44% were males. QTc values in supine and in standing positions are shown in Table 1. LOTS patients had a higher QTc interval after brisk standing than in supine position (p<0.0001 for both leads). In contrast, controls showed no significant increase in the QTc interval on standing. We also observed significant differences when compared the mean increase in the QTc interval between both groups (p<0.0001 for leads DII and V5). No significant differences in the increase of the QTc interval on standing were observed between LQTS1 or LQTS2 patients.

Table 1. QTc in supine and in standing positions

<table>
<thead>
<tr>
<th>Lead</th>
<th>QTc supine (ms)</th>
<th>QTc standing (ms)</th>
<th>ΔQTc (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DII</td>
<td>203±37</td>
<td>249±41</td>
<td>46</td>
</tr>
<tr>
<td>V5</td>
<td>203±37</td>
<td>249±41</td>
<td>46</td>
</tr>
</tbody>
</table>

Conclusions: Our population of patients with congenital LOTS had an abnormal QTc interval adaptation with the standing, showing a significant increase of these measures. These changes in the QTc interval were observed in both DII and V5 leads. Since our controls did not show this behavior, the performance of this test could be a useful tool in the diagnosis of individuals with baseline QTc interval at the upper limit of normal.

P6175 | BEDSIDE GRS fragmentation or epsilon potentials in Fontaine leads in arhythmogenic right ventricular cardiomyopathy

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Fontaine leads with highly amplified precordial leads and modified limb leads are often used to diagnose arhythmogenic right ventricular cardiomyopathy according to a publication of Marcus and Fontaine published in 1984. In standard ECG leads epsilon waves could be found in about 23% of cases according to recent
literature. If these special leads are used epsilon waves are documented in much more cases. QRSD segmentation in standard ECG leads could be found in 85% of cases in arrhythmogenic right ventricular cardiomyopathy.

The question is whether these special leads can be used not only to increase the rate of epsilon waves but also the rate of QRSD segmentation. QRSD segmentation is defined as a notchting of the Q wave, of the R wave or the S wave and includes epsilon waves, terminal activation delay and S wave upstroke.

Method: In a cohort of 128 patients (76 males, mean age of 46.3±13.1 years) Fontaine leads were used to diagnose arrhythmogenic right ventricular cardiomyopathy. Epsilon waves and QRSD fragmentation were analyzed in highly amplified precordial leads and in modified limb leads.

Results: Epsilon waves could be found in Fontaine leads in n=99/128 (77%) of cases. QRSD fragmentation could be demonstrated in n=127/128 (99%) of cases as defined by Fontaine leads. QRSD fragmentation included typical epsilon wave defined as notching of the S wave and beyond in the transition to the T wave.

Conclusions: If Fontaine leads are used in this cohort of patients with typical arrhythmogenic right ventricular cardiomyopathy the finding of epsilon waves increased dramatically by Fontaine leads but QRSD fragmentation increased to a rate of 99% superior to epsilon wave discrimination. If QRSD fragmentation in Fontaine leads are used the diagnosis of arrhythmogenic right ventricular cardiomyopathy can be made in almost all patients by highly amplified and modified ECG.

P6176 | BEDSIDE
Clinical significance of recurrence of extracardiac Ga-67 uptake in cardiac sarcoidosis during steroid therapy
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Background: Although the steroid administration has been established to improve prognosis in cardiac sarcoidosis (CA), there have been few reports of clinical indicators identifying inflammatory activity related to the titration of steroid. Clinical significance of recurrence of extracardiac Ga-67 uptake in CA, once disappeared by the introduction of steroid therapy, is not fully investigated.

Methods: We investigated 28 consecutive CA patients receiving steroid therapy in 2002-2012. Prednisolone was started at the dose of 30 mg/day for 1 month, and then tapered off by 5 mg every 4 weeks. Finally, the maintenance dose was 5 mg/day. The clinical examinations including Ga-67 scintigram were performed before the introduction of steroid, after the initial phase of prednisolone with 30 mg/day for 1 month, and then the tapering phase of 3 months a year.

Results: Although intra- and/or extracardiac Ga-67 uptake disappeared in all cases after the steroid therapy, extra-cardiac Ga-67 uptake, mainly in the mediastinum, recurred in 13 patients in the process of tapered steroid. During the follow-up of 3.9±2.8 years, 7 cardiac events were observed including 2 sudden deaths, 2 ventricular tachycardia, 1 hospitalization with exacerbated heart failure, 1 newly diagnosed complete atrioventricular block and 1 chest pain without ischemic heart disease. When divided into 2 groups based on Ga-67 re-uptake (R+ or R_), there were no significant difference of the echocardiographic parameters between the 2 groups. Cardiac events were significantly occurred in R+ than R_- (8/7% vs. 7/8% P<0.05), and left ventricular ejection fraction deteriorated more in R+ than R_- (-18±7% vs. -1±7%, P<0.01).

Conclusion: The recurrence of extra-cardiac Ga-67 uptake during the steroid therapy indicates poor prognosis, presumably through inadequate suppression of myocardial inflammation.

P6177 | BEDSIDE
Blood pressure alterations during heart failure treatment in patients with non-ischemic dilated cardiomyopathy
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Background: Most of cardiospecific protective agents to improve the prognosis of heart failure have no effect on left ventricular ejection fraction or on decreased systemic blood pressure (BP). Actually, the initiation and titration with optimal treatment were unfortunately limited in patients with low BP. We previously reported that systolic BP <113 mmHg classified in NYHA functional class I or II. All patients underwent laboratory examination, echocardiography, and cardiac catheterization before the titration. We determined the BP adaptation during cardiac protective treatment in HF patients with low BP.

Purpose: This study aimed to clarify the systolic BP alterations during the titration period of HF treatment and to investigate the prognostic value of BP alterations in low BP patients with asymptomatic or mildly symptomatic NIDCM.

Methods: We enrolled 65 NIDCM patients (22 female) with systolic BP <113Hg classified in NYHA functional class I or II. All patients underwent laboratory examination, echocardiography, and cardiac catheterization before the titration. We determined the BP adaptation during cardiac protective treatment in HF patients with low BP.

Results: The mean age, left ventricular ejection fraction, BNP levels were 48.4 years, 29.8%, 335pg/mL, respectively, ACEI/ARBs, β-blockers, and mineralocorticoid receptor antagonists were used in 80%, 94% and 62% of the patients before the titration and increased to 92%, 95% and 72% after the titration, respectively. The post-BP (102±14 mmHg) tends to be higher than the pre-BP (99±10 mmHg) (p=0.11) and BP levels in 37 (57%) patients were elevated after the titration. Univariate Q wave, of total hazard analysis revealed that post-BP and A/BP had inverse correlation with the risk of cardiac events (p<0.01 and p=0.03, respectively). In multivariate analysis, post-BP was an independent determinant of cardiac events (p=0.04).

Conclusions: BP levels were elevated after the optimal treatment of HF in about 50% of NIDCM patients with low BP. Additionally, higher post-BP was associated with a lower risk of cardiac events. Those results implicate that we should not hesitate to use cardiodprotection medications for NIDCM patients, even if their systolic BP is low.

P6178 | BENCH
Identification of novel markers in various cardiac pathologies for risk stratification and targeted therapy
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Purpose: Heart diseases are the leading causes of death worldwide. Dilated cardiomyopathy (DCM), myocarditis and ischemic cardiomyopathy (ICM) can be caused by various factors. The immune system is a key player with a central role after disease onset and during disease progression. Autoantibodies directed against various peptide-antigens present in cardiac tissue are found in these cardiac diseases.

Methods: Peptide Array analysis (PEPperMAP) with sera obtained from 10 DCM, 10 myocarditis, and ICM patients vs. 10 healthy, age-matched controls was performed against 26,364 different 15-mer peptides derived from 166 proteins associated with cardiovascular diseases.

Results: 1108 mAbs (n=8) were immunized on days 0, 7, 14 with peptide sequences (150/μg) derived from identified proteins. On day 28, mice were sacrificed, histopathological evaluation of the heart and antibodies were determined within the serum.

Conclusions: The myocarditis group various antigens were observed such as the giant sarcomeric signaling protein obscurin, the cytoplasmic protein dystrophin and laminin which is present in the basal lamina, as well as regulatory enzymes such as myosin light chain kinase and sodium/potassium transporting ATPase. Among the most promising candidate antigens in the DCM group were the structural proteins obscurin, dystrophin and laminin. In fact, over 30% of the top 50 antigenic peptides represent obscurin. In addition, we also identified 4 strongly reacting antigenic oligopeptides derived from RNA-binding protein 20. Sera from ICM patients reacted strongly to peptides derived from laminin, sodium/potassium transporting ATPase located in the plasma membrane of the cell and the voltage-gated potassium channel KCNQ1 required for repolarization of the cardiac action potential. Furthermore, we could identify the heat shock protein HSP27, the AMP-ATP-binding subunit of the AMP-activated protein kinase, and actin.

Conclusion: A/JOla mice (n=8) were immunized on days 0, 7, 14 with peptide sequences (150 μg) derived from identified proteins. Peptide Array analysis (PEPperMAP) with sera obtained from 10 DCM, 10 myocarditis, and ICM patients vs. 10 healthy, age-matched controls was performed against 26,364 different 15-mer peptides derived from 166 proteins associated with cardiovascular diseases. AU/Joala mice (n=8) were immunized on days 0, 7, 14 with peptide sequences (150 μg) derived from identified proteins. Peptide Array analysis (PEPperMAP) with sera obtained from 10 DCM, 10 myocarditis, and ICM patients vs. 10 healthy, age-matched controls was performed against 26,364 different 15-mer peptides derived from 166 proteins associated with cardiovascular diseases.

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noninvasive tests, the algorithm nosological diagnosis was developed. Isolated myocarditis diagnosed in 63% patients, its combination with genetic disorders in 17%, and genetic cardiomyopathy in 9%; in 11% patients a primary (idiopathic) cardiomyopathy was diagnosed. The anti-heart antibodies level had the most strong correlation with biopsy data.

In patients with inflammatory specific therapy was administered: methylprednisolone (32 [20; 40] mg/day), hydroxychloroquine 200 mg/day, azathioprine 108.3±34.2 mg/day, ganciclovir or acyclovir, IV immunoglobulin. Antiviral therapy was effective in 79.3% cases. Significant decrease (p<0.05) of left ventricle diastolic diameter (6.7±1.0 to 6.4±1.1), diastolic (202.7±85.0 to 177.9±96.4) and systolic volume (143.6±74.2 to 114.1±71.8), systolic pulmonary artery pressure (47.0±16.3 to 34.4±12.4), increase of EF (30.7±10.9 to 39.5±11.3) were found only in patients who received immunosuppressive therapy, both in virus-negative and virus-positive patients. With a mean follow-up 12.0 [5; 22] months mortality only in patients who received immunosuppressive therapy, both in virus-negative and virus-positive patients.

P6160 | BEDSIDE
Clinical significance of cardiac events and left ventricular systolic function improvement in newly-diagnosed dilated cardiomyopathy patients with prolonged QRS duration
T. Nabetza, T. Inomata, Y. Iida, Y. Ikeda, S. Ishii, T. Sato, T. Naruke, T. Mizutani, T. Koiatabashi. J. Ako. Kitasato University School of Medicine, Department of Cardiovascular Medicine, Kanagawa, Japan

Purpose: Prolonged QRS duration is a risk factor for poor prognosis in patients with non-ischemic dilated cardiomyopathy (DCM). Cardiac resynchronization therapy is widely used for patients with heart failure (HF) patients with impaired left ventricular ejection fraction (LVEF) <35% and prolonged QRS duration. It has been unclear, however, the association between prognosis and LVEF improvement in newly-diagnosed DCM (ND-DCM) patients treated only optimal pharmacotherapy (OPT) with prolonged QRS. Methods and results: One hundred and fifty three consecutive ND-DCM patients with LVEF <35% at baseline under OPT in 1996-2011 were enrolled. The patients were divided into 2 groups based on the QRS duration: ≥120 msec (Group C; n=40) or <120 msec (Group N; n=113). Group C was further divided into 2 groups based on LVEF <35% (Group C1; n=24) or LVEF ≥35% (Group C2; n=16) after completing OPT. None of Group C died during 6 months. During the observational period for 1787±1220 days, there were 4 deaths as the primary endpoint and 11 composite of cardiovascular events in acute phase. Kaplan-Meier curves indicated significantly fewer primary endpoint (P=0.016) or secondary endpoints (P=0.026) in Group C1 than in Group C2. On the other hand, there was no significant difference of both end points between the group N and group C1 (Fig. 1A; B).

Figure 1
Conclusion: There were some ND-DCM patients with QRS ≥120 msec at baseline whose LVEF improved after completing OPT. The clinical outcome of ND-DCM patients with QRS ≥120 msec with LVEF improvement during 6 months was equivalent to that of the ND-DCM patients with QRS <120 msec. Further studies will be necessary to identify patients with QRS ≥120msec who can respond to OPT.

P6181 | BEDSIDE
Low left ventricular function and high troponin I level in acute phase predict delayed recovery in patients with takotsubo cardiomyopathy
K. Kato1, Y. Saka2, I. Ishibashi2, Y. Kobayashi1. 1Chiba University Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan; 2Chiba Emergency Medical Center, Chiba, Japan

Background: Takotsubo cardiomyopathy (TC) is characterized by transient reversible systolic dysfunction of the apical and/or mid segments of the left ventricle (LV). However, there is little information about the details of its recovery process.

The present study evaluated recovery process and the contributing factors in TC patients.

Methods: A total of 16 consecutive patients with TC underwent serial cardiovascular magnetic resonance imaging (CMRI) (acute phase 3.25±1.88 day and follow-up 57.6±42.3 day) to assess global LV ejection fraction (LVEF) and regional LV wall motion. Furthermore, myocardial edema defined as high intensity area in T2-weighted CMR was evaluated.

Results: Between acute phase and follow-up, global LVEF improved from 48±13% to 68±9%. Regional wall motion abnormality remained in 4 patients (25.0%) in the follow-up CMRI. Myocardial edema was observed in 13 patients (81%) in acute phase and follow-up CMR showed it in 9 patients (69.2%). Of 16 patients, 12 had no regional LV wall motion abnormality in the follow-up CMRI and 4 had incomplete recovery. Lower global LVEF (34.5% vs 52.5%, p<0.01) and higher troponin I level (8.66 vs 2.61 ng/ml, p=0.04) in acute phase were observed in patients with incomplete recovery of regional LV wall motion.

Conclusions: Regional LV wall motion abnormality and myocardial edema do not disappear in all TC patients. Low global LVEF and high troponin I level in acute phase are predictors of delayed recovery in TC patients.

CARDIOMYOPATHIES IV

P6163 | BEDSIDE
Different response to adaptive servo-ventilation therapy according to the etiology of cardiomyopathy in patients with chronic heart failure
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Background: Beneficial effect of adaptive servo-ventilation (ASV) therapy in patients with chronic heart failure (CHF) has been reported. However, the difference in responsiveness to ASV therapy between the causes of cardiomyopathy is unexplored.

Methods: ASV therapy was successfully introduced in a total of 136 CHF patients between February 2009 and March 2013. Patients with LVEF >40%, valvular heart disease, or specific myocardial diseases were excluded; thereafter, 105 consecutive patients were enrolled in the study. They were divided clinically into dilated cardiomyopathy (DCM, n=70), dilated phase of hypertrophic cardiomyopathy (dHCM, n=16), and ischemic cardiomyopathy (ICM, n=19). Patients were followed up to a mean period of 300 days. Laboratory and echo data were obtained before and 6 months after ASV introduction. Baseline data including plasma BNP, hemoglobin, serum creatinine, serum sodium concentration, and medications were not different among groups.

Results: Six months of ASV therapy provided significant increase of LVEF in patients with DCM (6.1±1.1%, p<0.04) compared with dHCM (-0.1±3.0%) and ICM (0.4±2.5%). Kaplan-Meier analysis demonstrated that dHCM patients were associated with increased risk of death or heart failure readmission compared with DCM and ICM patients (p=0.02, Fig. 1).

Figure 1. Survival analysis.

Conclusions: ASV therapy improved cardiac function in DCM patients, while dHCM patients showed poor clinical outcome even after ASV therapy.

P6164 | BEDSIDE
Dried blood spot screening of Fabry Disease among patients with left ventricular hypertrophy of unknown cause
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Purpose: Identifying subjects and genotypic profiles compatible with Fabry Dis-
ease (FD) by dried blood spot (DBS) screening, among left ventricular hyper-trophy (LVH) patients >18 years, as candidates for genetic study of the α-galactosidase A gene (GLA) due to their gender and their low α-galactosidase A (α-Gal A) activity.

Methods: Screening study for FD among patients attending to cardiologist de-partments with unexplained left ventricular hypertrophy (≥14mm); DBS α-Gal A activity from patients was compared against controls matched by gender and medical center. Male patients with enzymatic activity <70% of controls and all female patients, underwent GLA gene sequencing characterization.

Results: A total of 269 patients were screened, 249 males (67.8%), which were younger than females (58±16 vs 65±15 years; p<0.001). Overall, patients were overwhelmingly on average (BMI = 28±8 kg/m²), the septal wall thickness was 19.4±4.7mm and the more frequent LVH geometry patterns were concentric and eccentric hypertrophy (46% and 40%, respectively). Females showed a higher presence-age of arterial hypertension (58.8% vs 45.4%; p<0.015), but no differences were shown in their creatinine levels 1.01±0.76 vs 1.12±0.71 mg/dl.

The GLA gene was sequenced for 67 males (26.9% among males) and all females, finding different variants in 18 males and 42 Females. Classical FD mutation c.376 A -> G (p.S126G), previously reported, was found in 1 subject (0.3%); 4 unrelated subjects were found carriers of c.937 G -> T (p.D313Y) variant, previ-ously associated with enzyme pseudo-deficiency; other 55 subjects showed vari-ants located in promoter and/or intronic regions. From these subjects, 15 patients showed a Complex Haplotype (CH) type I (-10 c.<A), 26 patients showed a CH II (-13 c.<A, c.548-125 C>G, c.639+66 A>G, c.1000-22 C>T), 17 patients showed a CH II (-136.71_77 del5, c.640-16 A>G, c.1000-22 C>T), 15 patients showed a CH III (-12 c.<A, -548-125 C>G, c.639+66 A>G, c.1000-22 C>T) and one patient showed a combined CH II and III. In addition, we have identified 2 novel variants c.34-1 C->T (p.Glu14->A) and c.640-25 A->G whose significance in FD pathophysiology remains unknown.

Conclusions: Only one subject (0.3%) showed a classical missense mutation in FD, however 48 subjects (13.3%) showed several complex haplotypes (CH) previously associated or described in individuals with FD symptoms. Further studies are needed to link these CH that might participate in the presentations of FD.


Background: Biomarker activation during stress cardiomyopathy is still not well known.

Carbohydrate-antigen (CA)-125, however, was studied as risk marker in subjects with chronic and acute heart failure. We therefore aimed to evaluate possible role of CA-125 in risk stratification and its possible correlations with other clinical characteristics in subject with stress cardiomyopathy.

Methods: Thirty-nine consecutive subjects (14 males, 25 females, 16±7.8 years, 1.376±1.77 del5, c.640±16 A>G, c.1000-22 C>T), 17 patients showed a CH II (c.376-1_77 del5, c.640-16 A>G, c.1000-22 C>T); 15 patients showed a CH III (-12 c.<A, -548-125 C>G, c.639+66 A>G, c.1000-22 C>T) and one patient showed a combined CH II and III. In addition, we have identified 2 novel variants c.34-1 C->T (p.Glu14->A) and c.640-25 A->G whose significance in FD pathophysiology remains unknown.

Conclusions: Only one subject (0.3%) showed a classical missense mutation in FD, however 48 subjects (13.3%) showed several complex haplotypes (CH) previously associated or described in individuals with FD symptoms. Further studies are needed to link these CH that might participate in the presentations of FD.

P6186 | BEDSIDE T-cell receptor Vbeta dominance indicates antigen specificity of infiltrates in myocarditis and dilated or inflammatory cardiomyopathy M. Noutsios1, C. Konstanta1, R. Pistilli1, H.R. Figulla2, V. Patitii2. 1 University Hospital Jena, Department of Internal Medicine I, Jena, Germany; 2 Genetics, Faculty of Biology, Philippus-Universitat Marburg, Marburg, Germany.

Introduction: Antiviral and autoimmune pathomechanisms contribute to the pathogenic link between myocarditis (MC) and DCM. Increased T-cell infiltrates, a key diagnostic criterion for inflammatory cardiomyopathy (DCMI), are detectable in a substantial fraction of patients presenting with dilated cardiomyopathy (DCM). T-cell responses targeting specific antigens can lead to a restriction of the T-cell receptor Vbeta (TCR Vb) repertoire. The former TCR Vb nomenclature has been updated by the TCR classification (ImMunoGeneTics). Diverse TCR Vbeta and TRBV dominant genes have been associated with several viral and autoimmune diseases.

Aims: Systematic evaluation of publications on TCR Vbeta / TRBV dominance in experimental and human MC / DCM / DCMI.

Results: Dominants of TCR Vb10, Vb8 and Vb13 were identified in Coxackievirus B (CVB) induced murine MC. Dominant TCR Vb4 infiltrates were eulicidated in experimental autoimmune MC in rats. CD3breptotyping revealed dominance of TCR Vb3, Vb7, Vb13.1 Vb1 and Vb5b in human DCM. This finding was associated with CVB infection (detected by immunohistology). In Chagas cardiomyopathy, abundance of TCR Vb 4, Vb 5, Vb 11, Vb 13, Vb 17 and Vb 20 have been analyzed. Significant associations between the immunohistologi-cal proof of DCMI and the expression of the constant TRB region (TRBC) and of CD3d have been established using a preamplified real-time RT-PCR for TRBC and TRBV gene expression. DCMI, however, was not characterized by a particu-lar TRBV dominance per se. In contrast, differential TRBV dominances were associated with the PCR proof of viral genomes in human DCMI: TRBV11 and TRBV14 with Parovirus B19 (B19V); TRBV4, TRBV10 and TRBV28 with human Herpes virus type 6 (HHV6); and TRBV14 with Entovirus. In a patient present-ing with acute myocarditis and B19V viremia, TRBV11 dominance was detected in the peripheral blood leucocytes.

Conclusions: Restrictions of TCR Vbeta repertoire of the T-cell infiltrates are present both in experimental CVB induced myocarditis and in autoimmune AMCs in rodents. CD3breptotyping permits detection of differential TRB Vb dominances in CVB and in Chagas induced human DCM. Increased TRBC expression is associated with the immunohistological criteria of DCMI. Furthermore, the detectability of diverse viral genomes by PCR is associated with differential TRBV dominances in human DCM. These data confirm the hypothesis that distinct antigens may induce and maintain the intramyocardial T-cell infiltrates both in experimental and in human MC and DCMI. These insights might be relevant for immunomodulatory treatment strategies targeting the T-cell response in MC and DCMI.
Surgical correction of HOCM in patients with severe hypertrophy and myocardial fibrosis

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**Background:** In patients with hypertrophic cardiomyopathy myocardial fibrosis is an independent predictor of adverse outcome. A new technique of HOCM surgical correction in patients with extreme hypertrophy and septal myocardial fibrosis has been proposed.

**Methods:** The excision of the asymmetrical hypertrophied area of the interventricular septum (IVS) causing obstruction was performed from the conal part of the right ventricle corresponding to the zone obstruction of the left ventricle (LV). This excision was carried out on the right side of the IVS and not trough the whole IVS thickness. The areas of septal myocardial fibrosis were removed corresponding to the zone of delayed enhancement (DE) imaging. Myocardial fibrosis was detected by cardiovascular magnetic resonance with DE imaging. Nine HOCM patients with extreme hypertrophy (NYHA Class 3.1), myocardial fibrosis and episodes of ventricular tachycardia (VT) underwent this procedure. Five patients had biventricular obstruction. The follow-up period was 39.9 months.

**Results:** Seven patients were free of symptoms (NYHA class 1) and two patients had only mild limitations. The mean echocardiographic gradient in LV decreased 43.4±5.2 to 4.3±1.3 mmHg. Echocardiographically determined septal thickness was reduced from 34.7±3.1 to 15.6±2.1 mm. Sinus rhythm without block of His bundle right branch was noted in all patients after surgery. VPCs were not registered. None of the patients needed implantation of a cardioverter-defibrillator.

**Conclusion:** This novel technique of HOCM surgical correction provides the precise removal of the areas of septal fibrosis and effective elimination of biventricular obstruction in patients with extreme hypertrophy who can not be treated with current surgical techniques. The approach avoids mechanical damage to the heart conduction system.

Prevalence and treatment of chromosomally integrated human herpesvirus 6 in patients with symptomatic heart failure


**Objective:** Investigation of prevalence, germline transmission and reactivation of HHV-6 in patients with persisting unexplained heart failure. Human herpesvirus 6 (HHV-6) A and B are two betaherpesviruses that are associated with many conditions including roseola, drug induced hypersensitivity syndrome, liver failure and myopathy.

**Methods:** We determined the prevalence of HHV-6 and ciHHV-6 genotypes in 1656 endomyocardial biopsies of patients with persisting unexplained heart failure. Inclusion criteria were: other reasons (arrhythmia, infections) for heart failure were excluded. HHV-6 DNA was detected by PCR in 273 of 1656 tissue samples (16.5%). HHV-6B (98.2%; HHV-6A: 1.8%) was identified by PCR. Nineteen of the 1656 patients (1.1%) presented HHV-6 infection. HHV-6 DNA was detected in 273 of 1656 cardiac tissues (16.5%, HHV-6B: 98.2%, HHV-6A: 1.8%) by PCR. Nineteen of the 1656 patients (1.1%) presented with persisting high HHV-6 copy numbers indicative of ciHHV-6. Sequencing confirmed ciHHV-6A in 7 patients (36.8%) which was considerably higher than detected in non-ciHHV-6 patients or described for normal populations. Inheritance was demonstrated in 3 selected families confirming ciHHV-6A chromosomal integration by PCR and by FISH. HHV-6 reactivation and chromosomal integration were confirmed in PBMCs and heart tissue. Virus particles were identified in degenerating myocytes and interstitial cells. Antiviral treatment abolished viral mRNA and ameliorated cardiac symptoms.

**Conclusion:** Virus replication in cardiac tissue of ciHHV-6 heart failure patients suggests that ciHHV-6 reactivation causes persistence of unexplained heart failure symptoms. We demonstrated that antiviral treatment, effective in decreasing viral transcripts and clinical complaints of cardiomyopathies, is a new therapeutic option for ciHHV-6 associated diseases.

Diagnostic value of multiplex ligation-dependent probe amplification of plakophilin-2 in arrhythmogenic cardiomyopathy

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**Background:** Arrhythmogenic Cardiomyopathy (ACM) is an autosomal dominant disease characterized by progressive fibro-fatty infiltration and high frequency of ventricular arrhythmias that can lead to sudden death. It is mainly caused by mutation in genes encoding desmosomal components, involved in only ~50% of patients.

**Aim:** The present study aimed to determine the frequency and prevalence of desmosomal genes mutations in a small cohort and to investigate whether copy number variations (CNVs) detection may increase the diagnostic yield of genetic screening in ACM.

**Methods:** 60 ACM consecutive patients underwent direct sequencing on a ABI-PRISM 3730 for 5 ACM-associated genes. Multiplex Ligation-dependent Probe Amplification by SALSA MLPA P168 ARVC-PK2 kit and quantitative Real-Time PCR (qPCR) on a LightCycler 480 were performed on genotype-negative probands in search of CNVs in Plakophilin-2 (PKP2).

**Results:** This comprehensive screening revealed pathogenic point mutations in 36 index patients (60%) distributed as follows: 5 mutations in Desmoglein-2 (DG2), 12 mutations in Plakophilin-2 (PKP2) (12%), 2 in Desmocollin-2 (3%), 2 in Plakoglobin (3%), 6 cases (10%) with multiple mutations, and 1 heterozygous large PKP2 exon deletion in 1 otherwise genotype-negative patient (2%). This new deletion was detected by MLPA technique and then confirmed by relative qPCR.

**Conclusions:** Screening analysis of ACM-related genes in 60 ACM index cases displayed approximately 60% of mutation carriers by conventional screening and another 2% by MLPA analysis, highlighting the potential of this CNVs analysis in increasing the diagnostic yield up to 10%.

Heart rate turbulence analysis as a markers of risk myocardium remodeling, electrical instability and sudden cardiac death in children with hypertrophic cardiomyopathy

I.V. Leonteva, V.A. Makarova. Moscow Institute for Paediatrics and Pediatric Surgery, Moscow, Russian Federation

**Purpose:** To evaluate the heart rate turbulence parameters in children with hypertrophic cardiomyopathy (HCM).

**Methods:** We examined 53 children with HCM (40 boys and 13 girls, mean age 13.7±7.7 years). Cardiac examination included standard electrocardiogram (ESG), Doppler echocardiography, 24-hour ESM monitoring. HRT parameters: turbulence onset (TO) - and turbulence slope (TS) were analyzed, if the number of ventricular premature complexes (VPC) was >5 and 2400 recording. Patients (pts) with atrial fibrillation or pacemaker rhythm or absence of VPCs were excluded. HRT was considered abnormal when TO ≥50 or TS ≤2.5 ms/RR interval.

**Results:** According to modern criteria HRT analysis was possible to make in 24 of 53 (45%) patients (pts) with HCM. The average values of TO were 2.47±0.94% (range from -8.45 to 8.15). Pathological values of TO - 0% (range from 0.84 to 8.5) were detected in 5 from 24 patients (20.8%). In all patients with abnormal values of TO were observed one or more major risk factors of sudden cardiac death: unexplained syncope (3pts), severe left ventricular hypertrophy (more than 30 mm) (4pts), non-sustained ventricular tachycardia (4pts), family history of sudden cardiac death (1pts). We obtained the relationship between pathological values of TO and non-sustained ventricular tachycardia (p=0.0076), and syncope (p = 0.05).

The average value of TS was 16.87±2.4 ms/RR (range from 3.8 to 42.3). TS value <2.5 was not revealed in all patients. The value TS ≤ -2 was observed in 3 cases of TO >0%.

**Conclusions:** Pathological values of THR (TO) revealed in 5 from 24 children with HCM. Abnormal parameters of TO were associated with non-sustained ventricular tachycardia and syncope. Electrical instability of myocardium according to TPT in the combination with other risk factors of sudden cardiac death may be a new indication for implantation of a cardioverter - defibrillator in children with HCM.

Various clinical features and echocardiographic profile of cardiomyomyxomas

M.T. Rahman, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

**Background:** Cardiac myxoma is a benign neoplasm that represents the most common primary tumour of the heart. Although the left atrium is the most commonly involved site of origin in 75% of cases, it can arise from any of the cardiac chambers.

**Aim:** To see clinical and echocardiographic profile of 72 cardiac myxomas.

**Methods:** 72 cardiac myxomas in 62 patients who admitted in National Institute of Cardiovascular Diseases from August 2003 to December, 2012 were studied clinically and by echocardiography.

**Results:** There were 18 males and 54 females, ages ranged from 17 to 76 years. The commonest symptom was dyspnoea (85%), followed by constitutional symptoms (42.4%), embolization (22.9%), palpitation (22.9%), syncope (13.2%), pedal oedema (18.6%) and chest discomfort (67.4%). The mean duration of symptoms displayed approximately 60% of mutation carriers by conventional screening and another 2% by MLPA analysis, highlighting the potential of this CNVs analysis in increasing the diagnostic yield up to 10%.

PERICARDIAL AND MYOCARDIAL DISEASE

Clinical features and echocardiographic profile of cardiac myxomas

M.T. Rahman, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

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myxomas except 5 were attached to the inter septal sheet. The site, size, shape, attachment, mobility, prolapse into ven tricle, and surface characteristic of myxoma were accurately assessed by 2D-echocardiography. When the morphological characteristic of myxomas were studied and correlated with clinical features large left atrial myxoma size was closely related with constitutional symptoms, con genital atrial septal defect, and mitral valve disease, whereas smaller myxoma size and irregular surface were associated with embolization.

Conclusion: Majority of myxomas mimic many cardiovascular diseases and were described in hypertrophy, so a high index of clinical suspicion is important for its early and correct diagnosis. The size and appearance of myxomas correlated with the presenting symptoms.

**P6194 | BEDSIDE**

Clandestine subaortic stenosis as a cause of left ventricular outflow tract obstruction in patients with hypertrophic obstructive cardiomyopathy

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Introduction: Hypertrophic cardiomyopathy (HCM) has a prevalence of 1/500 in the basic noninvasive tools for subaortic membrane detection. Resection of the subaortic membrane with myectomy should include histology of resected myxoma. The basic noninvasive tools for subaortic membrane detection. Resection of the subaortic membrane with myectomy should include histology of resected myxoma. The basic noninvasive tools for subaortic membrane detection. Resection of the subaortic membrane with myectomy should include histology of resected myxoma.

**Results:** 24 (14%) patients with non-obstructive HCM (mean septal thickness 20±6 mm, left atrial diameter 48±11 mm) while 138 (84%) pts had HOCM (mean septal thickness 21±4 mm, left atrial diameter 47±16 mm). L VOT gradient was 57±38 mmHg at rest and 100±46 mmHg with Valsalva. In 3 (2%) pts, a subaortic membrane, suspected with transthoracic and ascertained with transesophageal echocardiography, was the cause of LVOT obstruction. In those pts (mean septal thickness 25±12 mm, left atrium diameter 39±1 mm) L VOT gradient was 63±22 mmHg at rest and 83±18 mmHg with Valsalva, while pt had an IDC for primary prevention of sudden death. In this last pt subaortic membrane coincided with HOCM (histological proof of extensive disarray in the myometrium specimen).

Conclusions: Subaortic membrane is an important differential diagnosis of hypertrophic obstructive cardiomyopathy. Transthoracic and transesophageal echocardiography (including colour, CW and PW Doppler with focus on L VOT) are the basic noninvasive tools for subaortic membrane detection. Resection of the subaortic membrane with myectomy should include histology of resected myxoma, as diagnosis of coexistent HCM may have implications on risk stratification for sudden cardiac death.

**P6195 | BEDSIDE**

Left ventricular function in treatment-naive early rheumatoid arthritis

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Background: The role of inflammation in the pathogenesis of cardiovascular disease in rheumatoid arthritis (RA) remains unclear.

Objective: We investigated how disease activity, anti-cyclic citrullinated peptide antibodies (anti-CCP) status and coronary calcium score in treatment-naive early RA, impacts left ventricular (LV) systolic function.

Methods: Fifty-three patients with mean age 58±1.3 years and steroid- and disease-modifying antirheumatic drug (DMARD)-naive early RA were included. Disease activity was scored by the use of the Danish national DANBIO registry (number of swollen joints (NSJ (28)), number of tender joints (NTJ (28)), C-reactive protein (CRP) and Health Assessment Questionnaire (HAQ)). Pain, fatigue, physical and physician global assessment and a composite disease activity score (DAS28-CRP) were assessed by visual analog scales (VAS) 0–100. IgM rheuma factor (IgM-RF) and anti-CCP titer were evaluated by standardized techniques. Coronary calcium score was estimated by computed tomography (CT) by a single experienced cardiologist performed all the clinical assessments as well as all the transthoracic echocardiography (TTE) and coronary CT analysis.

Results: We found LV systolic function by conventional ejection fraction to be 54.1±9.2% and to be strongly correlated to disease activity (CRP: r=0.07, p=0.64; baseline NSJ: r=0.13, p=0.33; NTJ: r=0.08, p=0.58; HAQ: r=0.23, p<0.1; pain VAS: r=0.05, p=0.74; fatigue VAS: r=0.03, p=0.83; physician global assessment: r=0.09, p=0.54 and DAS28: r=0.03, p=0.84).

Univariate logistic regression (GLS) and sensitivity measurement of the LV function we found a significant correlation: HAQ (r=0.29, p=0.037), patient global assessment by VAS (r=0.35, p=0.011), patient fatigue assessment by VAS (r=0.3, p=0.03) and DAS28-CRP (r=0.28, p=0.043); all corrected for relevant confounders. Furthermore, anti-CCP was highly significantly correlated with GLS (r=−0.44; p=0.001) in univariate analysis. In multivariate analysis, it still remained significantly correlated (p=0.018), after correction for relevant founders.

Conclusion: We observed a significant correlation between increased disease activity and cardiac function in treatment-naive early RA without ischemic heart disease.

**P6196 | BEDSIDE**

Relationship between left ventricular mass index and cardiac toxicity from anticancer agents

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Purpose: Administration of cardiotoxic anticancer agents results in a significant increase in left ventricular mass (LVM), and the rate of change (%LVM) correlates with the total amount of anticancer agent (cyclophosphamide, epirubicin, and fluorouracil) (5-FU) PER LVM (5-LVM). This study investigated the relationship between left lower and higher LVM index (LVMi) patients.

Methods: We selected 276 consecutive breast cancer patients (all females; mean age, 52±9.7 years) who completed adjuvant chemotherapy with three drugs (CEF: cyclophosphamide, epirubicin, and fluorouracil) and performed both before and after several cycles of CEF, and the following parameters: absolute value of LVMi (LVM), absolute value of LVMi (LVMi), and absolute value of LVMi (LVMi). We observed a significant correlation between increased disease activity and cardiac function in treatment-naive early RA without ischemic heart disease.

Methods: We studied retrospectively 57 patients submitted to radical pericardectomy for constrictive pericarditis (CP). The aim of this study was to assess the utility of plasma BNP as a mortality risk predictor in CP patients submitted to pericardiectomy.

We observed a significant correlation between increased disease activity and cardiac function in treatment-naive early RA without ischemic heart disease.

Purpose: Brain natriuretic peptide (BNP) levels are usually low despite severe signs and symptoms of heart failure in constrictive pericarditis (CP). Many clinical and demographic data are well known as risk predictors of mortality after pericardiectomy for CP. Nevertheless, the role of BNP on this setting is not clear.

The aim of this study was to assess the utility of plasma BNP as a mortality risk predictor in CP patients submitted to pericardiectomy.

Methods: We studied retrospectively 57 patients submitted to radical pericardiectomy for CP between January 2002 and November 2013 in a tertiary hospital. All patients had blood tests for brain natriuretic peptide at admission. Clinical and sur- gical history, and cardiac catheterization data were collected from the patient’s medical records. All patients were followed- up by medical records or phone contact. Receiver operating characteristic (ROC) analyses was performed to identify the best BNP value in discriminating mortality.

Results: Mean age was 40.8±18 years with predominance of men (77.6%). CP etiology was: idiopathic (70.7%), tuberculosis (17.2%), post cardiac surgery (5.2%), systemic inflammatory disease (5.2%) and mediastinal radiotherapy (1.7%). There were 6 deaths in the first ninety days after surgery, 5 due to cardiac failure with a cardiac mortality of 9.2%.

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Pericardial and myocardial disease

P6198 | BEDSIDE
Cardiac involvement of systemic lupus erythematosus: echocardiographic findings of 75 cases

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Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by inflammation of multiple organs. The heart may be seriously involved.

Methods: We retrospectively reviewed the records of 75 patients with diagnosis of SLE based on the American College of Rheumatology criteria and who were referred to our echocardiography laboratory between 1993 and 2012. All echocardiographic exams were carried by transthoracic way.

Results: 16 cases were comprised of outside referrals specifically for Oncologic consultation. This search strategy identified 33 cases, including 17 patients (mean age 46; 6 males never suffered from heart failure and their systolic function was normal. Caesarean section was carried out because of breech presentation. These 4 females deliveries after LVHT had been diagnosed. Delivery was vaginal in 3, in the fourth, cesarean section was carried out because of breech presentation. These 4 female

P6199 | BEDSIDE
Echocardiographic features of cardiac angiosarcomas: Mayo Clinic experience

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Introduction: Cardiac angiosarcoma, though exceedingly rare, is the most common primary malignant cardiac tumor. The dismal prognosis and non-specific symptomatology underscores the need for an accurate and cost effective approach to the identification and characterization of these rare tumors.

Methods: We searched our clinic tissue registry for all histologically confirmed cases of cardiac angiosarcoma from January 1976 to December 2013. We searched our clinic tissue registry for all histologically confirmed cases of cardiac angiosarcoma from January 1976 to December 2013.

Results: Patients with SLE have an increased risk of cardiac involvement. In agreement with previous reports, our study shows that pericardial effusion is the most frequent cardiac complication of lupus. Valvular involvement is relatively frequent but the degree of valvular dysfunction is generally not important. Early diastolic left ventricular dysfunction threaten seriously these patients. Echocardiography should be used as a screening tool, including annual echocardiographic screening of asymptomatic individuals with SLE

P6200 | BEDSIDE
Emery dellfuss-6 with peculiar x linked cardiomyopathy

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Introduction: Emery dellfuss-6 is an X-linked muscular dystrophy (EMD) variant. We aim to describe a family with type EMD and severe cardiac phenotype.

Methods: Complete anamnesis and physical exam, blood tests, chest and spine X-ray, echo, echocardiogram, neurologic, pulmonary and clinical genetics evaluation were obtained.

Results: 14/28 (50%) subjects (3males/12females) were carriers of a FH1 p.Cys255Ser mutation (c.135292105G>A) (penetrance: 100% males; 29% females). Moderate (16-18mm max wall thickness) non-obstructive asymmetric hypertrophy with severe diastolic dysfunction and early severe systolic dysfunction was identified in all males and 1 (8%) female. Males had persistent CVP elevation (average: 304 UI/L). Early atrial flutter-fibrillation was identified in 100% of males and remarkable prolongation of the QT interval in 1 female. 1 male died suddenly aged 45yrs and 1 female died aged 45yrs after long-course cardiac disease. 1 male (proband) had resuscitated cardiac arrest (VF) aged 32yrs. Cardiac transplant was performed in 2 males aged 51 and 52yrs. Examination of the explanted heart diagnosed mixed cardiomyopathy with Arythrogenic Dysplasia and Left Ventricle non Compaction.

Conclusions: We present a family with a FH1 mutation causing EMD-6 and X linked severe cardiac phenotype characterized by moderate hypertrophy, restrictive physiology with progression to severe heart failure and transplant. Despite echocardiogram, pathology reveals fibrotrophy replacement of the myocardium and non-compaction.

P6201 | BEDSIDE
Left ventricular hypertrabeculation/noncompaction and pregnancy

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Background: Left ventricular hypertrabeculation/noncompaction (LVHT) is characterized by extensive trabeculations and a two-layered structure of the left ventricular myocardium. Aim of the study was to summarize outcomes of pregnancies in a LVHT cohort.

Methods: All females in whom LVHT was diagnosed in one echocardiographic laboratory when they were younger than 45yrs were contacted in July 2013. It was asked if pregnancy or delivery occurred after the diagnosis of LVHT had been established.

Results: From 1995-2013 LVHT was diagnosed in 207 patients. In 22 of the 63 female patients LVHT had been diagnosed when they were younger than 45yrs. In July 2013, 4 of the 21 surviving females reported uneventful pregnancies and deliveries after LVHT had been diagnosed. Delivery was vaginal in 3, in the fourth, cesarean section was carried out because of breech presentation. These 4 females never suffered from heart failure and their systolic function was normal. Clinical and echocardiographic findings did not differ between the females who did and did not become pregnant.

Conclusions: LVHT per se is no contraindication for pregnancy. If LVHT is diagnosed in females of childbearing age, cardiac risk associated with pregnancy can be estimated by scores considering previous cardiac events or arrhythmia, NYHA class of heart failure, presence of left heart obstruction and left ventricular ejection fraction. Since the data about pregnancy and LVHT are still rare, patients should be encouraged for cardiac follow-up and their data, including neurological findings, should be collected in registries.
Pericardial and pericardial disease

Objectives: To know the characteristics, natural history and prognostic implications of malignant pericardial effusions (MPE).

Methods: Patients with MPE were included from January 2010 to December 2013.

Results: 55 patients were analyzed (mean age 59 years, SD: 17.51% male) with a mean follow up of 7 months (SD: 8). The PE was the neoplasia’s first manifestation in 20%. Dyspnea was the most common symptom (33%). 51% required PE drainage, due to clinical (n=17) or echocardiographic (n=8) tamponade. 70% of the patients died, 3 of them due to cardiac tamponade and the rest as a consequence of disease progression. The mean time since diagnosis of MPE to death was 5 months (SD: 6). Only the type of tumor and the severity of PE were associated with higher mortality (p<0.05). 82% of patients received treatment for their underlying malignancy, which increased survival time (8 months vs 2 months, p<0.001).

Mortality and survival time

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Follow up (days)</th>
<th>Mortality</th>
<th>Survival (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung (n=22)</td>
<td>142 (2-927)*</td>
<td>20 (91%)</td>
<td>142 (SD: 119)</td>
</tr>
<tr>
<td>Breast (n=7)</td>
<td>148 (103-842)*</td>
<td>4 (57%)</td>
<td>129 (109-584)*</td>
</tr>
<tr>
<td>Leukemia (n=4)</td>
<td>103 (SD: 73)</td>
<td>3 (75%)</td>
<td>71 (SD: 41)</td>
</tr>
<tr>
<td>Lymphoma (n=7)</td>
<td>254 (SD: 167)</td>
<td>2 (29%)</td>
<td>264 (SD: 360)</td>
</tr>
</tbody>
</table>

(n = no. of patients. *Median if data do not meet criteria for normality.

Mortality of MPE is determined by the primary cancer and the severity of PE. Treatment of the underlying malignancy influences in survival time.

Conclusions: Mortality of MPE is determined by the primary cancer and the magnitude of the PE. Treatment of the underlying malignancy influences in survival time.

MYOCARDIAL AND PERICARDIAL DISEASE

P6204 | BEDSIDE

Pericarditis and myopericarditis/perimyocarditis: different prognosis?

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Introduction: Acute pericarditis (AP) and myopericarditis/perimyocarditis (MPPM) are inflammatory diseases of the heart whose natural history and prognosis are still poorly understood. The aim of the present study was to compare the prognosis of these two entities.

Methods: We retrospectively analyzed the clinical files of all patients admitted with AP and MPPM between January 2008 and December 2012. The diagnosis of AP was based on the presence of at least two of the following criteria: typical chest pain, pericardial rub, widespread ST-segment elevation or PR depression, and new or worsening pericardial effusion. MPPM was considered in the cases of suspected pericardial disease associated with elevated troponin levels, with or without left ventricular systolic function or wall motion abnormalities.

Results: Fifty nine patients were included, 27 with AP and 32 with MPPM. The groups had equal sex distribution and the median age was significantly superior in the AP population (54 Vs 41 years; p<0.039). During hospitalization heart failure and higher levels of pro-BNP were more frequent in the MPPM patients, although without statistical significance. There were 3 cases of supraventricular tachycardia in the AP group and 1 in the MPPM, 1 case of sinus bradycardia and 1 atrioventricular blockage in both populations. The median peak troponin T level was 0.98 mg/mL (minimum 0.127; maximum 7.48) in the MPPM population.

In this group, 7 patients (21.7%) presented left ventricular systolic dysfunction on echocardiogram which normalized/improved in a mean follow-up of 9 months (median initial ejection fraction 44%; final 58%). None of these cases had left ventricle dilatation. In a mean follow-up of 22 months heart failure diagnosis was made in 1 patient in each group. Recurrence was more common in the AP population (n=4; 14.8% Vs n=1) although without statistical significance. One patient with MPPM died during hospitalization and one patient admitted with AP died 10 months after the hospitalization due to a non-cardiovascular cause.

Conclusions: In our study MPPM and AP groups had similar outcomes. Elevated levels of troponin and reduced left ventricular function weren’t, in our patients, linked to a worse prognosis.

P6205 | SPOTLIGHT

Tuberculous pericarditis is associated with impaired left and right ventricular myocardial mechanics measured by 2D-Speckle tracking echocardiography

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Background: Tuberculosis (TB) is a serious problem in developing countries, which account for 95% of worldwide TB cases, and 99% of worldwide TB mortality. TB has not been on the list as one of the leading causes of left ventricular systolic dysfunction and two-dimensional speckle tracking echocardiography (2D-STE) imaging has not been used routinely to assess ventricular function in tuberculosis pericarditis. The main of this study was to use 2D-STE to evaluate both the left (LV) and right (RV) ventricular systolic function.

Methods: A total of eighty two patients with the diagnosis of tuberculosis pericarditis, and suitable standard two-dimensional echocardiographic images were included in the study. Mean age of 33years (56% males). Their retrospective images were analyzed offline using velocity-vector imaging technology. Student t-test, Pearson correlation coefficient (r) was used to describe the relationship between echocardiographic and strain parameters. Multivariate linear regression analysis was used to investigate the association global circumferential and radial strain with the patients’ symptoms and mortality.

Results: TB pericarditis is associated with significantly impaired LV strain both longitudinal and circumferential (p<0.001). Right ventricular free wall strain was also reduced in 40% of the patients. There was a strong negative correlation between LV systolic strain with LV ejection fraction (LVEF) based on the 2D-echocardiograph. There was a strong LV-RV and LV-Septal wall strain interaction (p<0.001). There was also no strong correlation between patients’ symptoms and the severity of LV strain impairment. The presents of concomitant human de-ficiency viral (HIV) infection pre-existing toxic exposure was also associated with more severe LV strain impairment. After adjusting for patients’ age, gender and body mass index LV systolic strain was predictive of poor LV function acutely.

Conclusion: Tuberculosis pericarditis is associated with both LV and RV strain impairment and the concomitant HIV status does play a role with the severity of LV dysfunction.

P6206 | BENCH

Myocardial performance index for detection of subclinical abnormalities in patients with sarcoidosis

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Aim: The aim of this study was to evaluate ventricular function in patients with sarcoidosis without an obvious heart disease by using tissue Doppler-derived left and right ventricular myocardial performance index (MPI).

Methods: The study population included 45 patient with sarcoidosis (29 men, 16 women; mean age, 44±10 years, mean disease duration, 4.2±2.7 years) and 45 healthy control subjects (31 men, 14 women; mean age, 41±8 years). Cardiac functions were determined using echocardiography, consisting of standard two-dimensional (2-D) and conventional Doppler tissue (TD) imaging and right ventricular MPI were impaired in sarcoidosis patients, although systolic function was significantly higher in patients with sarcoidosis than the control subjects. There was a correlation between the disease duration and right and left ventricular MPI (r=0.418, p=0.005; r=0.366, p=0.013, respectively) (Fig. 1). There was also a correlation between the systolic and diastolic function parameters and tissue Doppler measurements were similar between the patients and controls. Left ventricular MPI (0.490±0.092 vs. 0.396±0.088, p=0.010) and right ventricular MPI (0.482±0.132 vs. 0.368±0.090, p=0.006) were significantly higher in patients with sarcoidosis than the control subjects. There was a correlation between the disease duration and right and left ventricular MPI (r=0.418, p=0.005; r=0.366, p=0.013, respectively) (Fig. 1).

Conclusions: Tissue Doppler-derived myocardial left and right ventricular MPI were impaired in sarcoidosis patients, although systolic and diastolic function parameters were comparable in the patients and controls. We also showed a correlation between the systolic pulmonary arterial pressure and right ventricular MPI in patients with sarcoidosis.
P6207 | BEDSIDE
The relation of echocardiographic epicardial adipose tissue thickness and the coronary artery disease
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Background: Several studies suggested that epicardial adipose tissue (EAT) may be associated with coronary artery disease (CAD). EAT thickness can be measured by echocardiography. A meta-analysis was performed to investigate the relationship between echocardiographic EAT thickness and the CAD.

Methods: A systemic search of PubMed, Cochrane and Medline from January 2003 to May 2013 was conducted for reports on echocardiographic EAT thickness in patients with and without the CAD using specific search terms such as “epicardial adipose tissue”, “epicardial fat”, “coronary artery disease”. Data were extracted from applicable articles and mean differences or risk ratio, including 95% confidence intervals (CI), were calculated using RevMan 5.2 software.

Results: Seven studies were identified. The pooled population consisted of 1,144 subjects, of whom 693 had the CAD. Comparing with the non-CAD group, EAT thickness was significantly higher in patients in the CAD group (mean difference 1.66 mm, 95% CI 1.45 to 1.87, P<0.0001).

Conclusion: Echocardiographic EAT thickness is significantly higher in patients with the CAD, and seems to be effective marker in the prediction of CAD.

P6208 | BEDSIDE
Impact of modified immunosuppression and neurohumoral blockade on prevention of ventricular remodeling and improved clinical outcome in patients with cardiac sarcoidosis

Background: Several studies suggested that epicardial adipose tissue (EAT) may be associated with coronary artery disease (CAD). EAT thickness can be measured by echocardiography. A meta-analysis was performed to investigate the relationship between echocardiographic EAT thickness and the CAD.

Methods: A systemic search of PubMed, Cochrane and Medline from January 2003 to May 2013 was conducted for reports on echocardiographic EAT thickness in patients with and without the CAD using specific search terms such as “epicardial adipose tissue”, “epicardial fat”, “coronary artery disease”. Data were extracted from applicable articles and mean differences or risk ratio, including 95% confidence intervals (CI), were calculated using RevMan 5.2 software.

Results: Seven studies were identified. The pooled population consisted of 1,144 subjects, of whom 693 had the CAD. Comparing with the non-CAD group, EAT thickness was significantly higher in patients in the CAD group (mean difference 1.66 mm, 95% CI 1.45 to 1.87, P<0.0001).

Conclusion: Echocardiographic EAT thickness is significantly higher in patients with the CAD, and seems to be effective marker in the prediction of CAD.

P6209 | BEDSIDE
Detection of myocardial injury by three-dimensional speckle tracking echocardiography in chronic hepatitis C infection
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Purpose: Although recent reports highlighted extra-hepatic manifestations of hepatitis C virus (HCV) in a variety of organs, right ventricular involvement is the most frequent cardiac alteration whereas a clear-cut left ventricular (LV) involvement has been never reported. Accordingly, the aim of the study was to evaluate LV geometry and function by standard 2D and 3D echocardiography in a series of patients with HCV.

Methods: Twenty-four consecutive asymptomatic patients with chronic HCV (mean age ± SD: 60.9±6.5 yr) and 20 normal controls (NC), comparable for age and gender prevalence, were compared by standard echo-Doppler, 2D Speckle Tracking Echocardiography (STE) and 3D (both volumetric and STE) echocardiography. Global longitudinal strain (GLS) was calculated by 2D STE whereas LV volumes and ejection fraction (EF), sphericity index, LV mass and 3D STE-derived GLS, global circumferential strain (GCS), global area strain (GAS) and global radial strain (GRS) were also measured. Diagnosis of chronic hepatitis was based on liver biopsy or hepatic fibroScan. Cardiac images were acquired before the beginning of any kind of specific hepatic therapy. Coronary artery and valvular heart disease, heart failure, cardiomyopathies, atrial fibrillation, alcohol abuse, other causes of liver disease were exclusion criteria.

Results: The 2 groups were comparable for body mass index, heart rate and blood pressure. By standard 2D echocardiography no difference of 2D-derived EF, relative wall thickness, LV mass, LV velocity deceleration time and E/e' ratio was found between HCV and NC. Only transmural E/A ratio was marginally lower in HCV (0.84±0.2) than in NC (1.01±0.3) (p=0.04). The intergroup difference of 2D derived GLS and of 3D volumetric analysis (LV volumes, EF, sphericity index, LV mass) did not achieve the statistical difference. 3D STE showed lower GCS (HCV−15.3±2.2% vs NC−17.6±1.3% (p=0.02), GAS (25.5±2.6% vs 29.9±5.2% (p=0.03) and GRS (37.6±4.6% vs 44.9±12.2% (p=0.04) whereas HCV-related changes of GLS were not significant.

Conclusion: Our findings support the hypothesis that 3D STE is able to detect subclinical alteration of LV myocardial dysfunction which cannot be diagnosed by both standard echo and 2D STE-derived GLS. Alteration involves circumferential fibers of midwall (GCS) and the composite deformation component represented by GAS whereas the longitudinal fibers of the subendocardial layer of myocardium appears to be preserved.

P6210 | BENCH
The critical role of autophagy on cardiomyocyte death during longterm high-fat diet stimulation
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Autophagy is an important process in the pathogenesis of cardiovascular diseases, and high-fat diet (HFD)-induced obesity plays a causative role in the induction of cardiomyocyte autophagy. The aims of this study were to elucidate the role of autophagy on the HFD-induced apoptosis of cardiac cells.

Methods and results: C57B/6J male mice (5 wk old) fed with the HFD for 24 wks induced obesity, hyperglycemia, and dyslipidemia. Chronically feeding the HFD caused heart hypertrophy and increased the protein expression of LC3II, caspase 12, and PARP in the heart. In the in vitro cell model we further conducted to explore the role of autophagy on the HFD-induced cardiomyocyte death. Palmitate treatment (400 μM) for 24 hrs induced apoptosis in H9C2 cells, with increased expression of the autophagy markers LC3II and p62. An increase in the accumulative levels of autophagic vacuoles was observed in H9C2 cells exposed to palmitate. Palmitate decreased the expression of unfolded protein response (UPR) marker CHOP and GRP94, while increased the expression of endoplasmic reticulum (ER) stress-induced apoptosis marker caspase 12. Blocking this autophagic response with 3-methyladenine resulted in a significant increase in cell death and apoptosis of palmitate-treated H9C2 cells, with a further decreased expression of CHOP and GRP94. To summarize, the response of autophagy plays a critical role in HFD-induced apoptosis. Autophagy is essential for cardiomyocyte survival when exposed to the HFD; however, excessive autophagy damaged the cellular functions and caused the apoptosis of cardiac cells. In addition, there is a crosstalk between autophagy and ER stress when exposing to the HFD, and this underlying mechanism needs further study.

P6211 | BEDSIDE
Comprehensive echocardiographic and BNP monitoring of patients with chronic Chagas disease
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Purpose: The number of patients with Chagas disease residing in Europe has increased significantly. Early detection of myocardial involvement in these patients is crucial due to prognostic implications. Our aim was to evaluate changes in echocardiographic parameters, including diastolic function and 2D myocardial strain and BNP levels in the follow-up of patients with chronic Chagas disease.

Methods: 20 subjects (40±13 years, 67% women) from endemic areas of Chagas disease (8 in the undetermined form of Chagas disease, 8 with chagasic cardiomyopathy and 4 non-infected controls) were evaluated with echocardiographic parameters and autonomic function tests. Echocardiographic parameters and BNP quantification at baseline and 3.5 (range 2.6-4.6) years later. Echocardiographic analysis was performed, using EchoPac software, blinded to patients’ group and clinical or serologic results.
Results: There was a significant association between changes in circumferential and longitudinal myocardial strain, diastolic function and BNP levels (Fig. 1).

Conclusion: In the follow-up of patients with Chagas disease changes in myocardial strain correlates with changes in BNP and parameters of diastolic function. Those are complementary indices that may help to early detect myocardial involvement and to monitor mild left ventricular dysfunction in these patients.

P6212 | BEDSIDE Cardiovacular changes in patients with non-severe Plasmodium vivax malaria
A. Comte De Alencar Filho1, J.M. Barbosa Ferreira2, C. Fabbi3, W. Marcelo Monteiro4, K. Okoshi5, M.V. Guimarães De Lacerda6, M.P. Okoshi7,1, Amazonas Federal University, Manaus, Brazil;1 Amazonas State University (UEA), Manaus, Brazil;2 North University Center – Pharmacy School, Manaus, Brazil;3 Tropical Disease Center ‘Dr. Heitor Vieira Dourado’ - UEA, Manaus, Brazil;4 Medical School, UNESP, Botucatu, Brazil

Purpose: Cardiovascular system involvement in patients with Plasmodium vivax malaria has been poorly addressed. The aim of this study was to evaluate cardiac structures and function and serum markers of cardiovascular injury in patients with the non-severe form of Plasmodium vivax malaria.

Methods: We prospectively evaluated 26 patients with P. vivax malaria in an outpatient referral hospital from January 2012 to March 2013 and compared results with a control group of 25 gender- and age-matched healthy individuals. Patients underwent clinical evaluation, laboratory tests and transesophageal echocardiography at first evaluation after malaria diagnosis.

Results: Echocardiography showed higher left ventricular (LV) systolic diameter (8.8±2.82 vs 30.9±4.00 mm; p=0.03) and LV diastolic volume (82±12.3 vs 93.8±25.9 mL; p=0.05), and lower LV ejection fraction (Teicholz method: 73.2±6.59 vs 68.4±4.87; p=0.004) values in patients than controls. Right ventricle (RV) fractional area change (54.7±7.5.11 vs 50.5±6.71%; p=0.014) was lower, and RV myocardial performance index (0.21±0.71 vs 0.33±0.19; p=0.007), RV diastolic area (13.3±5.19 vs 15.3±9.66 cm²; p=0.008) and systolic area (6.41±1.27 vs 7.45±1.46 cm²; p=0.009), and pulmonary vascular resistance (1.13±0.25 vs 1.32±0.26 Woods unit; p=0.012) were higher in patients than controls. Patients presented higher serum levels of indirect bilirubin (0.24±0.15 vs 1.30±0.1 mL; p=0.001), soluble vascular cell adhesion molecule-1 (sVCAM-1: 453.1±143 vs 1983±880 ng/mL; p=0.001), N-terminal prohormone brain natriuretic peptide (0.59±0.86 vs 1.08±0.81 pg/mL; p=0.045), and troponin T (86.3±338 vs 1.037±264 pg/mL; p=0.045), and lower levels of nitric oxide (13.42±8.15 vs 5.98±5.97 uM; p=0.016) than controls.

Conclusion: Patients with non-severe Plasmodium vivax malaria present cardiac and endothelial functional alterations.

P6213 | BEDSIDE Parasympathetic incompetence detected by heart rate variability analysis in deceleration phase during head-up tilt table test in chronic Chagas disease
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Introduction: In chronic Chagas disease (CCD), autonomic function is compromised in both sympathetic and parasympathetic limbs. Phase-rectification of RR interval series allows separation of acceleration (AC) and deceleration (DC) phases, which reflects sympathetic and parasympathetic influence on heart rate, respectively. The aim of this study was to assess autonomic function using heart rate variability (HRV) driven by phase-rectification in healthy and CCD subjects.

Methods: RR interval series were analyzed using histogram distribution, split in 100ms-width classes, from 600ms to 1000ms. For each class, mean (MRR) and root-mean-squared difference (RMS) of consecutive normal RR intervals were calculated. Only pairs of consecutive RR intervals suitting a particular class were included. RMS was analyzed in the whole series (RMS-T), and in RR intervals pairs of AC (RMS-AC) and DC (RMS-DC) phases. Regression lines of RMS (T, AC, DC) vs. MRR were calculated, correlation coefficients tested, and angular coefficient compared between groups using Student t-test. RMS variables were log-transformed. (p<0.05)

Results: Correlation coefficient was significant for all regression lines (p<0.05). Mean RMS-AC showed significant difference between groups. In HG, RMS-T, RMS-AC and RMS-DC significantly increased proportionally to MRR (p<0.05). In HG, only RMS-AC showed significant increase as a function of MRR (Fig. 1).

P6214 | BEDSIDE Cardioversion of atrial fibrillation using dabigatran as thromboembolic prophylaxis
A.-K. Johansson1, T. Juhlin2, K. Hagwall3, J. Engdahl4, C. Rosmarin5, M. Ronquist1, M. Erick1, A. Danderyd University Hospital, Dept. of Cardiology, Stockholm, Sweden

Purpose: Cardioversion (DC cardioversion or pharmacological) of non-acute atrial fibrillation (AF) should be performed with preceding anticoagulation treatment, usually warfarin. An INR level between 2 and 3 during 3 to 4 weeks prior to cardioversion is usually requested. In practice, time to conversion is often delayed due to labile INR levels. With new oral anticoagulants (NOAC) the time to conversion can potentially be shortened. The safety of this strategy needs to be examined. Data from sub-group analysis from clinical trials with NOAC do not clarify whether 3 to 4 weeks’ treatment with NOAC is sufficient to prevent thromboembolism (TE) after cardioversion. The aim of this prospective study was to assess the incidence of TE in patients converted during treatment with Dabigatran (D).

Methods: We investigated the medical records of 436 patients from 4 hospitals where (D) had been used prior to cardioversion. TE within 30 days was the primary end point.

Results: 380 patients with persistent AF scheduled for DC cardioversion were included. The mean age was 64.6 years and 21.6% were women. The mean CHADS2VASC score was 1.8. 93.6% of patients had (D) 150 mg b.i.d. Time from initiation of (D) treatment to cardioversion was 33 days. In 93.6% cardioversion was performed in sinus rhythm. During 30 days of follow-up 1 TE (0.26%) occurred.

Conclusion: In this prospective study from a clinical material, not part of a clinical trial, we found a low incidence of TE when (D) was used as TE prophylaxis in association with cardioversion. These results indicate that 4 weeks of (D) treatment seems to be a safe alternative strategy to warfarin during cardioversion in patients with AF.

P6215 | BEDSIDE Cardioversion of atrial fibrillation using dabigatran as thromboembolic prophylaxis
A.-K. Johansson1, T. Juhlin2, K. Hagwall3, J. Engdahl4, C. Rosmarin5, M. Ronquist1, M. Erick1, A. Danderyd University Hospital, Dept. of Cardiology, Stockholm, Sweden

Purpose: Atrial fibrillation (AF) has been associated with cognitive impairment and we have recently shown that AF is associated with decreased brain volume independent of stroke in an elderly population. The causes may include multiple cerebral microemboli or hypoperfusion of the brain, but remain speculative. Previous data from our group have shown decreased cerebral blood flow in elderly patients with AF compared to those in sinus rhythm. The purpose of this study was to test the hypothesis that cerebral blood flow improves after direct current (DC) cardioversion for AF.

Methods: A prospective study involving patients undergoing elective DC cardioversion is ongoing at our institution. A magnetic resonance imaging (MRI) examination of the brain was performed immediately prior to DC cardioversion and repeated ten weeks later. Total cerebral blood flow was measured with phase contrast magnetic resonance imaging (PC-MRI) at the level of the skull base for direct flow measurements in the internal carotid arteries and basilar artery, providing the total sum of blood supply to the brain. In addition, we assessed brain perfusion...
with arterial spin labeling magnetic resonance imaging (ASL-MRI). ASL-MRI has the advantage over PC-MRI of measuring perfusion directly in the brain tissue capillary network.

**Results:** Currently 36 patients have been enrolled with a mean age of 64.3±7.5 years. Preliminary results for those patients who have undergone MRI, both before cardioversion and after successful cardioversion and remained in sinus rhythm, show that total cerebral blood flow measured with PC-MRI increased from 574±112 ml/min to 710±177 ml/min after CV. Total brain perfusion by ASL-MRI increased from 41±11 ml/100g/min to 46±10 ml/100g/min and total grey matter perfusion measured by ASL-MRI increased from 44±11 ml/100g/min to 50±11 ml/100g/min. Correlation between blood flow measurements with ASL-MRI and PC-MRI was 0.84, *p*<0.0001.

**Conclusions:** These preliminary data suggest that total cerebral blood flow and brain perfusion may improve after DC cardioversion for AF. Reduced cerebral blood flow and diminished perfusion may be an underlying mechanism in decreased brain volume seen in elderly individuals with AF and thus potentially play a causative role in the cognitive impairment seen in this arrhythmia. Further studies are needed to investigate this possible relationship.

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**P6217 | BEDSIDE**

**Utility of HAS-BLED score in evaluating the risk of major bleeding and death in patients with non-valvular atrial fibrillation undergoing direct-current cardioversion**

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1 General University Hospital of Alicante, Arrhythmia Unit, Cardiology Department, Alicante, Spain; 2 Hospital Clínico Universitario Virgen de la Arrixaca, Cardiology, Murcia, Spain; 3 University Hospital Morales Meseguer, Haematology, Murcia, Spain; 4 General University Hospital of Alicante, Cardiology, Alicante, Spain; 5 Birmingham City Hospital, Birmingham, United Kingdom

**Background:** The HAS-BLED score is well validated to predict the risk of major bleeding in patients with non-valvular atrial fibrillation (NVAF). Its utility to predict bleeding events and death in NVAF patients undergoing direct-current cardioversion (DC-CV) is unknown. We studied the role of HAS-BLED score in predicting major-bleeding and death in real-world individuals with NVAF undergoing DC-CV.

**Methods:** Between January 2008 and June 2012, 571 consecutive DC-CV procedures were performed to 406 patients (70.1% male; mean age 64.4±11.2) with NVAF. In 540 procedures, HAS-BLED was calculated, and related to the incidence of major-bleeding and death.

**Results:** During a median follow-up of 668 (IQR: 293-1168) days, there were 21 major bleeds (3.7%) and 26 deaths (4.6%), being annual rates of major bleeding and death of 2.02% and 2.51%, respectively. Bleeding was gastrointestinal in 11 (52.4%), neurological in 5 (23.8%) and other site in 5 (23.8%). Aetiology of death was vascular (or probably vascular) in 13 (50.0%), non-vascular in 11 patients (42.3%) and unknown origin in 2 (7.7%). The HAS-BLED score was significantly associated with major bleeds (HR: 2.03, 95%CI: 1.53-2.68; *p*<0.001) and death (HR: 2.44, 95%CI: 1.83-3.25; *p*<0.001). HAS-BLED performed well in predicting both major bleeding (c-statistic: 0.77, 95%CI: 0.66-0.88; *p*<0.001) and death (c-statistic: 0.82; 95%CI: 0.74-0.91; *p*<0.001).

**Abstract P6217 – Table 1**

<table>
<thead>
<tr>
<th>HAS BLED score</th>
<th>Annual rate of major bleeding</th>
<th>Annual rate of death</th>
<th>Patients in category (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>1</td>
<td>0.45</td>
<td>0</td>
<td>120</td>
</tr>
<tr>
<td>2</td>
<td>1.44</td>
<td>1.08</td>
<td>151</td>
</tr>
<tr>
<td>3</td>
<td>2.00</td>
<td>2.45</td>
<td>136</td>
</tr>
<tr>
<td>4</td>
<td>1.82</td>
<td>2.73</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>8.83</td>
<td>10.27</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>29.80</td>
<td>24.83</td>
<td>11</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>54.64</td>
<td>1</td>
</tr>
</tbody>
</table>

**Conclusions:** In patients with NVAF undergoing DC-CV, HAS-BLED score was a good predictor of the occurrence of both major-bleeding and death.

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**P6218 | BEDSIDE**

**Blood pressure increases after successful cardioversion for atrial fibrillation**

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**Background:** Atrial fibrillation (AF) and high blood pressure (BP) are both common conditions that co-exist to a large extent. Despite this, knowledge about how AF influences BP and how rhythm control affects BP is scarce. Further, 24-hour ambulatory BP (ABPM) is a well documented method that enhances risk prediction but is less well studied in patients with AF.

**Material and methods:** We studied 25 patients with AF who were referred for electric cardioversion (EC). Office BP as well as ABPM were recorded shortly before (within 1 week) and shortly after (within 1 week) EC. 19 patients had complete ABPM-recordings and were included for this analysis. Out of these 19 patients, 7 patients had a quick return of AF after EC and consequently had AF during the BP-measurements post EC (group 1). 12 patients had a successful EC and were restored to sinus rhythm (group 2).

**Results:** In group 1 mean 24-hour systolic BP was non-significantly lower at the recording post EC but in group 2, mean 24-hour systolic BP significantly increased by 10 mm Hg (*p*<0.01). See table 1. One patient in group 2 had an increase of antihypertensive medication between the ABPM before and after EC. The remaining 11 patients had unchanged medication and thus changes in medication could not account for the difference in BP. The changes in systolic office BP before and after EC was statistically not significant.

**Conclusion:** Patients with successful EC to sinus rhythm had a marked increase of their 24-hour systolic BP in contrast to patients that were still in AF after unsuccessful EC. It is possible that we either underestimate the "true" BP in patients with AF or that the hemodynamic changes after restoration to sinus rhythm lead to an increase in BP. In both cases, this may have important implications for adequate management of BP in patients with AF. These findings should be replicated in a larger study and further studies should elucidate the possible mechanisms involved.

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**P6220 | BEDSIDE**

**Low incidence of intracardial thrombus formation by direct oral anticoagulants in the setting of electrical cardioversion**

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**Purpose:** Data regarding the comparison of direct oral anticoagulants (DOAs)
with vitamin K antagonists (VKA) in the prevention of intracardiac thrombusformation (ICT) in atrial fibrillation (AF) in the setting of electrical cardioversion (DCCV) is sparse.

Methods: A total of 500 pts with indication for ECV were enrolled. 404 pts received a transesophageal echocardiography (TEE) to exclude ICT and to determine the left atrial appendage blood flow velocity (LAAV). 9 pts with a history of ICT were excluded. Endpoint was the TEE-guided detection of ICT and preformation.

Results: Endpoint was reached by 16 pts (4%). These pts showed a significantly higher CHADS2-VASc score and lower LAAV. 22.8% of all pts with pos. ICT result were under VKA therapy, whereas only 0.51% received DOAs (p=0.011). Dabigatran and Rivaroxaban showed a significant diminished incidence of ICT compared with VKA (p=0.003).

Table 1

<table>
<thead>
<tr>
<th>Total</th>
<th>Pos. ICT</th>
<th>Neg. ICT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n, %)</td>
<td>395 (100%)</td>
<td>16 (4.1%)</td>
<td>379 (95.9%)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>67.2±11.4</td>
<td>69.9±3.3</td>
<td>66.9±0.6</td>
</tr>
<tr>
<td>Male, %</td>
<td>278 (70.4%)</td>
<td>12 (75%)</td>
<td>266 (70.2%)</td>
</tr>
<tr>
<td>CHADS2-VASc score</td>
<td>2.3±1.6</td>
<td>4.0±0.5</td>
<td>2.0±0.1</td>
</tr>
<tr>
<td>EGRA</td>
<td>2.3±0.7</td>
<td>2.5±0.7</td>
<td>2.3±0.4</td>
</tr>
<tr>
<td>INR</td>
<td>1.6±0.7</td>
<td>1.6±0.2</td>
<td>1.6±0.4</td>
</tr>
<tr>
<td>LAAV, m/s</td>
<td>0.4±0.2</td>
<td>0.18±0.03</td>
<td>0.41±0.01</td>
</tr>
<tr>
<td>VKA, n (%</td>
<td>139 (35.2%)</td>
<td>56 (33.0%)</td>
<td>93 (34.0%)</td>
</tr>
<tr>
<td>Rivaroxaban, n (%)</td>
<td>117 (29.6%)</td>
<td>1 (6.3%)</td>
<td>116 (30.6%)</td>
</tr>
<tr>
<td>Dabigatran, n (%)</td>
<td>36 (9.1%)</td>
<td>1 (6.3%)</td>
<td>35 (9.1%)</td>
</tr>
<tr>
<td>Apixaban, n (%)</td>
<td>7 (1.8%)</td>
<td>0</td>
<td>7 (1.9%)</td>
</tr>
<tr>
<td>LMWH, n (%)</td>
<td>66 (16.7%)</td>
<td>3 (18.8%)</td>
<td>63 (16.6%)</td>
</tr>
<tr>
<td>ASA, n (%)</td>
<td>10 (2.5%)</td>
<td>2 (12.5%)</td>
<td>8 (2.3%)</td>
</tr>
<tr>
<td>No OAC, n (%)</td>
<td>25 (6.3%)</td>
<td>2 (12.5%)</td>
<td>23 (6.1%)</td>
</tr>
</tbody>
</table>

Conclusions: The rate of newly diagnosed ICT prior to ECV in pts managed with DOAs is significantly lower than in pts with VKA therapy. DOAs potentially prevents ICT more effectively than VKA.

P6221 | BEDSIDE

Dabigatran improves efficiency of an elective direct current cardioversion service

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Purpose: Direct current cardioversion (DCCV) is an effective method for treating atrial fibrillation. Anticoagulation prior to DCCV is mandatory to reduce the risk of thromboembolism. Historically, achieving and maintaining stable anticoagulation with Warfarin was challenging in some patients leading to high levels of procedure cancellations or rescheduling and long delays for DCCV. The recent introduction of novel oral anticoagulants such as Dabigatran offers a potential alternative to Warfarin therapy in this patient group. We aimed to examine the impact of the use of Dabigatran on our DCCV service as an alternative to Warfarin.

Methods: We analysed 242 DCCV’s performed on 193 patients over a 36-month period. Patients were divided into 2 cohorts. Cohort A included cases in the 22-month period prior to the introduction of Dabigatran. Cohort B included cases in the 14-month period after the introduction of Dabigatran. In patients in the later cohort were treated either with Warfarin or Dabigatran 150mg twice daily. Rates of cancellation and rescheduling, time taken to DCCV and outcomes were compared between the two cohorts and between the two anticoagulants.

Results: All patients in cohort A received Warfarin. In cohort B, 48.4% received Dabigatran; the other patients were established and stable on Warfarin or had reasons for taking Warfarin (e.g. metal heart valve). The average CHADS2-VASc score for all patients was 2.08. A small number of patients (10%) were cancelled in both cohorts due to non-anticoagulation issues (e.g. patients’ choice, refusal for ablation and spontaneous return to sinus rhythm). A significantly larger number of patients from cohort A were rescheduled due to subtherapeutic INRs compared to cohort B (42% versus 15%, p<0.001). Those who received Dabigatran also had significantly lower rates of rescheduling compared to those who received Warfarin (9.7% versus 34.4%, p=0.001). The length of time between initial clinic assessment and DCCV was 22 days shorter in patients taking Dabigatran compared to Warfarin (45 versus 67 days; p=0.0015). Outcomes in achieving and maintaining sinus rhythm were comparable in both cohorts and anticoagulants (p<0.05).

Conclusions: Cancellations of DCCV appointments due to subtherapeutic INRs disrupt clinical care and the resulting inefficiency can escalate treatment cost. This study demonstrates that the use of Dabigatran instead of Warfarin in patients undergoing DCCV reduced rescheduling and thus improved efficiency.

P6222 | BENCH

Czech AF 2012 registry: profile of atrial fibrillation patients receiving antithrombotic therapy before noac

J. Spinar, J.V. Vitovec, L.S. Spinarova. University hospital, Brno, Czech Republic

Purpose: Profile of Czech AF 2012 registry is an epidemiological survey conducted by 197 Czech internal medicine and cardiology specialists who aimed to provide a comprehensive view of patients with non-valvular atrial fibrillation in the Czech Republic with respect to the prevention of stroke, before new anticoagulants were available.

Methods: It involved 982 patients, average age 69.9±10.4 years. The population of men was slightly higher (n=543, 55.3%), especially in the age group under 65 years; women prevailed in the age group above 75 years (55.7%).

Results: One quarter (25.1%) of patients was diagnosed with atrial fibrillation for less than 2 years; 23.2% for 2-5 years; 13.5% for 6-10 years, and 8.6% for more than 10 years. 20.7% of patients had paroxysmal atrial fibrillation; 59.5% indicated permanent atrial fibrillation, i.e. lasting more than one year. 58.7% of patients received medication regulating the heart rhythm; 44.0% had another antirhythmic medication. 13.8% of patients used their medication once a day; 55.1% twice a day, and 29.6% three times a day. 38.7% of patients were after cardioversion, 7.9% were after ablation. 91.5% of patients received warfarin alone or as dual (1.4%) therapy. Only 8.7% of patients had medium or severe kidney impairment. Only 7.5% of patients used acetylsalicylic acid, 0.2% used dual antiplatelet treatment.

Only 3.0% of patients had CHADS2=0; 55.8% were at a medium risk (CHADS2=1-2), and 41.2% at a high risk (CHADS2≥2). 22.1% of patients had one associated condition; 27.5% had two associated conditions; 19.8% had three associated conditions; 28.7% had four or more associated conditions; and only 2.0% indicated no associated condition or gave no answer. The most common associated condition was hypertension (90.2%), followed by ischemic heart disease (50.9%) and diabetes mellitus (41.8%), 95 patients (9.7%) had a history of embolism while receiving antithrombotic therapy. 102 patients (10.4%) had another antiarrhythmic therapy. 91.5% of patients received warfarin alone or as dual therapy, 3.9x per year.

Conclusion: Atrial fibrillation patients are commonly elderly, polymorbid and high-risk patients on a pharmacological medication two to three times a day in more than 80% INR monitoring was close to the level described in large international studies, almost 2/3 of patients were within the therapeutic range.
Purpose: To investigate the safety and efficacy of low-intensity warfarin therapy (INR 1.6-2.6) in elderly Korean patients with nonvalvular AF.

Methods: A total of 583 NVAF patients (mean age 69.5 ± 12.8 years) with an INR ≤ 2.6 and a CHADS2 score ≥ 1 were enrolled. The primary endpoint was the incidence of hemorrhagic events at 1 year. Safety was defined as the occurrence of all-cause mortality and major bleeding events.

Results: The median follow-up period was 12 months. The incidence of hemorrhagic events was 3.9% (11 of 284 patients) at 1 year. Major bleeding occurred in 3.0% (8 of 284 patients). No life-threatening bleeding occurred. All deaths were non-heart-related. The incidence of major bleeding was significantly lower in the INR 1.6-2.6 group than in the INR > 2.6 group (0% vs. 5.2%, p = 0.017).

Conclusions: Low-intensity warfarin therapy (INR 1.6-2.6) is safe and effective for the primary prevention of hemorrhagic events in elderly Korean patients with nonvalvular AF.
Anticoagulants in atrial fibrillation

P6229 | BENCH

Antithrombotic treatment of atrial fibrillation in general practice: application of the GRASP-AF audit tool

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Purpose: Despite compelling evidence of the efficacy of oral anticoagulation (OAC) for stroke prevention in atrial fibrillation (AF) not all suitable patients receive appropriate antithrombotic therapy. We examined the utilization of antithrombotic therapy in AF patients in general practice, based on the computerized GRASP-AF (Guidance on Risk Assessment and Stroke Prevention in Atrial Fibrillation) audit tool available for UK general practitioners to assess stroke risk and antithrombotic therapy use.

Methods: 2259 AF patients [mean (SD) age 76 (12) years, 46% female, represent 2.15% of the total general practice population] identified by the GRASP-AF tool from 11 general practices were followed-up for 12 months.

Results: Most patients were moderate-high risk of stroke (92.5%) based on the CHADS2-Vasc score (≥1 if male, ≥2 if female, 86% based on CHADS2 score ≥1). Only 1080 (48%) patients received OAC and 921 (41%) received antiplatelet agents. OAC was declined by 113 (5.0%) patients and contraindicated in 187 (8.3%). Based on CHADS2, OAC (+ antiplatelets) was prescribed to 51% of patients at moderate-high risk of stroke; with CHAD2Ds2-Vasc, OAC was prescribed to 50% of moderate-high risk patients, and approximately 28% of low risk patients (Table). Over a 12 month period, 67 (3.0%) developed stroke, including 5 (0.2%) hemorrhagic strokes. Use of antiplatelet agents was associated with a significantly increased risk of stroke on univariate analysis (odds ratio 1.88, 95% CI 1.14-3.09, p=0.016).

Antithrombotic therapy and stroke risk

<table>
<thead>
<tr>
<th>CHADS2 score</th>
<th>None</th>
<th>OAC</th>
<th>OAC + antiplatelet agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>126 (39%)</td>
<td>108 (33%)</td>
<td>80 (25%)</td>
</tr>
<tr>
<td>Moderate-high risk</td>
<td>240 (12%)</td>
<td>736 (39%)</td>
<td>891 (46%)</td>
</tr>
<tr>
<td>CHA2DS2-Vasc score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk (if male, 1 if female)</td>
<td>86 (51%)</td>
<td>38 (22%)</td>
<td>40 (24%)</td>
</tr>
<tr>
<td>Moderate-high risk</td>
<td>281 (13%)</td>
<td>774 (37%)</td>
<td>931 (45%)</td>
</tr>
</tbody>
</table>

Conclusion: OAC therapy in AF remains suboptimal in the UK general practice settings, with sub-optimal treatment of high-risk patients and inappropriate OAC use in low-risk patients. Aspirin monotherapy use remained excessive in high-risk patients, despite exposing such patients to an increased risk of stroke.

P6231 | BENCHMARK

Left atrial sphericity improves CHADS2 score stroke prediction in patients with atrial fibrillation

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Introduction: Left atrial sphericity (LASP) is a new remodeling parameter that has independent predictive value for atrial fibrillation (AF) recurrence after AF ablation. We sought to evaluate whether LASP adds prognostic information to CHADS2 score and LA appendage (LAA) characteristics.

Methods: Twenty-nine patients with history of prior stroke and 29 age- and gender-matched controls were included. All patients underwent cardiac MRI prior to the AF ablation procedure. LASP was calculated using a 3D left atrial (LA) reconstruction that excluded pulmonary veins and the LAA. Manual LAA segmentation was used to calculate the volume. LAA morphology was classified as previously reported: chicken wing, cauliflower, windsock, and cactus. Area under the ROC curve (AUC) was calculated for LASP, LAA volume, LAA volume and CHAD score (Stroke2 excluded). A cut-off value was determined for optimal stroke prediction.

Results: Mean age of the study population was 61±11 years, 79.3% were male, 53.4% had hypertension, and 8.6% had diabetes. Compared to controls, patients with history of prior stroke had significantly higher LASP (80.2±3.1 vs 82.5±3.3, p<0.008); there were no differences in CHADS2 score (0.66±0.76 vs 0.90±0.86, p=0.28). LA volume (85.1±24.1 vs 94.8±25.1, p=0.07), LAA volume (5.9±2.9 vs 5.5±2.9, p=0.66), or LAA morphology (p=0.514). LASP had the only significant ROC curve for stroke prediction (AUC 0.706 [0.571-0.842], p=0.007). The cut-off value for LASP was 83.6% (52% sensitivity, 90% specificity). A significantly greater proportion of patients with high LA sphericity (>83.6%) had prior stroke (83.3% vs 35.0% below the cut-off; P=0.001). Logistic regression showed predictive value for LASP (OR 1.26 per each 1% increase [1.85-52.20], P=0.013), but not for CHAD score (OR 1.457 [0.755-2.81]; p=0.262). The combination of both parameters (CHAD-LASP) increased the predictive value over CHAD score alone (AUC of 0.719 [0.585-0.852], p=0.004).

Conclusion: LA sphericity is associated with history of prior stroke in patients undergoing AF ablation and increases the predictive value over CHAD score alone.
P6233 | BEDSIDE
Profile and outcome of anticoagulated patients admitted to the emergency department of a tertiary hospital for bleeding complications
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Purpose: Advance age and comorbidity are known risk factors for bleeding in patients taking oral anticoagulants (OAC). The aim of this study was to describe the profile of patients with bleeding events seen in our emergency department (ED) and to identify factors associated with major bleeding (MB).

Methods: We included patients receiving OAC for non-valvular atrial fibrillation (NVAF) or higher bleeding risk. Patients were included in the study if they presented to the ED for a bleeding event from June 2012 to January 2014. MB was defined as a reduction in Hb level ≥20 g/dL, requirement of ≥2 units of packed red cells, requirement of invasive procedures, or bleeding in a critical site. All other bleeding episodes were considered minor (MB). Age, performance of activities of daily living (Barthel), comorbidity (Charlson), comedication, and HASBLED score were recorded.

Results: 73 patients (57% men) were seen in the ED for bleeding complications. 66 patients received vitamin K antagonists (VKA) for NVAF (56 patients) or MP (10 patients) and 7 patients received dabigatran (all for NVAF). Bleeding sites were: intracranial (IC) (13), gastrointestinal (40), urtic tract (9), lung or airway (3), others (8). MB occurred in 44 patients (91% required admission for a mean of 11±9 days) and 29 patients had MB. There were no significant differences between patients with MB and mB in terms of age (80±9 vs 78±8), Barthel index (88±22 vs 88±28), and Charlson index (2.5±1.9 vs 1.8±1.5). 22% of patients were taking antplatelet agents and 8% NSAID, but there were not significant differences between patients with MB or mB regarding the use of these drugs. In patients receiving VKA, there were not significant differences between patients with MB and mB neither in terms of INR level (4.2±2.4 vs 3.8±2.3) nor in the percentage of patients with INR within therapeutic range (INR 2.3±0.8 for NVAF and 2.5±3.5 for MP). The HASBLED score did not show significant differences between patients with MB or mB (2.6±0.9 vs 2.9±1.2). IC bleeding was the cause of death in 4 patients. In 50% of patients with IC bleeding the INR was above the therapeutic range but only in 25% the INR was >4. HASBLED was >3 in a 38% of patients with IC bleeding.

Conclusions: In this study, the severity of bleeding was not related to comorbidity or bleeding risk. In a year to year basis. The most serious complication of anticoagulation, was neither related to a higher HASBLED score nor to the intensity of the anticoagulation. One limitation of the study is the small number of patients included. More studies are needed to define which patients are at a higher risk of MB while taking OAC.

P6234 | BEDSIDE
Left atrial appendage thrombus in the modern anticoagulant era

Background: Transesophageal echocardiography (TOE) guided direct current cardioversion (DCCV) following variable duration anticoagulation has become the modern standard of care for many patients with atrial fibrillation. Agents used include warfarin, heparins, and more recently dabigatran and rivaroxaban. During a single anaesthetic, if left atrial appendage (LAA) thrombus is excluded by TOE, patients scheduled for DCCV in the modern era. Operator risk aversion regarding “missing a clot” (false negative) with potential catastrophic clinical repercussions (stroke etc), led to relatively high inter-observer variability (with a tendency to excess false positive studies) compared to retrospective expert review.

P6235 | BEDSIDE
CHA2DS2-VASc as a predictive score system for the clinical outcomes in acute myocardial infarction patients with atrial fibrillation

Purpose: CHA2DS2-VASc score system has been used in the assessment for the development of stroke in patients with atrial fibrillation (AF). Substantial patients with AF experience acute myocardial infarction (AMI). However, little is known about the prognostic impact of CHA2DS2-VASc score system on the clinical outcomes in AMI patients with AF.

Methods: We analyzed a total of 1,021 patients (71.0±12.0 years old, 693 males) AMI with AF enrolled in Korean AMI Registry (KAMIR). In-hospital outcome was defined as in-hospital mortality and complications including death, major- or minor-bleeding, and new onset cerebrovascular accidents (CVA). One-year clinical outcomes were analyzed according to CHA2DS2-VASc score in a linear correlation method, and defined as the composite of major adverse cardiac events (MACEs) including death, myocardial infarction (MI), target vessel revascularization (TVR) and coronary artery bypass graft (CABG). CHADS2, CHA2DS2-VASc, Framingham, and Framingham-IV model were calculated and the predictive accuracy for one-year clinical outcomes and major adverse cardiac events (MACEs) of them were analyzed by Receiver Operating Characteristics Curve.

Results: Patients with one year MACEs had significantly higher CHADS2 (2.5±1.4 vs 1.8±1.3, p < 0.001), CHA2DS2-VASc (3.6±1.7 vs 2.6±1.7, p < 0.001; non ST segment elevation MI 3.6±1.1 vs 3.1±1.1, p < 0.001) than the patients without one year MACEs. In-hospital mortality was higher in patients with CHADS2 score >2 (13.1% vs 6.4%, p < 0.001) without differences in the rate of CVA, major bleeding, and new onset heart failure. Both one year mortality (linear p < 0.001) and the composite of MACEs (linear p < 0.001) were increased as stepwise manner according to CHA2DS2-VASc score. The predictive accuracy of CHADS2 score was better for one year mortality (area under curve (AUC) 0.715, 95% confidence interval 0.67-0.76, p < 0.001) than CHADS2 (AUC 0.674) and TIMI score (AUC 0.712). Also, the predictive accuracy of CHA2DS2-VASc score was better for one year MACEs (AUC 0.671, 95% confidence interval 0.63-0.70, p < 0.001) than CHADS2 (AUC 0.651) and TIMI score (AUC 0.664).

Conclusions: CHA2DS2-VASc score can provide simplicity with accuracy for the prediction and risk stratification of one year mortality and MACEs as well as in hospital mortality in AMI patients with AF. CHA2DS2-VASc score could be utilized for the prediction of both clinical outcomes and stroke in AMI patients with AF.

P6236 | BEDSIDE
Why are oral anticoagulants restrained from patients with atrial fibrillation - outcome of a population based assessment in a geographically well-defined catchment area
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Purpose: Atrial fibrillation (AF) affects about 3% of the adult western population and incurs an annual stroke risk of 5%. Use of oral anticoagulants (OAC) significantly reduces this risk. As only about 50% of patients with AF in Europe are prescribed OAC, an opinion of “inappropriate underutilization” has been set. Little is known about why AF patients are not prescribed OAC more frequent in routine clinical management. The aim of this study was to assess this issue in a geographically well-defined catchment area.

Methods: The FHN-registry records all identified patients with AF in a catchment area of 65532 people. Of the 1616 patients with an identified AF on December 2010, 588 (36%) were not prescribed OAC. The physicians (n=22) responsible for their treatment were identified, and requested to complete a standardised questionnaire to assess the reason of restraining OAC in each individual case.

Results: This analysis is based on the 520 first returned questionnaires. The Table 1.

Table 1. Reasons of restraining OAC in patients with CHADS2 0, 1 and ≥2

<table>
<thead>
<tr>
<th>CHADS2=0</th>
<th>CHADS2=1</th>
<th>CHADS2 ≥2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>88</td>
<td>152</td>
</tr>
<tr>
<td>No medical indication (%)</td>
<td>75.0</td>
<td>44.7</td>
</tr>
<tr>
<td>Bleeding (%)</td>
<td>2.2</td>
<td>8.6</td>
</tr>
<tr>
<td>Side effects of OAC/interaction (%)</td>
<td>11.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Poor compliance (%)</td>
<td>3.4</td>
<td>10.5</td>
</tr>
<tr>
<td>Repeated falls (%)</td>
<td>0.0</td>
<td>3.3</td>
</tr>
<tr>
<td>Patient decline OAC treatment (%)</td>
<td>0.0</td>
<td>7.2</td>
</tr>
<tr>
<td>Converted to sinus rhythm (%)</td>
<td>9.1</td>
<td>6.6</td>
</tr>
<tr>
<td>Malaginy (%)</td>
<td>1.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Severely declined general condition (%)</td>
<td>2.3</td>
<td>7.2</td>
</tr>
<tr>
<td>Other specified reason (%)</td>
<td>4.5</td>
<td>3.9</td>
</tr>
<tr>
<td>No reason identified (%)</td>
<td>1.1</td>
<td>4.6</td>
</tr>
</tbody>
</table>
given reasons of restraining OAC in patients with CHADS2 0, 1 and ≥2, respectively, are given in Table 1.

**Conclusion:** This is, to our knowledge, the first study to assess causes of restraining OAC in a geographically well-defined population, thus including hospital- and as well as non-hospital based healthcare. In patients with CHADS2=2 the main causes of restraining OAC were severely declined general condition, a history of bleeding and poor compliance.

**P6237 | BEDSIDE**

Prognostic impact of CHA2DS2Vasc and renal impairment in non valvular atrial fibrillation patients: which is the best equation to stratify the risk of future events?

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**Purpose:** Renal dysfunction (RD) is associated with an increased risk of thromboembolic (TE) and haemorrhagic (HE) events in non valvular atrial fibrillation (NAVF). Which method of RD evaluation can better stratify the risk of cardiovascular (CV) events in NAVF is still unknown. We evaluated the additive prognostic role of RD (1 point) to CHA2DS2VASc score considering pts that experienced past thromboembolic or hemorrhagic events.

**Methods:** Between 2009 and 2013, we enrolled 3399 consecutive NAVF patients (pts). Clinical data were derived from the E-data chart for outpatient clinic of our cardiovascular center. In 1509 pts glomerular filtration rate (GFR) was available at first clinic evaluation with Cockcroft-Gault (CG); Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology collaboration (CKD-EPI) equations. Renal dysfunction was defined as GFR ≤60ml/min. We recalcified CHA2DS2Vasc score, adding 1 point for RD using all the equations. The median follow-up was 15 months (IR 15-40). We evaluated incidence of death, CV hospitalization (CVH), Thromboembolic event (TE) and major HE.

**Results:** The median age was 75 years (IR 68-81), 39.7% were male; 1217 (80.1%) pts had hypertension, 466 (30.8%) diabetes mellitus, 295 (19.5%) heart failure, 196 (13%) prior stroke or transient ischemic attack and 23 (1.5%) previous bleedings. Median GFR was 61.8±ml/min (IR 47-77) with CG, 72.4 (IR 59-87) with MDRD and 69.1 (IR 55-84) with CKD-EPI. Median HAS-BLED score was 3 (0-5) and >3 in 70% of the pts; median CHA2DS2Vasc score was 4 (IR 3-5) and >2 points in 91.1% pts. 623 (41%) pts were on anticoagulant therapy (OAC). During follow-up we recorded 531 (35%) deaths or CVH, 113 (7.5%) TE and 24 (1.6%) major HE. Adding 1 point for RD to CHA2DS2Vasc score pts were reclassified in a worse-class of risk in 47% with CG, 34% with CKD-EPI and 27% with MDRD (p<0.001). Pts with combined TE/HE during follow-up were reclassified by the presence of RD in a worst class of risk in 62% with CG, 46% with CKD-EPI and 35% with MDRD (p<0.001). Stratifying these pts by OAT, CG and CKD EPI reclassification were associated to a significant higher risk of TE/HE (p=0.006) only in not OAT pts; conversely MDRD identified an higher risk only in OAT pts (p=0.04). Adding 1 point for CHA2DS2Vasc score considering pts that experienced prior death, CV hospitalization, TE and major HE, the overall incidence of major CV events was 30.2% and was 36.4% in pts with RD.

**Conclusions:** In NAVF pts the risk reclassification by CHA2DS2Vasc and RD shows an additive predictive prognostic impact. CG was the best formula to reclassify pts risk of events.

**P6238 | BEDSIDE**

High-sensitivity cardiac troponin T levels do not increase after elective, biphasic, direct-current cardioversion for atrial fibrillation/flutter

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**Background:** The kinetics of high-sensitive cardiac troponin T (hs-cTnT) levels after elective, biphasic, direct-current cardioversion for persistent atrial fibrillation/flutter remains unknown.

**Methods:** We examined hs-cTnT kinetics in 24 patients at baseline and at 2, 6, and 24 hours post-cardioversion, and again at 7 and 30 days. We also examined levels of high-sensitive cardiac troponin T (hs-cTnT), troponin-I, troponin-I, cTnT, and cTnT, as part of a general rise in biomarkers, such as BNP and hs-CRP , in 30 patients.

**Results:** The cardioversion procedure was successful in all of the patients, and 70% of the patients remained in sinus rhythm at 30 days following cardioversion. Mean baseline hs-cTnT concentration was 21.7±12.7 ng/L with 14 patients presenting with levels above the detection level (13 ng/L). hs-cTnT levels did not change significantly over time although they tended to decrease by 30 days (16.6±6.1 ng/L). There was no significant risk in other markers of myocardial injury. Similarly, BNP and hs-cTnT levels were elevated at baseline and tended to decrease over the longer period.

**Conclusions:** Patients with persistent atrial fibrillation/flutter have elevated hs-cTnT levels, as part of a general rise in biomarkers, such as BNP and hs-cTnT, without a further rise after cardioversion. After cardioversion, there is a gradual, nonsignificant decrease in levels of these biomarkers over time.

**ANTI-CoAGULANTS AND STROKE IN ATRIAL FIBRILLATION**

**P6241 | BENCH**

Relationship between deteriorating renal function and adverse events in atrial fibrillation patients using novel oral anticoagulants

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**Introduction:** Renal function is crucial to use novel oral anticoagulants (NOAC) in patients with non-valvular atrial fibrillation (NAVF).

**Methods and results:** This study consists of 689 NAVF patients (68±11 years old) receiving NOAC ( dabigatran: 442, rivaroxaban: 217, apixaban 30 patients) in our hospital. The mean estimated creatinine clearance (eCCr) before NOAC was 74±26 ml/min. The eCCr ≤50 ml/min was present in 113 of 689 (16%). The eCCr was measured again in the remaining 576 patients with eCCr >50 ml/min before NOAC, and eCCr fell into ≤50 ml/min in 27 patients (3.9%) at 295±250 days after NOAC (Table). Adverse events were observed in 39 of 113 patients (35%) with eCCr <50 ml/min before NOAC, 12 of 27 patients (44%) with eCCr fall <50 ml/min after NOAC, and 121 of 549 patients (22%) with preserved eCCr >50 ml/min after NOAC. Major bleeding was observed in 2 of 113 patients (2%) of eCCr <50 ml/min before NOAC, 2 of 27 patients (7%) of eCCr fall <50 ml/min before NOAC.

**Patients with eCCr <50 ml/min Patients with preserved eCCr ≥50 ml/min P value**

<table>
<thead>
<tr>
<th>Patients with eCCr &lt;50 ml/min Patients with preserved eCCr ≥50 ml/min</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients number</td>
<td>27</td>
</tr>
<tr>
<td>Age, years old, mean±SD</td>
<td>76±9</td>
</tr>
<tr>
<td>Race, n (M/F)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Serum Cr (mg/dl) at baseline</td>
<td>0.87±0.20</td>
</tr>
<tr>
<td>eCCr (ml/min) at baseline</td>
<td>56±5</td>
</tr>
<tr>
<td>Previous stroke or TIA, n (%)</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>11 (41)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>16 (59)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>CHADS2score, mean</td>
<td>2.3±1.3</td>
</tr>
<tr>
<td>CHADS2-VASc score, mean</td>
<td>3.8±1.4</td>
</tr>
<tr>
<td>Thromboembolic event, n (%)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Adverse event, n (%)</td>
<td>12 (44)</td>
</tr>
<tr>
<td>Major bleeding, n (%)</td>
<td>2 (7)</td>
</tr>
</tbody>
</table>

**Downloaded from https://academic.oup.com/euroheartj/article-abstract/35/suppl_1/851/541962 by guest on 07 February 2019**
after NOAC. On the other hand, no major bleeding event was observed in patients with preserved CCR <50 ml/min after NOAC.

Conclusion: Deteriorating renal function is associated with increasing adverse events. Repeated measurement during NOAC is important to avoid adverse effects.

P6242 | BEDSIDE

Characterizing patients who do not do well on a vitamin-K antagonist therapy in a community based cohort of patients with non valvular atrial fibrillation


Background and aim: In atrial fibrillation (AF) the risk of complications increases an INR (International normalized ratio) values are out of therapeutic range. Mean time in therapeutic range (TTR) below 60% indicates that vitamin-K antagonist (VKA) is inefficient. We aimed to determine TTR values in patients who were on VKA treatment and had non-valvular AF and to identify the factors affecting TTR in these patients.

Methods: Retrospective, between June 2012 and December 2013, 534 consecutive patients with non-valvular AF who were attending the out-patient Cardiology clinics of a tertiary hospital were enrolled. For the purpose of the present study, only patients who were on uninterrupted AVK in at least 12 months and had 9 consecutive INR values were included. TTR values were determined using the fraction of INR's in range (the number of INR's within target range / [2 to 3] divided by the total number of INR's). A cut off value of 60% was used to assess efficacy of TTR. Thereafter, patients were classified into two groups according to their TTR values (<60% vs. >60%) and the characteristic features of these groups were compared. Independent predictors of having TTR <60% were identified using a binary logistic regression analysis.

Results: The mean age of the patients was 73 ± 11 years and 40.4% were female. 64% of the patients had 15 INR’s consecutive tests, and the average number of INR’s tests was 13.9 ± 1.8. Mean TTR value was 59.1 ± 16, and 44.8% (n=239) had TTR values below 60%. In the univariate analysis, patients with TTR <60% were younger (72 ± 12 vs. 74 ± 11 years; p<0.03) and more commonly women (65% vs. 54%, p<0.01) than those patients with TTR >60%. History of congestive heart failure, chronic obstructive pulmonary disease, moderate with alcohol consumption, being on home amiodarone, hyperuricemia, and a history of prior malignant disease, were significantly associated (p<0.05) with TTR <60%. Prior coronary artery disease and smoking status showed a tendency to be associated with TTR <60% (p<0.10). After a multivariate adjustment, the independent predictor of having a TTR >60%, were moderate alcoholism consumption (odds ratio 5.3 [95%CI 1.2-4.8]), history of malignant disease (odds ratio 2 [95%CI 1.2-4.0]), on home amiodarone (odds ratio 1.6 [95%CI 1.3-2.1]), and age <65 years (odds ratio 1.5 [95%CI 1.1-1.8]).

Conclusions: We found that about 45% of our study patients had inefficient TTR values and that TTR values were associated with some potentially modifiable factors such as alcohol consumption and amiodarone treatment.

P6243 | BEDSIDE

Cost-effectiveness of non-Vitamin-K oral anticoagulants compared to warfarin in patients with non-valvular atrial fibrillation

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Non-Vitamin-K antagonist oral anticoagulants (NOAC) demonstrated in edoxaban’s ENGAGE-AF trial, apixaban’s ARISTOTLE trial, rivaroxaban’s ROCKET-AF trial and dabigatran’s RE-LY study non-inferiority or superiority for the prevention of the primary endpoint of stroke and systemic embolic events, for occurrence of severe bleeding complications and mortality in patients with non-valvular atrial fibrillation (NVAF) compared to warfarin adjusted to an INR (International normalized ratio) of 2 to 3. The pharmacoeconomic aspects of dabigatran, rivaroxaban and apixaban demonstrated to be cost effective in many countries for the health care system mainly. Here we determined the cost-effectiveness of 60mg od and 30mg od edoxaban from a German payer perspective and compared the results with those obtained for the approved NOAC.

We used the Markov decision model to analyse the quality adjusted life years (QALY), total costs (one time costs for treatments, rehabilitation costs for inpatient and ambulatory care, inpatient medical treatment costs, daily costs for drugs) and incremental cost effectiveness ratio (ICER) based on the data of the ENGAGE-AF study. The present analysis was compared with data previously derived from ROCKET-AF and ARISTOTLE studies under a German health care insurance perspective.

The base-case analyses of a 65 years old person with a CHADS2 score >1 gained 1.7 lives over warfarin for 30mg od and 60mg od edoxaban, respectively. The ICER was 50,000 and 68,000 Euro per QALY for the higher and lower dose of edoxaban based on the results of the Monte Carlo Simulation (MCS). The results of the one-way sensitivity analysis showed that the costs for edoxaban (both doses), the quality of life utilities, the treatment of ischemic stroke and of major and intracerebral bleeding complications were important values in our model. The various willingness-to-pay thresholds were analysed by using the probabilistic sensitivity analysis (PSA) in the MCS by varying all variables simultaneously. Edoxaban 60mg od and 30mg od were cost effective at willingness-to-pay thresholds of 52,000€/QALY and 67,000€/QALY. The results for apixaban were in between the 2 edoxaban doses and higher for dabigatran both doses and rivaroxaban.

Apixaban in addition to apixaban may be regarded as the most cost-effective NOAC from a German public health care insurance perspective. The larger reduction in medical cost was mainly driven by reductions in the risks major bleeding events. Additional real life use of NOAC has to substantiate the present results for specific countries.

P6244 | BEDSIDE

An analysis of net clinical benefit of new oral anticoagulants versus warfarin in atrial fibrillation phase III trials

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Purpose: We estimated the net clinical benefit (NCB) of new oral anticoagulants (NOAcs) vs warfarin across phase III clinical trials, evaluating composites of efficacy and safety in patients with non-valvular atrial fibrillation (AF).

Methods: We considered the incidence rates (IR) per 100 patients years for major vascular outcomes, systemic embolic events and hemorrhagic stroke, adjusted major bleeding (major bleeding minus hemorrhagic stroke) and myocardial infarction for each treatment. We first calculated the Rate Ratio (RR) of NOAcs vs warfarin for a composite outcome (CO) of such events. We then attributed to each event a weight according to its reported impact on death, as derived from previous studies. Ischemic stroke (IS) was used as the reference value. The NCB was defined as the weighted sum of IRs for each NOAC (dabigatran 150mg and 110mg, rivaroxaban 20mg, apixaban 5mg, edoxaban 60mg and 30mg) minus the weighted sum of IRs in the respective comparator (warfarin), NCB was expressed as IS equivalents prevented per 100 patients years of treatment.

Results: Expressed as RR, 95%CI, the CO was significantly lower than warfarin for 150mg dabigatran (0.91, 0.79-0.99), apixaban (0.82, 0.73-0.89), and both 60mg and 30mg edoxaban (0.89, 0.79-0.96; 0.83, 0.73-0.89). There was a favourable, but not significant, trend for better NCB vs warfarin as to 110mg dabigatran (0.92, 0.80-1.00) and rivaroxaban (0.93, 0.82-1.01). According to weighted NCB estimates, IS equivalents were significantly lower for all NOAcs compared with warfarin (Figure). There were no significant differences in CO and NCB between the two doses of dabigatran and edoxaban.

Conclusions: Considering a weighted NCB, all NOAcs showed a better compounded efficacy/safety profile than warfarin in patients with AF.
they were patients of the higher risk profile: older (mean age 73.7 vs. 65.0, p < 0.0001), more frequently with the history of hypertension (77% vs. 70%), dia-
betes mellitus (34% vs. 24%), ischemic heart diseases (25% vs. 14%), previous MI (21% vs. 15%), heart failure (19% vs. 6%), and stroke (8% vs. 3%). They were also less frequently treated invasively (PCI in 52% vs. 73% in patients without FA). The follow-up data concerning rehospitalization, cardiac procedures and mortality up to 3 years following index MI are shown in the table. Significantly more patients with FA were hospitalized due to stroke (9.8% vs. 2.9% in patients without FA, p < 0.0001).

Conclusion: Survivors of AMI who had FA during the acute phase are patients of high initial risk profile and higher long-term mortality and morbidity. Every 10th patient with FA in AMI is hospitalized due to stroke during 3 years following MI.

P6246 | BEDSIDE

Truly low-risk patients with newly diagnosed non-valvular atrial fibrillation at risk of stroke: 1-year outcomes from the GARFIELD Registry

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Purpose: To study 1-year outcomes in truly low-risk patients with non-valvular atrial fibrillation (AF).

Methods: In the ongoing, international registry, GARFIELD, a total of 12,458 prospective patients with AF were enrolled at 739 sites in 30 countries between March 2010 and January 2013. Results are reported at 1-year follow-up. CHADS2 and CHA2DS2-VASc scores were calculated in 12,195 and 12,184 patients, respectively.

Results: A total of 6.6% and 3.6% of patients had CHADS2 and CHA2DS2-VASc scores of 0, respectively ("low-risk"). Low-risk patients were younger and more likely to be male. Approximately 75% of these patients received antithrombo-
bitic or antiplatelet therapy. The unadjusted 1-year incidence of all-cause death, stroke/systemic embolism (SE) and major bleeding increased significantly when risk scores were ≥1. The 1-year incidence of stroke/SE was lower in those with CHA2DS2-VASc of 0 vs CHADS2 of 0 (0.7% vs 1.2%).

Table 1

<p>| CHADS2 = 0 | CHA2DS2-VASc = 0 |</p>
<table>
<thead>
<tr>
<th>n=79712</th>
<th>n=4351218</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA2DS2-VASc = 0 vs CHA2DS2-VASc ≥1 and CHADS2 ≥1 vs CHADS2 of 0</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
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<tr>
<td>VKA</td>
<td>228</td>
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<tr>
<td>VKA-AP</td>
<td>58</td>
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<tr>
<td>FXa or DTT</td>
<td>60</td>
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<tr>
<td>FXa or DTT + AP</td>
<td>17</td>
</tr>
<tr>
<td>AP</td>
<td>252</td>
</tr>
</tbody>
</table>

No antithrombotic therapy

1-year outcomes (unadjusted) (n=50712195) vs CHADS2 ≥1 and CHADS2 ≥1 |

| All-cause death, n% | 25 | 21 | 0.343 (0.343–0.989) |
| Stroke/SE, n% | 10 | 12 | 0.19 (0.139–1.362) |

Major bleeding, n% | 0 | 0 | 0.02 |

P6247 | BEDSIDE

Effectiveness of apixaban compared to edoxaban for stroke prevention in non-valvular atrial fibrillation

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Purpose: The European Society of Cardiology guidelines recommend consideration of novel oral anticoagulants (NOACs) including dabigatran, rivaroxaban and apixaban instead of warfarin for stroke prevention in non-valvular atrial fibrillation (NVAF) patients. Several published economic evaluations have deemed apixaban to be the most cost effective drug amongst the current anticoagulants. Edoxaban may be the 4th NOAC to the market based on recently published ENGAGE-AF trial. Limited data exists about its relative economic value versus apixaban. We assessed the cost-effectiveness of apixaban 5 mg BID versus edoxaban 60 mg or 30 mg QD as intended starting dose strategies for stroke prevention in NVAF patients, from a UK NHS perspective.

Methods: A Markov model was developed to evaluate the lifetime clinical and economic impact of apixaban versus both daily twice versus edoxaban (30mg and 50mg once daily) in NVAF patients. A pair-wise indirect treatment comparison was con-
ducted for the following end-points: ischemic stroke, systemic embolism, intracra-
nial hemorrhage, other major bleeds, clinically-relevant non major bleeds, myo-
ocardial infarction and treatment discontinuations. Price parity was assumed be-
tween apixaban and edoxaban. Outcomes estimated over lifetime horizon were healthcare costs, life years gained, and quality-adjusted life years (QALY) gained.

Results: Apixaban was predicted to increase life expectancy and QALYs ver-
sus low dose and high dose edoxaban over a lifetime horizon. These gains were achieved at cost-savings versus low dose edoxaban, thus dominating it in the analysis. Apixaban was cost effective versus edoxaban 60 mg QD with incremen-
tal cost effectiveness ratio (ICER) of £6,763/QALY gained, well below commonly
**Conclusion:** Among patients with atrial fibrillation (AF), significant predictors of AF included age ≥65 years and a longer PR interval at enrollment were independent predictors of AF. In multivariable analysis, age ≥65 years (HR 2.8 [95% CI 1.2-5.2], P < 0.01), CHADS2 score (HR 1.9 per one point [1.3-2.8], P < 0.001), PR interval (HR 1.2 per 10ms [1.1-1.4], P < 0.0001), and diabetes (HR 2.3 [1.0-5.2], P < 0.05). In multivariable analysis, age ≥65 (HR 2.5 [1.2-5.2], P < 0.01), and PR interval (HR 1.3 [1.2-1.4], P < 0.0001) remained significant and together yielded an area under the ROC curve of 0.73 (95% confidence interval 0.69-0.76, P < 0.001).

Conclusion: Age ≥65 years and a longer PR interval at enrollment were independently associated with an increased propensity for AF in CS patients, however they offered only moderate predictive ability in determining which CS patients had AF detected by the ICM in the CRYSTAL AF study.

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**P6251 | BEDSIDE**

**Predictors for detection of atrial fibrillation in cryptogenic stroke patients:** insights from insertable cardiac monitor data in the CRYSTAL AF study

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**Purpose:** Undiagnosed atrial fibrillation (AF) may be responsible for a significant proportion of cryptogenic strokes (CS). However, the clinical, electrocardiographic, and echocardiographic factors associated with the occurrence of AF in CS are not well understood. We assessed these factors in CS patients who received an insertable cardiac monitor (ICM, Reveal XT) for arrhythmia surveillance in the CRYSTAL AF study.

**Methods:** ICM patients ≥40 years old with CS or transient ischemic attack within 90 days prior to enrollment were studied. We assessed whether age, gender, race, body mass index, type and severity of index ischemic event, CHADS2 score, PR-interval, and the presence of diabetes, hypertension, congestive heart failure, or PFO predicted AF detection within the initial 12 months of follow-up using univariate and multivariable Cox proportional hazards models and receiver operator characteristic (ROC) curves.

**Results:** Among 221 ICM recipients (age 61.6±11.4 years, 64% male), adjudicated episodes of AF were detected in 29 patients within 12 months. In univariate analysis, significant predictors of AF included age ≥65 years (HR 2.8 [95% confidence interval 1.2-5.8], P < 0.01), CHADS2 score (HR 1.9 per one point [1.3-2.8], P < 0.001), PR interval (HR 1.2 per 10ms [1.1-1.4], P < 0.0001), and diabetes (HR 2.3 [1.0-5.2], P < 0.05). In multivariable analysis, age ≥65 (HR 2.5 [1.2-5.2], P < 0.01), and PR interval (HR 1.3 [1.2-1.4], P < 0.0001) remained significant and together yielded an area under the ROC curve of 0.73 (95% confidence interval 0.69-0.76, P < 0.001).

**Conclusion:** Age ≥65 years and a longer PR interval at enrollment were independently associated with an increased propensity for AF in CS patients, however they offered only moderate predictive ability in determining which CS patients had AF detected by the ICM in the CRYSTAL AF study.
Of the 90 patients in the study (age 78 ± 7), 50% were women; the avg. CHA2DS2-VASc score and HAS-BLED-score were 4.7 and 2.8. 8 patients (8.8%) had suffered from previous strokes. The most common indication for LAA closure was recurrent gastrointestinal bleeding with OAC (33%). In 83/90 (92%) patients a device was successfully implanted. 3 patients had a previously undetected LAA thrombus in the main LAA-lobe. In 4 patients the procedure was stopped due to unfavorable LAA-morphology (i.e., ≤ 15mm depth/width).

Overall 83 devices of all sizes were implanted (10x21mm/22x24mm/22x27mm/19x30mm/10x33mm). As periprocedural complications, one pseudoaneurysm and one AV-fistula of the A. femoralis sup. occurred. One patient developed a reactive polysteris 10 days after the implantation which resolved after bilateral thoracoscopic (non-hemorrhagic aspirin). No other implantation related complications did occur. 45 patients received a TEE control 2-3 months post-procedure. No device displacement/protrusion and no relevant periventricular flow in color-doppler echo (all < 3mm). In one case (1.1%) we found an asymptomatic thrombus on the LAA-device (spherical, approx. 17x18mm), which completely resolved after 3 months of OAC and did not recur.

Conclusions: In a real-world scenario percutaneous LAA-closure can be safely and effectively used as alternative to OAC. In our high-risk group of elderly patients with atrial fibrillation, dual platelet inhibition can be used directly instead of OAC after implantation. To ensure a good result and detect device-related thrombus, TEE monitoring should be recommended to all patients after 2-3 months.

P6254 | BEDSIDE
Status of anticoagulation therapy and incidence of events in Japanese elderly patients with non-valvular atrial fibrillation: a report from the J-RHYTHM Registry
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1 Nippon Medical School, Tama-Nagayama Hospital, Dept. of Internal Medicine and Cardiology, Tokyo, Japan; 2University of Toyama, the Second Dept. of Internal Medicine, Toyama, Japan; 3Hiroaki University, Cardiology, Respiratory Medicine and Nephrology, Hiroaki, Japan; 4The Cardiovascular Institute, Tokyo, Japan; 5University of Toyama, Division of Biostatistics and Clinical Epidemiology, Toyama, Japan

Background: Although novel oral anticoagulants (NOACs) have been available for a few years, the status in patients with non-valvular atrial fibrillation (NVAF), with lower usage of NOACs has been limited in elderly patients due to lack of evidence of its safety. Warfarin has been still widely used in real-world clinical situation and is the most reliable anticoagulant especially in very old patients with aged >85 years. However, there is little information about the status of anticoagulation therapy in very old NVAF patients.

Aim: To elucidate the status of anticoagulation therapy and to clarify the incidence of events in elderly NVAF patients using the data from the J-RHYTHM Registry, a multicenter, nationwide, prospective, observational study.

Method: Consecutive series of all type AF patients were enrolled from 158 institutions of whole 7,937 patients, 4,056 NVAF patients (men 70.8%, 69.8±10.0 years) were eligible for analysis and divided into 3 age groups: <70 years (group Y: 3,365 patients, 70–84 years (group O: 3,711 patient), and ≥ 85 years (group VO). The primary comparison of baseline discalecation/protrusion and the occurrence of events in different international normalized ratio (INR) levels (≤ 1.6, 1.6–1.99, 2.0–2.59, 2.6–2.99, and ≥3.0). Patients were followed for 2 years or until an event of endpoint occurred. In case of any event, an INR value at the event was recorded. Results: The incidence of events in different INR levels (≤ 1.6, 1.6–1.99, 2.0–2.5, 2.6–2.99, and ≥3.0) were higher than those with FIR ≥70%.

Conclusions: Rate of both target INR level of 1.6–2.6 was lower in groups VO (57.8%) than in groups Y (65.1%) and O (66.7%). During a 2-year follow-up period, rates of chronic kidney disease, II–III/IV–V , % 75.7/87.8 24.3/12.2 0.003 and also reduced cost to healthcare service as compared to patients on warfarin.

P6255 | BEDSIDE
International normalized ratio control and 1-year outcomes in patients with newly diagnosed atrial fibrillation: the GARFIELD Registry
1 Technical University of Munich, Munich, Germany; 2Tokai University School of Medicine, Department of Medicine, Kanagawa, Japan; 3University of Birmingham, Birmingham, United Kingdom; 4McMaster University, Hamilton, Canada; 5Aarhus University, Aarhus, Denmark; 6Osaka National Hospital, Osaka, Japan; 7MD Strzshesko Institute of Cardiology, Kiev, Ukraine; 8Ramathibodi Hospital of Mahidol University, Bangkok, Thailand; 9Catholic University Clinical Hospital, Santiago, Chile; 10University of the Witwatersrand, Johannesburg, South Africa

Purpose: To investigate frequency in range (FIR) of international normalized ratio (INR) measurements in relation to demographic, care settings and outcomes after 1 year in patients taking vitamin K antagonists (VKAs) for newly diagnosed non-valvular atrial fibrillation (AF).

Methods: In total, 6305 of 12,458 prospective patients were treated with VKAs at 1-year follow-up in the GARFIELD REGISTRY, and INRs were available for 5115 VKA-treated patients. In this analysis, the target INR range was defined as 2.0–3.0, and the cut-off for poorly controlled INR was FIR <70% and for well controlled INR was FIR ≥70%.

Results: Age and gender did not have a significant influence on FIR, whereas increasing alcohol use and worsening chronic kidney disease were associated with lower FIR. Overall, 25% of VKA-treated patients had FIR <70%. Compared with other settings, a greater proportion of patients (35%) treated at an anticoagulant clinic or thrombosis centre had FIR >70%. Unadjusted rates of death, stroke/systemic embolism, and major bleeding at 1-year follow-up were significantly higher in patients with FIR <70% than those with FIR ≥70%.

Conclusion: These real-world data confirm that suboptimal INR control is associated with an increased risk of severe adverse outcomes. Further analyses for different FIR cut-offs are ongoing.
P6257 | BEDSIDE
The use of dabigatran according to body mass index: the RE-LY experience
1Thomas Jefferson University Hospital, Philadelphia, United States; 2University of British Columbia, Canada; 3Tulane University, New Orleans, Louisiana, USA; 4University of British Columbia, Canada; 5University of Toronto, Toronto, Ontario, Canada; 6Master Hospital, Manchester, United Kingdom; 7Boehringer Ingelheim GmbH & Co, Ingelheim am Rhein, Germany; 8Upstate University, Upstate, Sweden

Introduction:
Many pharmaceuticals (not including dabigatran) are dosed according to body weight.

Objective:
The purpose of this analysis was to understand efficacy and safety outcomes of dabigatran in a specific subset of patients with atrial fibrillation.

Methods:
In the RE-LY trial, 18,113 patients were randomly assigned to 110 mg or 150 mg dabigatran bid vs warfarin dose adjusted to INR 2.0-3.0. The overall sample mean weight was 79.5 kg (10.6 kg). The dabigatran group was categorized into three groups based on the bottom 10% (<22.5 kg/m²), middle 80% (22.5 to <36 kg/m²), and upper 10% (>36 kg/m²). Kaplan-Meier estimated event rates of major bleeding and stroke/SEE (systemic embolization) at 1 year from randomization were reported in BMI groups by treatment. Due to the exploratory nature of the analyses, no p-value adjustment for multiple comparisons was made.

Results:
One year bleeding and stroke/SEE rates were higher in patients with the bottom 10% BMI values compared to middle, and upper BMI subgroups (all P-values ≤0.001). Within each BMI subgroup, the 1 year major bleeding rate trends were comparable or lower in those that received 110 mg dabigatran compared to 150 mg dabigatran and warfarin. In contrast, one year stroke/SEE rates were lower in those that received 150 mg dabigatran, compared to the other two treatments in each BMI subgroup (Table). Conclusion: Patients receiving oral anticoagulation for AF, with a BMI <22.5 kg/m² have an increased risk of major bleeding and stroke/SEE at 1 year, compared to patients with a BMI ≥22.5 kg/m². Differences between treatments within each BMI subgroup are consistent with results in the overall trial.

P6259 | BEDSIDE
The thrombogenic influence of female patients with atrial fibrillation may be caused by left ventricular diastolic dysfunction. Evaluated by propensity score matching
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1Korea University, Anam Hospital, Seoul, Korea, Republic of Korea; 2Korea University Ansan Hospital, Ansan-Si, Korea, Republic of Korea

Background: Female gender is a risk factor for thromboembolism (TE) in atrial fibrillation (AF). But the pathophysiological basis for increased embolic risk in women is not well known, especially in cardiac anatomy and function. The aim of study was to evaluate the cardiac structural and hemodynamic differences between sexes in AF by eliminating well-known clinical risk factors for TE.

Methods: 168 (F: 84; 84) patients with non-valvular AF were matched by age, presence of diabetes or hypertension and type of AF, using propensity score. The size and function of left ventricle (LV) and left atrium (LA) were measured by echocardiography. Parameters of aortic stiffness (Aortic strain, distensibility coefficient) and stiffness index were calculated from ascending aortic diameters in M-mode echocardiography.

Results: The LV mass index and ejection fraction were similar in both groups, but LA volume index was larger in female. Peak mitral E wave velocity, the ratio peak E wave velocity and mitral annular tissue velocity (E/e) to the expiratory flow were higher in female. The deceleration time was shorter in female than that of male. The presence of SEC tended to be more frequent in female than male (p=0.051). Aortic distensibility was lower and aortic stiffness index was higher in female (Table 1).

Table 1

Overall (N=84)
Female (N=84)
Male (N=84)
P-value
Left ventricular mass index (g/m²)
92.3±19.1
94.5±18.9
92.5±19.0
0.926
Left ventricular ejection fraction (%)
51.9±6.9
54.2±5.8
51.7±6.8
0.439
Left atrial volume index (mL/m²)
41.5±14.5
34.4±10.1
41.8±14.5
0.001
Peak mitral E wave velocity (m/s)
72.9±17.4
65.1±16.2
72.6±17.4
0.005
Deceleration time (ms)
162.9±42.3
180.6±41.8
162.9±42.3
0.007
E/e' 10.7±3.1
9.0±3.6
10.6±3.1
0.002
The presence of spontaneous echo contrast (n,%) 34 (40.5)
23 (27.5)
34 (40.5)
0.051
Aortic strain (%) 7.33±3.44
8.06±3.22
7.33±3.44
0.106
Aortic distensibility (cm²·dyn⁻¹·10⁴) 3.33±1.74
3.95±1.95
3.33±1.74
0.018
Aortic stiffness index 3.68±1.28
2.98±1.93
3.68±1.28
0.026

Conclusion: Despite the similar clinical settings, LV diastolic function was worse in female than male. The worse diastolic LV function may induce LA stagnant and this may contribute greater risk of LA thrombus formation in female. LV diastolic dysfunction could be explained by the higher aortic stiffness in female than male.

P6260 | BEDSIDE
Usefulness of the New SAMe-TT2-R2 risk score in identifying patients who do well with vitamin K antagonist therapy in a community-based cohort of patients with non-valvular atrial fibrillation
1Hospital Universitario de Santiago de Compostela, Spain

Background:
Oral anticoagulant therapy (OAC) is the cornerstone treatment in atrial fibrillation (AF) patients at risk of thromboembolic events. However, in therapeutic range (TTR) for OAC therapy is critical to prevent the devastating consequences of AF-related thromboembolic complications. There is now a great interest in identifying patients at risk of having a poorer TTR and therefore could be potential candidates for prescribing a new OAC. Recently, a new predictive model, the SAMe-TT2-R2 was conceived for this purpose. However, the performance of this risk score in an independent datasets is poorly known.

Objective:
To examine the validity of the new SAMe-TT2-R2 score in identifying the probability of anticoagulation, in a sample of outpatients with non-valvular AF.

Methods: Retrospective: Between June, 2012 and December 2013, all consecutive patients with non-valvular AF on a vitamin-K antagonist who were attending the outpatient Cardiology clinics of a tertiary hospital were recruited. We calculated the SAMe-TT2-R2 score in 534 ambulatory patients with non-valvular AF who had ≥12 months of uninterrupted VKA and >7 consecutive INRs at the moment of the study. The Sam-e-TT2-R2 score was validated by checking its discriminative power (c-index) and calibration ability (Hosmer-Lemeshow goodness-of-fit test) with regard to the 25th, 50th, and 75th percentile as the TTR cut-off points.

Results: Mean INR values was 13.9 (SD 1.8); 342 (64%) patients had 15 INR values. The mean TTR (% in Range) was 60% (SD 18). The 25th, 50th, and 75th percentile of the TTR were of 46.7%, 33.3% and 26.7%, respectively. The SAMe-TT2-R2 score values ranged from 0 to 5 (201 [39% patients had >2 points]). The c-index values for the 25th, 50th, and 5th percentiles of the TTR were 0.58 (95%CI 0.52-0.63), 0.65 (95% CI 0.57-0.74), and 0.66 (95%CI 0.58-0.75), respectively. The risk score performed well in terms of calibration as all the p-values of the Hosmer-Lemeshow of test were >0.05 and the c-index was 0.58 (95%CI 0.52-0.63). The performance of the new SAMe-TTR2 score predicts acceptably poor INR control and could potentially aid decision-making in the management of patients with non-valvular AF.

Conclusion: Evaluation of the new SAMe-TT2-R2 score in non-valvular AF patients could potentially aid decision-making in the management of patients with non-valvular AF.
P6261 | BEDSIDE
Analysis of antithrombotic therapy prescription for the prevention of stroke and systemic embolism in patients with atrial fibrillation in clinical practice
R. Linchak, D. Komkov. National Research Center for Preventive Medicine, Moscow, Russian Federation

Antithrombotic therapy (ATT) prescription in patients with atrial fibrillation (AF) is the only medical intervention affecting the prognosis. CHA2DS2-VASc score is commonly used for stroke risk stratification in patients with AF. The latest review of practice guidelines extended the number of indications for anticoagulant therapy, especially for novel anticoagulants (NOAC) prescription.

Purpose: The purpose of this study was to analyze physician’s tactics in ATT prescription for cardiogenic embolism prevention in patients with AF.

Materials: This study involved an anonymous survey conducted among 382 physicians (160 cardiologists and 262 internists). The first question was: “In what number of cases do you use CHA2DS2-VASc score to stroke risk stratification in patients with AF?” The second question asked: “Which antithrombotic drugs do you recommend for cardiogenic embolism prevention in patient with AF?”

Results: The received data showed that 113 physicians (50%) didn’t use CHA2DS2-VASc score, 78 physicians (20%) used it less than in 50% of cases, 111 specialists (29%) – more, than in 50% of cases and 80 (21%) respondents evaluated ATT in all patients with AF. The most prescribed drug for cardiogenic embolism prevention was warfarin (30%), second and third place took acetylsalicylic acid (19%) and clopidogrel (16%) in monotherapy. Dabigatran and rivaroxaban recommended 10% and 8% of physicians respectively. 8% of respondents preferred acetylsalicylic acid and clopidogrel combination, and a small number of physicians recommended other drugs, such as telnine (4%), syncumar (1%), diprydamole (2%), pentoxifylline (2%).

Conclusions: According to results of our study, only 1 of 5 physicians always uses CHA2DS2-VASc score for stroke risk stratification in patients with AF. One third of them recommended warfarin, every fourth prescribed drugs which safety and efficacy for stroke prevention in patients with AF hadn’t been validated in large studies, and only 18% of specialists preferred NOAC as it recommended in actual clinical practice guidelines.

P6262 | BEDSIDE
Silent cerebral infarcts and its association with clinical and echocardiographic factors in patients with non valvular atrial fibrillation
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Purpose: In addition to overt stroke atrial fibrillation (AF), may also cause "silent" cerebral ischemic areas with some neuropsychological consequences. The aims of the study were to evaluate prevalence of large (>15mm) silent cerebral infarcts (SCI) and its association with clinical and echocardiographic factors in patients with AF.

Methods: We examined 134 patients with non valvular AF. Among them 15.67% (n=21) of patients had paroxysmal AF, while others 84.33% (n=113) persistent and long lasting persistent AF. The mean age was 60 ± 10 years, mean left ventricle ejection fraction (LVEF) 55.34%, mean left atrial appendage size (LAAV) 35.63 cm³, mean anamnesis of atrial fibrillation 3.72 years, mean duration of arrhythmia episode 6.78 month, mean CHA2DS2-VASc score 2.23, mean International Normalized Ratio (INR) was 1.5, 70.15% (n=94) of patients were males and 29.85% (n=40) were females. 23.13% (n=31) had diabetes. Arterial hypertension was found in 82.09% (n=110) of patients. There were no cases of prior stroke among patients. All patients underwent anamnesis, neurological, biochemical examinations, transoesophageal (in a case of persistent form), transthoracic echocardiography and multispectral computed tomography of the brain. Severe carotid stenosis was excluded by carotid duplex scanning. According to current recommendations SCI was defined as imaging ≥30 mm in patients with AF, associated with these lesions.

Results: SCI were detected in 33.58% (n=45) of patients, and in total infarcts ≥15mm were detected in 11.19% (n=15) of patients. SCI≥15mm were found in 19.05% of patients with paroxysmal AF and in 9.73% of patients with persistent AF, p=0.2. By neurological examination all patients with SCI≥15mm had some evidences of chronic neurological deficit. SCI≥15mm were significantly associated with CHA2DS2-VASc score ≥2 OR=8.82 (95% CI 6.8-10.9), p=0.014; LAAV≥30 cm³ OR=4.89 (95% CI 3.6-6.2), p=0.012; creatinine clearance (CCI) <90 ml/min OR=4.85 (95% CI 3.3-6.4), p=0.007; complex plaque in aorta ≥5 mm OR=3.34 (95% CI 2.2-4.5), p=0.035; LV wall motion abnormalities OR=4.94 (95% CI 1.8- 5.0), p=0.045; and was not associated with severe SEC 4+ and low LVEF<45%, p=0.05. In the multivariate logistic model, LAAV ≥30 cm³, p=0.017 and CCI<90 ml/min, p=0.035 were independently associated with SCI ≥15mm.

Conclusions: Large SCI ≥15mm were not rare findings in patients with AF. Left atrial appendage dysfunction and chronic renal impairment were independently associated with these lesions.

P6263 | BEDSIDE
Is oral anticoagulation needed in patients with atrial fibrillation, stent implantation and low-moderate risk of stroke?
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Thromboprophylaxis for patients with coronary artery disease and atrial fibrillation (AF) may often be antiplatelet therapy when there is a low or moderate risk of stroke (CHA2DS2 score=0 or 1), particularly when patients experience an acute coronary syndrome or undergo intracoronary stent placement. Some physicians may be reluctant to prescribe oral anticoagulation (OAC) in these patients and several recent guidelines propose slightly different management in such settings. Our goal was to evaluate whether treatment with an OAC is appreciably beneficial in these AF patients.

Methods: All patients with AF and stent implantation seen between 2000 and 2010 in 3 academic hospitals were identified in a database and followed up for mortality, stroke and bleeding events. The CHA2DS2 score was calculated for each patient as initially described, based on 2 points for a history of stroke or TIA, and 1 point each for age >75, hypertension, diabetes, and cardiac failure.

Results: Among all patients seen between 2000-2010, 343 had AF, coronary stent placement and CHA2DS2 score=0 or 1. In these patients, OAC was prescribed on an individual basis for 144 patients (42%) and no OAC in the remaining 199 patients (58%). During a 1-year follow-up, 17 strokes/thromboembolic events (5.0%), 29 major bleedings (8.5%) and 30 deaths (8.7%) were recorded. Patients under OAC had a non significant lower risk of stroke than those not treated with OAC (2.8% vs 6.5%, p=0.14), a non significant higher risk of bleeding (11.8% vs 6.0%, p=0.08) and a lower all-cause mortality (4.9% vs 11.6%, p=0.03).

Conclusions: In one of the largest series of AF patients with coronary stent implantation and a CHA2DS2 score=0-1, prescription of oral anticoagulation was associated with a trend towards lower risk of stroke and higher risk of bleeding, and with a significantly lower mortality.

P6265 | BEDSIDE
Use of novel oral anticoagulants in patients undergoing atrial fibrillation catheter ablation

Background: Novel oral anticoagulants (NOACs) for stroke prevention in atrial fibrillation (AF) are increasingly used in the general AF population, but experience in patients undergoing AF catheter ablation is limited. Here, we report practice patterns and short-term outcomes of different anticoagulation strategies before and after AF ablation.

Methods: Pre- and postablation oral anticoagulation was assessed in 893 consecutive patients (63% male, age 62±10 years). Intravenous heparin use and ac- chieve a therapeutic range of anticoagulation during time of ablation. 30-day bleeding and thromboembolic complication rates were assessed.

Results: Patients presented with Vitamin-K-antagonists (VKA), NOACs or antiplatelets/no anticoagulation in 45%, 39% and 16%, respectively. Among the pa- tients on NOACs, dabigatran, rivaroxaban and apixaban was used in 41%, 56% and 3%, respectively. Among patients with VKA, INR was 2 – 3 in 80%, while NOACs were discontinued 24 hours before the procedure. Using 1414±64540 units of heparin, ACT >300 sec was achieved in 63% of the total population. ACT >300 sec was more frequently achieved with VKA (81%) compared with dabiga- tran (64%), apixaban (67%) or rivaroxaban (53%), although patients treated with NOACs required more heparin (14703 in dabigatran, 15838 in rivaroxaban, 16750 in apixaban vs. 12303 in VKA). While there was only one thromboembolic complica- tion, there were 1.6 bleeding complications (0.9% pericardial tamponade, 0.7% groin); Bleeding rates were 0.6% with dabigatran, 1.4% with rivaroxaban, 1.5% with VKA, 3.2% with low-molecular weight heparin and 3.1% with no prior anticoagulation. NOACs were initiated within 12 - 18 hours after ablation and in- cluded dabigatran, rivaroxaban and apixaban in 25%, 30% and 2%, respectively, while 43% remained on VKA.

Conclusions: There is substantial use of NOACs before and after AF catheter ablation. While bleeding and thromboembolic complications are rare with different regimens, heparin use and ACT are substance-dependent. Further studies are needed to better define the role and specific management of NOACs in the setting of AF catheter ablation.

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P6266 | BEDSIDE
Trends in antithrombotic management of atrial fibrillation after the last update of ESC guidelines: follow-up data from the PREFER in AF registry
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Purpose: The 2012 focused update of the ESC guidelines for the management of atrial fibrillation (AF) recommended the use of anticoagulant therapy for the prevention of thromboembolic events for all patients with AF except those at low risk. However, implementation tends to be incomplete or only applied to a subset of patients. We evaluated the impact of these recommendations in clinical practice of different European countries.

Methods: The PREvention of thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF) recruited unsolicited patients diagnosed as AF in Austria, France, Germany, Italy, Spain, Switzerland and the United Kingdom from Jan 2012 to Jan 2013. We report the data collected at enrolment into the study and follow-up performed 1 year later.

Results: 7243 patients were enrolled from 461 sites. The mean age was 71.5±11 years, 60.1% were male and the mean CHA2DS2-VASc score was 3.4±1.8. Antithrombotic therapy consisted of vitamin K antagonists (VKA) in 65.8% of those with CHA2DS2-VASc score ≥4 (4793 of 5600), and 70.1% of those with CHA2DS2-VASc score of 1 (468 of 668) at the baseline visit. The overall anticoagulation rate at follow-up was slightly lower as compared with baseline (from 82.3 to 80.0%). There was a significant reduction in the use of vitamin K antagonists (VKA) alone (from 66.3 to 61.8%). In parallel, the use of novel oral anticoagulants (NOACs) raised from 6.1 to 12.6%, mainly due to a marked increase of oral factor Xa inhibitors [rivaroxaban, apixaban] (from 1.9 to 6.0%), and in lesser amount due to oral thrombin inhibitors [dabigatran] (from 2.6 to 6.5%). Substantial inter-country differences were noted with higher uptake of NOACs in Germany, France and Spain. Most of the combination treatments judged inappropriate according to the last ESC guidelines were progressively discontinued, such as the combined long-term use of VKA and antiplatelet (AP) agents (from 9.5 to 5.7%), and the use of APs agents as monotherapy (from 11.2 to 8.0%).

Conclusions: The antithrombotic management of AF patients in 2013 in Europe has been substantially adapted to guideline recommendations, and oral anticoagulants are administered to a majority of eligible patients. However, implementation is not complete and there are still prescription patterns that should be adequately targeted.

P6267 | BEDSIDE
Anticoagulation treatment safety with vitamin K antagonists and novel oral anticoagulants within the registry of patients with non-valvular atrial fibrillation
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Background: Thromboembolic events (TEE) in patients with atrial fibrillation (AF) are associated with increased cardiovascular mortality by means of cardioembolic stroke. However, in Russia very small amount of patients are taking anticoagulants. By the way, now cardiologists may also prescribe novel oral anticoagulants (NOAC) with no need of routine laboratory monitoring and dose changing but routine clinical experience with NOAC is still limited.

Aim of the study: For detализation of actual state of art in routine clinical practice of anticoagulant treatment registry (RAFAC – Registry of patients with Atrial Fibrillation with and without AntiCoagulants) of patients with non-valvular AF was organized on the basis of anticoagulant clinic.

Subjects: Up to date 681 patients with non-valvular AF are included in the RAFAC registry; 70.2% are women (mean age – 70.4 years) and 29.8% - men (mean age – 63.2 years). 667 patients (98%) had at least 1 point according to CHA2DS2-VASc score. Among those only 423 (63.4%) were taking anticoagulants: 309 patients (73.0%) were taking warfarin and 114 patients – NOAC (27.0%); 22.4% from all anticoagulated patients took dabigatran and 4.6% - rivaroxaban.

Results: Within 1 year no TEE were registered in all the patients in the Registry. Minor bleedings were seen in 6.5% of anticoagulated women and 9.5% of anticoagulated men, major bleedings were not registered. Only few (21%) patients on warfarin had war time within the therapeutic range (TTR) more than 60% as it should be. Bleedings occurred significantly higher in patients on warfarin (8.6%) in comparison with patients on NOAC (4.3%; p<0.05). As expected, mostly frequent bleedings occurred in patients with 6 points according to CHA2DS2-VASc (12.7% of patients with bleedings). However, patients with only 1 point according to CHA2DS2-VASc had also rather high bleeding rate (8.5%) that should be discussed in terms of necessity of anticoagulation in these patients with low-intermediate risk of TEE.

Conclusions: Registry RAFAC data confirm significant underuse of oral anticoagulants for thromboembolism prevention in patients with non-valvular AF even in routine medical care of large cardiovascular centers. Less than quarter of patients on warfarin are in >60% of TTR that may partly explain higher bleeding rates in patients of vitamin K antagonists and in future may also leads to low efficacy of such treatment. NOAC (dabigatran and rivaroxaban; apixaban has been registered in Russia only in the end of 2013) confirm their safety in routine practice in this group of patients.

P6268 | BEDSIDE
Comparison of atrial fibrillation patients with and without an initial awareness of rhythm disturbance in the PREFER in AF registry for outcomes and management differences

Background: Patients with atrial fibrillation (AF) may present initially with or without symptomatic awareness of AF related stroke. A 64-slice CT was performed to evaluate the Embolic risks in atrial fibrillation 1113 (volume at P wave beginning -minimal volume)/volume at P wave beginning ±1.8. An- d 2 (4793 ±267) patients had permanent AF . Percentages were 22%, 26%, 7% and 45% in the asymptomatic patients, respectively. CHA2DS2-VASc scores on average were 3.4 for S and 2.9 for AS patients.

To date, at follow-up of 6412 patients with 1 year data, additional strokes had occurred in 0.9% (54/5695) of S and 1.6% (8/501) of AS patients with respective TIA rates of 0.6% (37/5695) and 1.2% (6/501). Re: medications, 11% of S and 9% of AS were not on anti-platelet or anti-thrombotic medications, with 13% in both groups on a novel oral anticoagulant (NOAC) at the follow-up visit (Table 1).

Table 1. Medication intake at Baseline and Follow-up

<table>
<thead>
<tr>
<th></th>
<th>Patients with symptoms (S) N=5695</th>
<th>Asymptomatic patients (AS) N=501</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No anti-platelet or anti-thrombotic medication</td>
<td>337</td>
<td>5.9</td>
</tr>
<tr>
<td>NOAC</td>
<td>357</td>
<td>6.3</td>
</tr>
<tr>
<td>Follow-up Visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No anti-platelet or anti-thrombotic medication</td>
<td>540</td>
<td>11.2</td>
</tr>
<tr>
<td>NOAC</td>
<td>628</td>
<td>13.0</td>
</tr>
</tbody>
</table>

Conclusions: Our data show that in a large registry of contemporary management of AF, stroke and TIA outcomes are similar for patients with and without symptomatic awareness of AF over 1 year follow-up. Similar low proportions of patients are started on novel oral anti-coagulants (NOAC), but more patients are not taking either anti-platelet or anti-thrombotic therapy, which is a cause for concern.

P6269 | BEDSIDE
Functional remodeling rather than morphological character of left atrium is a powerful predictor for the occurrence of stroke in patients with atrial fibrillation
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Introduction: Optimal identification of the high risk patients for stroke is a crucial issue in management of atrial fibrillation (AF). In addition to the clinical risk stratification schemes, multi-detector computed tomography (MDCT) can also confer additional information to select the vulnerable patients for stroke.

Methods: We studies 118 patients (80 male). Group I included 21 controls, group II included 68 patients with AF and no history of stroke, group III included 29 patients with AF related stroke. A 64-slice CT was performed to evaluate the Functional remodeling rather than morphological character of left atrium (LA) is a powerful predictor for the occurrence of stroke in patients with atrial fibrillation 1113. The pouch of LA and four types of LAA morphologies (Cactus, Chicken Wing, Windsock and cauliflower) were depicted. In addition, the active transport function [volume at P wave beginning - minimal volume]/volume at P wave begin-
ning] and passive transport function [(maximal volume- volume at P wave beginning)/(maximal volume)] of LA and LAA were assessed by dynamic CT.

**Results:** The gender, body mass index were similar among three groups. However, the age was elder and CHADS2 score was higher in group III. The incidence of LA pouch was similar among the three groups (33% vs 29% vs 28%, p=0.90). The distribution of different LAA morphologies were also similar among the three groups (p=0.11). On the other hand, the active transport function of LA and LAA (LA: 0.31±0.06 vs 0.23±0.14 vs 0.11±0.10; LAA: 0.48±0.17 vs 0.34±0.21 vs 0.13±0.19, both p<0.001) were significantly reduced in patients with AF and stroke. But the passive transport function of LA and LAA were similar among the three groups (P=0.14 for LA, p=0.43 for LAA)

**Conclusion:** LA pouch is not an uncommon finding and it is not associated with the stroke in patients of AF. The categories of LAA morphologies among the three patient groups are not significantly different. Our findings showed that the impaired active transport function of LA and LAA correlated significantly with the occurrence of stroke in patients with AF.

**P6270 | BEDSIDE**

**Prevalence of left atrial appendage thrombus according to CHADS2 score level in patients with atrial fibrillation**


Transesophageal echocardiography (TEE) is performed routinely in patients with AF of >48h in order to exclude left atrial appendage thrombus (LAA-T) prior to cardioversion. The purpose of this study was to assess the prevalence of LAA-T according to the CHADS2 score.

**Methods:** We analyzed all TEEs performed for patients with AF of >48h, prior to cardioversion. Patients with significant valvular disease, prosthetic valve, or atrial fibrillation who are on anticoagulation were excluded.

**Results:** A total of 1504 TEEs were reviewed. The mean age was 73.6±10 years, 708 (47%) females, and mean CHADS2 score was 2.3±1.2. (median [interquartile range] was 2 [1–3]). LAA-T was detected in 165 (11%). Figure 1 summarizes the % of patients with LAA-T at each CHADS2 score level. Multivariate logistic regression with all components of CHADS2 score as covariates revealed 3 independent risk factors for LAA-T: prior stroke (OR 2.32 95%CI [1.52–3.58], p<0.0001), CHF (OR 1.70 95%CI [1.22–2.38], p=0.002), and DM (OR 1.55 95%CI [1.10–2.02], p=0.012).

**Conclusion:** The odds of finding an LAA-T in patients with AF of >48h increased with the CHADS2 score level. No LAA-T was detected in patients with AF and CHADS2 score of 0. It might be reasonable to omit TEE as a screening examination prior to cardioversion in AF patients with CHADS2 score of 0, but patients with score ≥1 require TEE in order to exclude LAA-T prior to cardioversion.

**P6271 | BEDSIDE**

**CHA2DS2-VASc vs. CHADS2 at predicting the risk of stroke and death in a community-based cohort of patients with non-valvular atrial fibrillation who are on anticoagulation**


**Background:** CHA2DS2-VASc risk score was seen to be more reliable than the CHADS2 score for identifying patients with non valvular atrial fibrillation (AF) who are at risk of stroke. The predictive superiority of the CHA2DS2-VASc over the CHADS2 in anticoagulated patients with non valvular AF is not well known.

**Aim:** To assess the predictive ability of CHA2DS2-VASc and CHADS2 in predicting the composite endpoint of stroke and death in non valvular AF patients on vitamin K antagonist.

**Methods:** Retrospectively, from June/2012 to December/2013, 534 patients with non-valvular AF on vitamin-K antagonist who were attending the outpatient Cardiology clinics of a tertiary hospital in Spain were recruited. The Cox regression analyses were used to assess the association (in terms of hazard ratio “HR”) between each of the two risk schemes and the study endpoint. Data regarding stroke and death was collected at 10 (SD=3) months. The performance of both risk scores was computed by using area under the ROC (receiver operating characteristics) curves [AUC].

**Results:** Mean age was 74 (SD 11) years, and 216 (40.4%) were women. CHADS ranged from 0 to 6 points, while CHADS-VASc ranged from 0 to 12 points. According to CHADS scheme there were 8.8% at low risk (0 points), 20% at intermediate risk (1 point), and 71.2% at high risk (>2 points) of non fatal stroke and death at 10 (SD 3) months. However, according to CHA2DS2-VASc, 5.4%, 5.8%, and 89% of patients were classified as having low, intermediate and high risk, respectively. At 10 (SD 3) months, 14 events were recorded: 5 patients suffered a non fatal stroke and 9 patients died. 13 out of the 14 events were found in the high risk category of the CHA2DS2-VASc (one event in the intermediate risk category). In contrast, using the CHADS2 classification system, 11 of 14 events occurred in the high risk strata, 2 of 14 in the intermediate risk strata, and 1 of 14 in the low-risk category. HR for the association between the CHA2DS2-VASc (as a continuous category) and stroke/death during follow-up was 1.4 (95%CI 1.007–2.041; p=0.046), similar to the HR obtained by using the CHADS2 score (HR 1.4 [95%CI 1.001–2.248]; p=0.049). CHA2DS2-VASc exhibited a better predictability than did CHADS2 as was shown by the AUC: 0.67 [95%CI 0.52 to 0.86; p<0.03] vs. 0.63 [0.46 to 0.79; p=0.11].

**Conclusion:** In our study the rate of stroke in patients with non valvular AF was nearly 1% despite anticoagulation. CHA2DS2-VASc outperformed the old CHADS2 in predicting the risk of stroke and death in these patients.
### Abstract P6274 – Table 1

<table>
<thead>
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<th>Outcome (ITT)</th>
<th>Pacemaker or ICD</th>
<th>Annual rate dabigatran 110 mg bid</th>
<th>Annual rate dabigatran 110 mg bid</th>
<th>Annual rate warfarin</th>
<th>DE 110 mg vs. warfarin</th>
<th>DE 150 mg vs. warfarin</th>
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<tbody>
<tr>
<td>Stroke &amp; systemic embolism</td>
<td>Yes/No</td>
<td>1.47/1.55</td>
<td>1.18/1.10</td>
<td>2.20/1.65</td>
<td>0.67 (0.38, 1.17)/0.94 (0.76, 1.17)</td>
<td>p-inter = 0.26</td>
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<tr>
<td>Death</td>
<td>Yes/No</td>
<td>3.83/3.74</td>
<td>3.87/3.61</td>
<td>4.54/4.07</td>
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<td></td>
</tr>
<tr>
<td>Vascular death</td>
<td>Yes/No</td>
<td>1.87/2.37</td>
<td>2.49/2.22</td>
<td>3.55/2.92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI (including silent)</td>
<td>Yes/No</td>
<td>1.10/0.79</td>
<td>0.92/0.79</td>
<td>0.99/0.59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke/SEE. MI (incl. silent) or vascular death</td>
<td>Yes/No</td>
<td>4.71/14.11</td>
<td>3.67/3.56</td>
<td>5.68/4.10</td>
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</table>

#### Conclusions:
In patients with atrial fibrillation, initiating treatment with dabigatran was not associated with higher frequency of subsequent PPI use, as compared with warfarin. However, among those who shifted from warfarin to dabigatran; PPI use was more frequent than those initiated on warfarin. The results indicate that dabigatran is not associated with a higher risk of gastrointestinal adverse reactions, compared with warfarin, while shifts from warfarin to dabigatran, may have higher propensity for gastrointestinal adverse reactions.

### P6276 | BEDSIDE

#### Atrial fibrillation and anticoagulation under use in patients with permanent pacemaker: risk factors - cognitive impairment?

N. Diaconu1, C. Grati1, A. Grosu1, V. Racila1, O. Gherman2, G. Pavlic2

1 Institute of Cardiology, Chisinau, Moldova, Republic of; 2 State University of Medicine and Pharmacy, Chisinau, Moldova, Republic of; 3 Institute of Neurology and Neurosurgery, Chisinau, Moldova, Republic of

#### Introduction:
Atrial fibrillation (AF), in addition to macroembolic complications, may also produce multiple cerebral ischemic areas due to microembolic phenomena and transient hyperfusion, eventually leading to a progressive cognitive impairment and even to claimed vascular dementia.

#### Aims:
To determine whether atrial fibrillation (AF) in stroke-free patients with cardiac pacing is associated with impaired cognition and structural abnormalities of the brain and to determine the proportion of these patients who were receiving anticoagulation to prevent thromboembolic stroke.

#### Methods:
Patients with non-valvular atrial fibrillation (NVAF) with permanent pacemaker and no history of stroke, and transient ischemic attacks were consecutively examined. To investigate the cognitive status, subjects underwent the neuropsychological rating scale Mini Mental State Examination (MMSE). Patients with cognitive disturbances underwent cerebral CT and TEE.

#### Results:
The patients with AF and ECS (mean age 68 ± 1.06 years; 54% M) were evaluated. Forty five patients (42%) diagnosed with AF had no prior documented diagnosis of AF, and the majority had no symptoms suggesting AF. According to CHADS2-VASC score 73.1% of patients were in high thromboembolic risk (group I), 22.3% in moderate risk (group II) and 4.6% in low risk (group III).

#### Conclusion:
Atrial fibrillation is a factor which correlating with low cognitive function and even to claimed vascular dementia. This might prevent not only major cerebrovascular accidents, but also the less obvious clinical outcome of cognitive function loss.
tional risk factor for stroke were randomized to apixaban or warfarin and followed for a median of 1.8 years. Plasma concentrations of IL-6 and CRP were analyzed in samples obtained at randomization. Association between quartile groups of IL-6 and CRP and clinical outcomes were analyzed by Cox regression adjusted for known cardiovascular risk factors and other cardiac biomarkers.

**Results:** The IL-6 median value was 2.3 ng/mL with interquartile range 1.5-3.9 ng/mL. The CRP median value was 2.2 mg/mL with interquartile range 1.0-4.8 mg/mL. The relations between the IL-6 and CRP quartiles and outcomes are shown in the table. There was no interaction between inflammation marker levels and the effects of apixaban versus warfarin on outcome events.

**Conclusions:** In anticoagulated patients with AF, inflammatory activation markers are not associated with increased risk of stroke, despite the significant association with mortality. The IL-6 level is also related to the risk of bleeding.

---

**Table 1. Outcomes according to IL-6 and CRP**

<table>
<thead>
<tr>
<th>Outcome IL-6 (quartiles in rows)</th>
<th>CRP (quartiles in rows)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Events</strong></td>
<td><strong>HR (G group 1 as reference)</strong></td>
</tr>
<tr>
<td>(%)/yr</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Stroke or systemic embolism</td>
<td>85 (1.06)</td>
</tr>
<tr>
<td>88 (1.30)</td>
<td>1.02 (0.77–1.36)</td>
</tr>
<tr>
<td>121 (1.71)</td>
<td>1.37 (1.02–1.83)</td>
</tr>
<tr>
<td>Death</td>
<td>137 (1.70)</td>
</tr>
<tr>
<td>+0.16 (0.90–1.44)</td>
<td>148 (2.36)</td>
</tr>
<tr>
<td>1.14 (0.90–1.44)</td>
<td>148 (2.36)</td>
</tr>
<tr>
<td>1.14 (0.90–1.44)</td>
<td>148 (2.36)</td>
</tr>
</tbody>
</table>

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**P6279 | BEDSIDE**

The morphological and decreased flow velocity of left atrial appendage are strong predictors of stroke in nonvalvular atrial fibrillation

**Introduction:** Left atrial appendage (LAA) is an important source of thromboembolism in patients with atrial fibrillation (AF). However, the remodeling of LAA in nonvalvular AF patients with stroke is not completely revealed. This study evaluated whether LAA remodeling is affected by stroke and LAA flow velocity (LAAFV) in nonvalvular AF patients.

**Methods:** In 238 AF patients, transesophageal echocardiography and cardiac computed tomography were performed. The dimension, morphology and flow velocity of the LAA in NOAC patients were compared with NOAC patients with stroke group (n=67, mean age 66.0 ± 9.3 years) and without ischemic stroke (no-stroke group, n=151, mean age 55.9 ± 10.0 years). LAA morphologies were divided into chicken-wing and other types including cuff-like, sinusoid and cactus.

**Results:** Compared with no-stroke group, the stroke group had larger LAA dimension (4.7 ± 0.8 cm vs. 4.3 ± 0.6 cm, p < 0.001), larger LAA orifice area (4.5 ± 1.5 vs. 3.0 ± 1.1 cm², p < 0.001), and slower LAA flow velocity (36.3 ± 19.1 vs. 54.7 ± 19.8 cm/s, p < 0.001). Patients with chicken-wing type LAA (n=101) had lower proportion of stroke than those with other type LAA (n=137) (18%, vs. 40%, p < 0.001). LAA flow velocity was negatively correlated with LAA orifice size (R= -0.46, p < 0.001). Patients with chicken-wing LAA had smaller LAA orifice area (3.6 ± 1.6 vs. 3.2 ± 1.0 cm², p < 0.001) and higher LAA flow velocity (55.2 ± 21 vs. 44.2 ± 21 cm/s, p < 0.001) than those with other type LAA. After adjustment for multiple potential confounding factors including CHA2DS2-VASC score, persistent AF, LAA velocity, LAA morphology other than chicken-wing was found to be significant risk factor of stroke (OR 2.9, 95% CI 1.5-6.0, p=0.003).

**Conclusion:** LAA morphology was closely related with stroke. This finding might be explained by the change of orifice enlargement and LAA flow velocity according to the LAA morphology.

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**P6280 | BEDSIDE**

Clinical management and outcome of major bleeding in patients on oral anticoagulant treatment: results from the climbing study

**Introduction:** The incidence of major bleeding (MB) is about 3% per year in patients on oral anticoagulant treatment: results from the climbing study (CLIMBING). Major bleeding was defined according to ISTH definition. The primary outcome of the study was death occurring during the hospital stay. Secondary outcomes were major thromboembolic complications (acute coronary syndrome, ischemic stroke, systemic cardioembolism, and pulmonary embolism).

**Results:** As for February 1st, 2014, 312 patients were included in this study, 186 with intracranial hemorrhage (ICH). All patients were on treatment with vitamin K antagonists.

**Conclusion:** This meta-analysis suggests that NOAC may be preferable to warfarin for peri-AF ablation anticoagulation. They are associated with a decrease in bleeding and no significant increase in embolic events compared to WB.
INR (OR 1.24; 95% CI 1.07-1.43) were independently associated with non-ICH MB. Among HASSBLED items, previous stroke (OR 2.16; 95% CI 1.07-4.34; p 0.03) was independently associated with INCH while abnormal renal function (OR 2.13; 95% CI 1.18-3.85; p 0.01), previous bleeding (OR 4.15; 95% CI 9.29-8.95; p <0.001), antiplatelet (OR 3.31; 95% CI 1.19-9.18; p 0.02) and NSAIDS usage (OR 13.69; 95% CI 1.38-135.91; p 0.02) were independently associated with non-ICH MB.

PCCs were most commonly used in patients with ICH (52 vs. 24%; p <0.001) while fresh frozen plasma was most commonly used in patients with non-ICH MB (10 vs. 7%; p 0.01).

In-hospital death occurred in 68 patients (21%), ICH (OR 4.28; 95% CI 1.90-9.66; p <0.001), trauma (OR 2.09; 95% CI 1.06-4.15; p 0.03) and re-bleeding during the hospital stay (OR 4.13; 95% CI 1.99-8.58; p <0.001) were independent predictors of mortality. ICH at admission (p=0.001) and ICH at discharge (p=0.001) were independent predictors of outcomes. Among the 312 study patients, 7 had an acute coronary syndrome (2 ICH patients), 5 an ischemic stroke (3 ICH patients), and 4 a pulmonary embolism (3 ICH patients) during the hospital stay. The incidence of thromboembolic complications was 7% in patients receiving and 3.6% in those not receiving PCCs.

Conclusions: Among patients with MB while on oral anticoagulant treatment the risk for death is not associated with HASSBLED score. The association between thromboembolic complications and PCC use need further evaluation.

P6281 | BEDSIDE
Long term follow-up in patients with atrial fibrillation under 55 years old: Can we predict mortality?
G. Vaneiro, Casmu Arrhythmia Service, Montevideo, Uruguay

Atrial fibrillation in young patients is no so common; incidence is below 0.5% according to the age group considered. Compared to older patients differences are numerous. They have less co-morbidities, and a lower incidence of thrombo-embolic and bleeding. In the young AF is most often paroxysmal and mortality is lower. Our objective was to evaluate mortality in young patients with diagnosed AF and a extended follow-up, particularly the relationship with thrombo-embolic risk scores and the type of AF.

Patients and methods: We studied 399 patients who were diagnosed with AF below age 56. The population belongs to our AF-cohort of 3196 patients, which started on Nov-1995. Data was collected until Jan-2014. Demographics, EHRA symptoms, comorbidities, medication and the CHADS2/CHA2DS2VASc score, type of AF at the first consult and at the last consultation were annotated as well as complications, hospital admissions and mortality.

Results: Mean age was 45±9 (range 17-55 years), with a mean follow up of 98±52 (8-229 months), ten patients were lost to follow-up. 22% of the patients were females.

A CHADS2/CHA2DS2VASc score equal or above 2 was calculated in 28% of the population. 53% presented with paroxysmal AF, 42% with persistent and 3.5% with permanent AF. On the last evaluation 51% had paroxysmal, 23% persistent and 24% permanent AF.

27 (6.9%) patients died, the Kaplan-Meier survival curves showed that a CHADS2/CHA2DS2VASc score 2 was significantly associated with survival. We also observed that the progression to permanent AF was significantly associated with mortality. When we combined both variables the survival curves were significantly different.

Conclusion: In young patients with AF, the combination of a high CHADS2/CHA2DS2VASc score and the progression to permanent AF appears to have a detrimental effect on survival.

P6282 | BEDSIDE
The prognostic significance of cardiac structure and function in atrial fibrillation: the ENGAGE AF-TIMI 48 Echocardiographic Substudy

Atrial fibrillation (AF) is associated with increased risks for thromboembolic complications. Measurement of endothelial dysfunction has been validated in large population studies as strong predictor of adverse cardiovascular outcomes. Although paroxysmal AF usually evolves to chronic AF, the role of endothelial dysfunction remains undetermined.

Methods: In this cohort study we enrolled 152 consecutive subjects with AF. Thirty-five subjects had paroxysmal AF and 117 chronic (long standing persistent or permanent) AF. Flow mediated dilation (FMD) was measured as an index of endothelial function. All subjects underwent two-dimensional echocardiographic assessment.

Results: Mean age was 79±10 years vs. 65±15 years, p=0.002, had impaired LVEF (44±14 vs. 53±10, p=0.001) increased LAdiam/BSA (18±3 vs. 20±3, p=0.001), decreased LAVol/BSA (17±3 vs. 16±3, p=0.001), increased LVMass/BSA (126±44 vs. 118±35, p=0.001), and impaired creatinine clearance (64±18 ml/min/1.73m² vs. 83±20 ml/min/1.73m², p=0.001). Importantly, subjects with chronic AF had impaired FMD compared to subjects with paroxysmal AF (4.0±1.76% vs. 6.83±1.38%, p<0.001). In addition, there was an inverse correlation between FMD and LAdiam/BSA (r=-0.53, p<0.001), LAVol/BSA (r=-.48, p<0.001), LVMass/BSA (r=-0.36, p=0.007) and a positive correlation between FMD and LVEF (r=0.30, p=0.003).

Conclusions: Endothelial dysfunction is associated with atrial remodeling in patients with AF and is implicated in the progression from paroxysmal to chronic AF.

P6285 | BENCH
Depressed pitx2 levels in patients with 4q25 risk variants is linked to hallmarks of atrial fibrillation such as right atrial myocyte hypertrophy and increased frequency of transient inward currents

Purpose: Atrial fibrillation (AF) has been associated with 4q25 risk variants that presumably modulate the expression or activity of the transforming growth factor beta type 1 receptor (TGFβR1). The relationship between 4q25 variants, pitx2 levels and cardiac electrophysiology in patients with AF has not been previously assessed.

Methods: Perforated patch-clamp technique was applied to right atrial myocytes from patients with or without AF or atrial chamber-specific pitx2+/− mice in order to measure cell capacitance, ionic currents, or spontaneous action potentials. Protective (CCGG) and risk (non-CCGG) 4q25 variants were identified by DNA sequencing and pitx2 expression was assessed on various samples in order to measure cell capacitance, ionic currents, or spontaneous action potentials. Protective (CCGG) and risk (non-CCGG) 4q25 variants were identified by DNA sequencing and pitx2 expression was assessed in various samples in order to measure cell capacitance, ionic currents, or spontaneous action potentials.

Results: Eight samples with 4q25 risk variants had twofold lower pitx2 levels than those with protective 4q25 variants. Moreover, myocytes from 13 risk variants without AF had larger cell capacitance than myocytes from 14 patients with the protective variant (79±10 vs. 53±6 pF, p<0.05). Myocytes from AF patients had a larger cell capacitance than those from control patients with the protective variant (107±10 pF) and 7 protective (103±9 pF) variants. As expected, L-type calcium current amplitude was smaller in patients with than without AF (1.3±0.3 vs. 2.8±0.3 nA/pF, p<0.01), but there were no differences among risk and protective variants in patients with AF.

Conclusions: Non-CCGG (risk) 4q25 variants are associated with a smaller cell capacitance, larger cell area and larger cell capacitance in patients with AF. Moreover, myocytes from AF patients had a larger cell capacitance than those from control patients.
out AF (2.6±0.4 vs. 3.0±0.4 pAF/P, p=0.5). By contrast, myocytes from the same patients with risk variants had a significantly higher frequency of spontaneous transient inward currents (II) than those with the protective variant (1.2±0.4 vs. 0.2±0.1 events/min, p<0.05). Comparison of right atrial myocytes from 6 atrial-specific pig2f−/− and 4 wild type (WT) mice confirmed that partial loss of pig2 function increases cell capacitance (89.6±8 vs. 44.1±5 pF, p<0.02). Moreover, the frequencies of spontaneous membrane depolarizations and II were proportional, and spontaneous action potentials were more frequent in pig2f−/− mice than in WT (1.7±0.7 vs. 0.2±0.1 events/mm, p<0.05). In addition, the voltage threshold for spontaneous AF firing was shifted from -60±5 mV in WT to -75±3 mV in pig2f−/− (p<0.05).

Conclusions: Patients with 4q25 risk variants have reduced pig2 levels and right atrial myocytes from those without AF already have cellular electrophysiological hallmarks of spontaneous activity, such as increased size and II frequency. These features are reproduced in heterozygous pig2f−/− mice, demonstrating that pig2 deficiency in 4q25 variants increase the risk of arrhythmicogenic afterdepolarizations.

P6286 | SPOTLIGHT
New inflammatory predictors for non-valvular atrial fibrillation: echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio

1 Hault Acet1, 2 Faruk Ertas1, 3 Mehmet Ata Akil1, 4 Mustafa Oylumlu1, 5 Nihat Pelev1, 6 Mehmet Zihni1, 7 Murat Yıksı1, 9 Zeynep Kaya1, 10 Mehmet Siddik Ulgen1, 11 Dicle University, cardiology, Diyarbakir, Turkey; 2Mevlana University Faculty of Medicine, Cardiology, Konya, Turkey

Objectives: The objective of this study was to investigate the relationship of echocardiographic epicardial fat thickness (EFT) and neutrophil to lymphocyte ratio (NLR) with different types of non-valvular atrial fibrillation (AF) in a clinical setting.

Methods: A total of 197 consecutive patients were enrolled in the study. Seventy-one patients had paroxysmal non-valvular AF, 63 patients had persistent/permanent non-valvular AF, and 63 patients had sinus rhythm (control group). EFT was measured with echocardiography, while NLR was measured by dividing neutrophil count by lymphocyte count.

Results: EFT was significantly higher in patients with paroxysmal non-valvular AF compared with those in the sinus rhythm group (6.6±0.7 mm vs. 5.0±0.9 mm, p<0.001). Persistent/persistent non-valvular AF patients had a significantly larger EFT compared with those with paroxymal AF (8.3±1.1 mm, vs. 6.6±0.7 mm, p<0.001). EFT had a significant relationship with paroxysmal non-valvular AF (odds ratio 4.672, 95% CI: 2.329 to 9.371, p<0.001) and persistent/permanent non-valvular AF (OR 24.276, 95% CI: 9.285 to 63.474, p<0.001). NLR was significantly higher in those with paroxysmal non-valvular AF compared with those in the sinus rhythm group (2.5±0.6 vs. 1.8±0.4, p<0.001). Persistent/permanent non-valvular AF patients had a significantly larger NLR when compared with paroxysmal non-valvular AF patients (3.4±0.5 vs. 2.5±0.6, p=0.001). NLR (≥2.1) had a significant relationship with non-valvular AF (OR: 11.313, 95% CI: 3.205 to 42.306, b: 2.426, p=0.001).

Conclusion: EFT and NLR are highly associated with types of non-valvular AF independent of traditional risk factors. EFT measured by echocardiography and NLR appear to be related to the duration and severity of AF.

P6288 | BEDSIDE
Role of masked coronary heart disease in patients with recent onset atrial fibrillation and troponin elevations

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Background: Patients with recent onset atrial fibrillation (AF) and troponin (cTnI) elevations show poor outcomes. Coronary heart disease (CHD) might be cause, consequence or innocent bystander.

Objective: To recognize and treat CHD to avoid adverse events.

Methods: Patients with recent onset AF participated in the study. The exclusion criteria were acute coronary syndrome and severe comorbidities. Patients managed with standard care (Group 1, n=1086, 2010-2011 years) were compared to patients managed with tailored care inclusive of echocardiography and stress testing (Group 2, n=217, 2012-2013 years).

End-point: The composite of ischaemic vascular events inclusive of stroke, acute coronary syndrome, revascularization and cardiovascular death at six-month follow-up.

Results: Out of 4008 patients considered, 2141 with recent onset atrial fibrillation were enrolled; 183 showed cTnI elevations, 92 in group 1 and 91 in group 2. At univariate analysis abnormal cTnI elevations, known coronary heart disease, age, hypercholesterolemia, diabetes mellitus were independent predictors of the primary end-point. However, only cTnI elevations, known ischaemic heart disease and age were predictors of the end-point at multivariate analysis. Overall 2 versus 7 patients in group 1 and 2 respectively, (p=0.033), underwent revascularisation. Eventually, 16 patients in group 1 versus 5 patients in group 2 reached the end-point (p=0.019 table). Patients of group 2 were managed as follow: 35 were admitted of whom 15 with positive stress testing and 20 with high cTnI values (mean values: 0.64±1.01 ng/ml). Fifty-six patients were discharged with negative stress testing (n=13) or very low cTnI values (n=43, mean values 0.29±0.30 ng/ml).

Primary composite end-point

<table>
<thead>
<tr>
<th>Total</th>
<th>Stroke</th>
<th>CHD</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=98)</td>
<td>16 (17.4%)</td>
<td>4 (4.3%)</td>
<td>10 (10.7%)</td>
</tr>
<tr>
<td>Group 2 (n=91)</td>
<td>5 (5.5%)</td>
<td>1 (1.1%)</td>
<td>4 (4.4%)</td>
</tr>
<tr>
<td>p value</td>
<td>0.019</td>
<td>0.368</td>
<td>0.163</td>
</tr>
</tbody>
</table>

CHD, coronary heart disease; Death, cardiovascular death.

Conclusions: In patients with AF and cTnI elevations, tailored care inclusive of echocardiography and stress testing succeeded in recognizing and treating “critical” masked CHD avoiding adverse events.
P6290 | BEDSIDE

Left atrial phasic functions and plasma NT-proBNP levels predict atrial fibrillation development in patients with hypertrophic cardiomyopathy: A prospective follow-up study

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Purpose: Atrial fibrillation (AF) is the most common arrhythmia in patients with hypertrophic cardiomyopathy (HCM) and associated with morbidity. NT-pro-BNP levels are shown to be elevated in patients with HCM. We investigated if left atrial (LA) phasic functions and plasma NT-proBNP levels could predict future development of AF in HCM.

Methods: Seventy patients with HCM who were in sinus rhythm at the time of their recruitment were enrolled. The following LA volumes (LAVs) were measured by Simpson’s rule: maximal volume (Vmax) during left ventricular (LV) end-systole, minimal volume (Vmin) just before mitral valve closure and LA volume before atrial contraction (VpreA) at the onset of the P wave on the simultaneously recorded ECG. Left atrial total emptying fraction (LATEFI), LA active emptying fraction (LAAEFI), LA passive emptying fraction (LAPEIF) were calculated by using these LAVs. LV mass index (LVM) was calculated by the method of Devereux. E/E' ratio of the LV septal wall (E/E' septal) was obtained to characterize LV filling by using tissue Doppler. NT-pro-BNP levels of the patients were measured on the same day with echocardiographic study.

Results: The patients were followed up for 37.1±1.9 months. During follow-up 16 patients (8 men, 54.8±12.05 years) developed AF. When patients with AF (group 1) were compared with the ones without AF (group 2, n=54) significant differences were observed between groups in terms of LAEF (p=0.002), LAVI (p<0.001), LAAEFI (p=0.005), E/E' septal (p=0.035), LVM (p=0.032) and logNT-proBNP (p=0.004). Intraobserver analysis LAVI (odds ratio [OR], 1.04; 95% confidence interval [CI]: 0.99-1.09; p=0.002), LAEF (OR), 0.99; 95% CI: 0.89-1.08; p=0.007), LATEFI (OR), 1.01; 95% CI: 0.89-1.13; p=0.018 and NT-proBNP levels (OR), 4.25; 95% CI: 0.68-26.71; p=0.005) predicted AF development. An NT-proBNP cut-off value of 980 pg/mL predicted future AF occurrence with 72% specificity and 83% sensitivity [AUC=0.772 (95% CI: 0.651-0.893)]; a LATEFI cut-off value of 49% with 63% specificity and 76% sensitivity [AUC=0.755 (95% CI: 0.63-0.879)]; a LAAEFI cut-off value of 34% with 63% specificity and 74% sensitivity [AUC=0.702 (95% CI: 0.579-0.887)]; a LAVI cut-off value of 48 mL/m² with 72% specificity and 88% sensitivity [AUC=0.818 (95% CI: 0.707-0.93)].

Conclusion: In patients with HCM, LA reservoir and pump functions and plasma NT-proBNP levels predict AF development. This observation might be helpful in early detection of patients who are prone to AF development.

P6291 | BENCH

Degree of fatty infiltration contributes to complexity of the substrate for atrial fibrillation in goat left atria


Purpose: Progression of atrial fibrillation (AF) is caused by electrical and structural remodeling. Fibrosis and altered connexin expression are known alterations in atrial tissue structure contributing to the development of an AF substrate. To date, the effect of fatty infiltration on AF conduction has not been studied. We hypothesize that the degree of fatty infiltration is an important determinant of AF progression and AF complexity in goat left atria (LA).

Methods: LA epicardial high-density contact mapping (256 electrodes) was performed in goats with acutely induced (aAF, n=6) and persistent AF (persAF, n=5). After analysis of unipolar AF electrograms, AF cycle length (AFCL) and number of fibrillation waves per second (waves/s) were quantified. Mapped tissue regions were excised and reconstructed by high-resolution MRI (voxel size [78×78×78]m³), allowing myocardial fat quantification within the atrial wall using a Fatty Infiltration Score (FIS, quantification of proportion fat per electrode grid).

Results: AFCL (ms) was shorter in persAF than in aAF (103±27 vs. 127±15, P<0.05) and waves/s were higher in persAF than in aAF (102±27 vs. 41±14, P<0.01). The degree of fatty infiltration was much higher in persAF than in aAF (FIS-44±3±87 vs. FIS-20±4±835, P<0.01). Waves’ correlated well with fatty infiltration (bivarate r=0.96, P<0.01; see Figure) & corrected for the 2 groups (partial r=0.87, P<0.01). AFCL correlated inversely with fatty infiltration (r=0.81, P<0.01).

Conclusion: Persistence of AF is associated with fatty infiltration in goat left atria. Fatty infiltration seems to be an important determinant of AF complexity that deserves further targeted investigation.

P6292 | BENCH

Vidarabine, an anti-herpesvirus agent, prevents catecholamine-induced atrial fibrillation in mice

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Objectives: Atrial fibrillation (AF) is one of the most common arrhythmias in clinical practice. In recent years, catecholamine-induced hyperphosphorylation of cardiac ryanodine receptor (RyR) and oxidative stress, which is related to the ‘leaky’ RyR, has been suggested to play a critical role in AF-mediated signaling. Previously, we found that Vidarabine, an anti-herpesvirus agent, is a selective inhibitor of cardiac RyR. Here, we evaluated the anti-arrhythmic effect of Vidarabine using our mouse model of AF induced by transesophageal atrial burst pacing.

Methods and results: After treatment with Vidarabine (15 mg/kg/day) or Metoprolol (10 mg/kg/day, 1h-interrupted administration) for 5 days, spontaneously implanted osmotic minipump for 6 days, we assessed the duration of AF in mice. The transesophageal atrial burst pacing reproducibly induced self-sustaining AF. Sympathetic activation by intraperitoneal administration of norepinephrine (NE) (1.5 mg/kg), strikingly elongated the duration of AF (control 39 sec vs NE 739 sec, P<0.001). Both Vidarabine and Metoprolol shortened the duration of NE-elongated AF (control 674 sec vs Vidarabine 364 sec, P<0.05; vs Metoprolol 167 sec, P<0.05). Metoprolol significantly decreased left ventricular ejection fraction even at the lower dose (3 mg/kg/day for 2 days), whereas Vidarabine did not affect them. Vidarabine blunted the NE-induced RyR phosphorylation in atria (~20% and ~25% lower than vehicle-treated control at Ser 2808 and Ser 2814, respectively, P<0.05). In atrial myocytes, Vidarabine attenuated isoproterenol (ISO)-enhanced diastolic Ca²⁺ leak from sarcoplasmic reticulum (SR) (~27% lower than myocytes without Vidarabine treatment; P<0.01). Meanwhile, ISO increased the production of reactive oxygen species in neonatal rat cardiomyocytes. Intraoperineal administration of Tempol (24 mg/kg), a superoxide dismutase mimetic, inhibited NE-elongated AF (~66% shorter than control; P<0.03). Interestingly, to co-administration of Vidarabine and Tempol had no additive inhibitory effect on the NE-elongated AF, indicating that Vidarabine may suppress NE-elongated AF through antioxidative mechanisms.

Conclusions: These results indicate that Vidarabine inhibits AF via suppressing diastolic Ca²⁺ leak from SR without deterioration of heart function. The amelioration of oxidative stress may be involved in the mechanism.

P6293 | BENCH

Fluctuation in QT interval at onset and termination of paroxysmal atrial fibrillation

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Purpose: To compare the QT interval before, during and after episodes of paroxysmal atrial fibrillation (PAF).

Methods: A total of 35 patients (age 53±12 years, 48% female) who had documented PAF on Holter monitoring were enrolled. QT interval was measured at: SR immediately prior to the onset and after the termination PAF episodes (SRbaseline and SRpostAF respectively) and during AF. QtC was calculated in all patients by using three formulas: Bazett’s, Fridericia and Framingham.

Results: None of the patients was on drug that altered QT interval. QtC was longer during AF comparing to that during SR (SRbaseline and SRpostAF). QtC-SRpostAF was shorter than QtC-SRbaseline (Table 1). QtC shortening during AF was not affected by SR without deterioration of heart function. The amelioration of oxidative stress may be involved in the mechanism.

Table 1

<table>
<thead>
<tr>
<th>P Value</th>
<th>SRbaseline vs. SRpostAF</th>
<th>SRpostAF vs. AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.001</td>
<td>Bazett</td>
<td>Fridericia</td>
</tr>
<tr>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
<td>0.05</td>
</tr>
<tr>
<td>0.5</td>
<td>0.001</td>
<td>0.5</td>
</tr>
</tbody>
</table>

(Bazett’s vs. Fridericia vs. Framingham)
QRS duration and more often presented nonsustained supra ventricular arrhythmias as markers of heart failure, i.e. higher troponin and NT-pro-BNP. Furthermore, severity of illness, medical and technical support therapies were recorded.

Measurements and Main Results: NAF was defined as an AF episode lasting >2h and reoxygenation for 2h. RhAngptl4 (1 μg/ml), PPARα inhibitor MK886 (1mM) were supplemented. HCMECs apoptosis was detected by TUNEL. Endothelial monolayer permeability was assessed by VE-cadherin internalization was detected by confocal microscopy. ZDF rats underwent 45min ligation and 3h reperfusion.

Conclusions: We recruited 76 age-matched subjects from outpatient cardiology clinic (male, 64±11 years, n=53; postmenopausal female, 65±12 years, n=23). Peripheral blood mononuclear cells were isolated using Ficoll density gradient centrifugation and grown on fibronectin-coated plates. EPCs were counted using flow cytometry of CD34+ and KDR+ markers. Colony forming unit (CFU) assay was performed to determine EPC function. EPCs were treated with Tβ4 (1000ng/ml) for 3 days.

Results: Despite the significantly lower FRS in female, EPC number (%CD34+/KDR+) and function (CFU) were not statistically different between genders (Table 1). We also did not establish a significant association between FRS and CFU (r=-0.28; r≤-0.25; P=0.05) and with EPC number (r=-0.25; r≤-0.22; P=0.05) in either male or female subjects. In male subjects, Tβ4 treatment increased the EPC function by 8% (14.6±2.3). This improvement was similar compared to Tβ4-treated CFU from female subjects (15.0±3.2) (P=0.05).

Table 1. Baseline clinical characteristics and endothelial progenitor cell number and function of recruited subjects

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Conclusions: EPC number and function were not significantly different between genders, despite the higher Framingham risk score observed in male subjects. Tβ4 treatment improved EPC function in both genders.

P6297 | BENCH Role of Angptl4 in cardioprotection of Rosuvastatin in replenished diabetic hearts

K. Qi, Y.J. Yang, X.D. Li, H.H. Cui, Fu Wai Hospital, Center of Coronary Heart Disease, Beijing, China, People’s Republic of China

Purpose: Functional disruption of microvascular barrier caused by ischemia/reperfusion results in ischemia/reperfusion injury (IRI). Hyperglycemia may aggravate myocardial IRI since it worsens the barrier function. Angiopoietin-like 4 (ANGPTL4) has the potential to improve endothelial barrier function and may be involved in replenished diabetic heart protection. To confirm the effect of ANGPTL4 in ROSU-mediated cardiac protection, studies in vitro and in vivo were conducted.

Methods: HCMECs were cultured in normal (5.5mM) and high glucose (18mM) for 48h respectively followed by glucose-oxygen-serum deprivation (GOSD) for 2h and reoxygenation for 2h. RhAngptl4 (1μg/ml), PPARα inhibitor MK886 (1mM) were supplemented. HCMECs apoptosis was detected by TUNEL. Endothelial monolayer permeability was assessed by VE-cadherin internalization was detected by confocal microscopy. ZDF rats underwent 45min ligation and 3h reperfusion. SIRNA was used to knock-down Angptl4 expression in rat hearts. High permeability size and intact size were determined by FITC-dextran and TTC staining.

Results: HCMECs apoptosis significantly increased after the GOSD/reoxygenation treatment in a time and glucose concentration-dependent manner. Compared with control, ROSU dramatically decreased HCMECs apoptosis (21%±5 vs. 56%±6), fluorescence intensity (1925±6 vs. 3560±182) and VE-cadherin internalization. These protective effects of ROSU were inhibited by MK886. ROSU markedly reduced size of hyperpermeability (24%±2 vs. 35%±6) and infarction (41%±6 vs. 56%±8) of ZDF rats in AMI/reperfusion model compared with control.

Conclusions: ROSU protects replenished diabetic heart through attenuating HCMECs apoptosis and paracellular hyperpermeability. This protection may be related to ROSU-mediated upregulating of Angptl4 via PPARα pathway.

ENDOTHELIAL FUNCTION – BASIC II

P6298 | BEDSIDE Incidence and predictors of new-onset atrial fibrillation in septic shock patients in a medical ICU: data from 7-day Holter ECG monitoring

C. Guenancia1, C. Binkust1, G. Laurent1, S. Vinault2, R. Bruyere3, S. Prin3, A. Pavon1, P.E. Charles1, J.P. Quenol1, 1University Hospital Center, Department of Cardiology, Dijon, France; 2University Hospital of Dijon, Centre d’investigation clinique, Dijon, France; 3University Hospital of Dijon, Medical ICU, Dijon, France

Objectives: New-onset atrial fibrillation (NAF) is a common complication of septic shock and incidence is underestimated. We sought to investigate the real incidence, associated risk factors for NAF, and its prognostic impact during septic shock in patients hospitalized in a Medical Intensive Care Unit (ICU).

Design: Prospective, single-center, observational study.

Setting: Medical ICU in a large university teaching hospital.

Patients: All consecutive patients presenting between March 2011 and May 2013 with septic shock were eligible for inclusion, with the following exclusion criteria: patients aged <18 years, prior history of AF (paroxysmal or sustained), and patients transferred from another ICU with prior septic shock.

Intervention: After inclusion, all patients were equipped with long-duration Holter ECG monitoring for 7 days.

Conclusion: QTC is prolonged during PAF comparing to that during preceding SR, then shortened after index AF episode terminates and becomes shorter than the QTC during SR prior to AF. The results suggest a shortening of ventricular repolarization time after a prolongation of QTC during the preceding AF.

P6299 | BENCH Are there gender difference in endothelial progenitor cell number and function and the effect with thymosin beta-4 treatment?

P.S. Lee1, L. Ye2, T.C. Yeol1, H.C. Tan1, A.M. Richards1, K.K. Poh1, 1National University Heart Centre, Cardiac, Singapore, Singapore; 2University of Minnesota, Cardiology, Minneapolis, United States of America

Purpose: There are gender differences in incidence and progression of cardiovascular disease (CVD). Since endothelial dysfunction is associated with CVD, there may be gender-related difference in endothelial progenitor cells (EPCs). We aim to correlate EPCs with Framingham risk score (FRS) and hypothesize that treatment of human EPCs with thymosin beta-4 (Tβ4), a novel peptide may improve EPC number and function.

Methods: We recruited 76 age-matched subjects from outpatient cardiology clinic (male, 64±11 years, n=53; postmenopausal female, 65±12 years, n=23). Peripheral blood mononuclear cells were isolated using Ficoll density gradient centrifugation and grown on fibronectin-coated plates. EPCs were counted using flow cytometry of CD34+ and KDR+ markers. Colony forming unit (CFU) assay was performed to determine EPC function. EPCs were treated with Tβ4 (1000ng/ml) for 3 days.

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Conclusions: EPC number and function were not significantly different between genders, despite the higher Framingham risk score observed in male subjects. Tβ4 treatment improved EPC function in both genders.
P6289 | BENCH
Endothelial cell functions are differentially affected by shed microvesicles and exosomes in coronary artery disease

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1 University of Zurich, Center for Molecular Cardiology, Zurich, Switzerland; 2 Heart Centre, Department of Cardiology, Leipzig, Germany; 3 University Hospital Zurich, Heart Center, Zurich, Switzerland; 4 Asklepios Klinik, Weissenfels, Germany.

Background and purpose: Shed microvesicles (SMV) and exosomes are released from cells by different mechanisms. Thus, quantitative as well as qualitative changes of each particle population in patients with coronary artery disease (CAD) may reflect an altered activation status of the endothelium, platelets and leukocytes and exosomal and vesicular differential endothelial phenotype. Yet, alterations in both populations have not been studied side-by-side so far.

The aim of the present study was therefore to compare the impact of SMVs and exosomes from healthy subjects and CAD patients on endothelial cell (EC) functional characteristics, thought to be important in atherosclerotic vascular disease.

Methods: Exosomes and SMVs were isolated from plasma of patients with stable CAD and age-matched healthy control (HC) subjects (n=34-44 per group) by stepwise filtration and ultracentrifugation (particle identity verified by electron microscopy and dynamic light scattering). Functional effects of vesicle fractions on cultured human arterial ECs were analyzed. In parallel, levels of total, platelet-derived (PMVs), endothelial-derived (EMVs) and leukocyte-derived (LMVs) SMVs were assessed by flow cytometry. Moreover, the impact of therapeutically relevant changes in vesicle counts and their functional effects were monitored in patients with CAD randomized into optimal medical treatment (OMT; n=15) or by OMT with an additional supervised exercise program (ET; n=18).

Results: In CAD patients, plasma counts of EMVs and LMVs (p<0.05 vs. con for both), but not of PMVs or total SMVs were increased versus HC. SMVs of HC, but not of CAD patients supported in vitro re-endothelialization by (30±10% and 9±9% vs. PBS, respectively, p<0.05). ET, but not OMT, improved CAD SMV capacity to support in vitro re-endothelialization (by 30±12% and 16±14% vs. begin, respectively, p<0.05). Over the whole study population, LMV plasma count was negatively correlated with overall SMV effect on re-endothelialization (p=0.001, r=−0.53). Exosomes of CAD as well as HC upregulated ICAM-1 (by 19±5 and 21±5%, p<0.05) and VCAM-1 (by 31±7% and 29±4%, p<0.05) expression by HAECS. Similarly, for EC death, particle type (p=0.02), not disease status was determined as source of variation by ANCOVA, indicating a differential biological effect of SMVs and exosomes.

Conclusions: SMVs and exosomes differentially impact on endothelial cell functions. In CAD, SMV capacity to support re-endothelialization was impaired, but partially rescued by exercise training.

P6290 | BENCH
Association of eNOS uncoupling with endothelial dysfunction in atherosclerotic plaques of human arteries

M. Stepnowska1, A. Siekierczyka1, I.T. Dobrucki1, J. Wojciechowski2, A. Szeftler1, M. Wozniak1, J. Rogowski1, L.W. Dobrucki1, L. Kalinowski2.
1 Medical University of Gdansk, Department of Medical Laboratory Diagnostics, Gdansk, Poland; 2 Beckman Institute of Advanced Science and Technology, Urbana; United States of America; 3 Medical University of Gdansk, Department of Cardiovascular Surgery, Gdansk, Poland; 4 University of Illinois, Department of Bioengineering, Beckman Institute of Advanced Science and Technology, Urbana, United States of America.

Purpose: The bioavailability of nitric oxide (NO) determines the function of the endothelium in the vessel wall. Endothelial dysfunction accompanied with decreased availability of NO may occur either because of decreased expression or impaired function of endothelial nitric oxide synthase (eNOS). There are inconclusive experimental and clinical observations showing that eNOS protein levels are decreased, normal or even increased in the endothelium overlying atherosclerotic lesions in arteries. This study was established to determine the exact mechanism underlying decreased NO bioavailability in the endothelium covering atherosclerotic lesions in human arteries.

Methods: Fragments of atherosclerotic and non-atherosclerotic (control) carotid arteries were isolated from patients undergoing carotid endarterectomy. Kinetics of NO2-/O2- and ONOO- radicals were measured in vitro with highly sensitive electrochemical nanosensors near the surface of a single endothelial cell. Total eNOS enzyme activity and eNOS dimmers and monomers was determined using low-temperature SDS-PAGE electrophoresis under both reducing and nonreducing conditions.

Results: The measurement of NO2-/O2- and ONOO- radicals revealed reduced release of bioactive NO (214 vs. 556 nmol/L) and increased levels of both NO2- (71 vs. 21 nmol/L) and ONOO-- (648 vs. 288 nmol/L) after activation of eNOS in endothelial cells from atherosclerotic plaques in comparison to cells from control samples. Immunoblotting with eNOS mRNA and protein expression was much higher in the endothelium of atherosclerotic arteries (0.15±0.04 arbitrary units) than in control (0.09±0.02 arbitrary units). The determination of the state of functional eNOS expression with the use of western blot technique revealed a significantly elevated monomer-to-dimer ratio in cells from atherosclerotic lesions (0.20±0.04) in comparison to control cells (0.01±0.005).

Conclusions: In summary, our data show that endothelial dysfunction in atherosclerotic lesions is associated with decreased level of bioavailable NO and elevated production of O2- and ONOO- after eNOS activation. Although the expression of both eNOS mRNA and protein is enhanced in cells from atherosclerotic plaques, the production of O2- and ONOO-- may be explained by the disruption of the dimeric structure of the eNOS enzyme.

P6300 | BENCH
Aerobic training increases blood nitric oxide and prevents the impairment in vascular reactivity caused by fructose intake in rats

A.C.L. Nobrega1, R.F. Medeiros2, T.G. Gaquei1, T. Bento-Bernades1, N.A.V.C. Motta1, F.C.F. Brito1, T.S. Miguel1, A.C.C. Albuqueruqe1, K.F. Gomes1, K.J. Oliveira1, F. Flumiren Federal University, Department of Physiology and Pharmacology, Niteroi, Brazil; 2 Postgraduate Program in Cardiovascular Sciences, Fluminiren Federal University, Niteroi, Brazil.

Purpose: The high intake of fructose is associated with cardiometabolic disorders. But it is uncertain if the effect of fructose overload on vascular reactivity and possible effects of non-pharmacological treatments. Thus, the aim of this study was to investigate the effect a high-fructose diet on vascular reactivity and the possible effects of aerobic exercise training in rats.

Methods: Wistar rats (n=7x4 groups), males, were distributed in Control group (C: tap water), Fructose group (F: water with 10% fructose) for 10 weeks; FT (0.8-6M) and CT (0.69-6M) groups. Those groups were randomly divided into two subgroups: F0 (NO2- and ONOO- were measured in vitro with highly sensitive electrochemical nanosensors near the surface of a single endothelial cell. Total eNOS enzyme activity and eNOS dimmers and monomers was determined using low-temperature SDS-PAGE electrophoresis under both reducing and nonreducing conditions. Functional effects of vesicle fractions on cultured human arterial ECs were analyzed. In parallel, levels of total, platelet-derived (PMVs), endothelial-derived (EMVs) and leukocyte-derived (LMVs) SMVs were assessed by flow cytometry. Moreover, the impact of therapeutically relevant changes in vesicle counts and their functional effects were monitored in patients with CAD randomized into optimal medical treatment (OMT; n=15) or by OMT with an additional supervised exercise program (ET; n=18).

Results: In CAD patients, plasma counts of EMVs and LMVs (p<0.05 vs. con for both), but not of PMVs or total SMVs were increased versus HC. SMVs of HC, but not of CAD patients supported in vitro re-endothelialization by (30±10% and 9±9% vs. PBS, respectively, p<0.05). ET, but not OMT, improved CAD SMV capacity to support in vitro re-endothelialization (by 30±12% and 16±14% vs. begin, respectively, p<0.05). Over the whole study population, LMV plasma count was negatively correlated with overall SMV effect on re-endothelialization (p=0.001, r=−0.53). Exosomes of CAD as well as HC upregulated ICAM-1 (by 19±5 and 21±5%, p<0.05) and VCAM-1 (by 31±7% and 29±4%, p<0.05) expression by HAECS. Similarly, for EC death, particle type (p=0.02), not disease status was determined as source of variation by ANCOVA, indicating a differential biological effect of SMVs and exosomes.

Conclusions: SMVs and exosomes differentially impact on endothelial cell functions. In CAD, SMV capacity to support re-endothelialization was impaired, but partially rescued by exercise training.
icant increase was evident, CD31+/Annexin+ EMP levels were 0.119% (±0.043 SEM, p<0.0188, n=15). No significant differences were found for CD31+/Annexin- EMPs.

**Conclusions:** These experimental results could provide explanation for the elevated level of EMPs in STEMI patients, showing that temporary hypoxic conditions might act as an endogenous survival signal. On the experimental results of this current study we believe that the release of CD31+/Annexin+ EMPs also in healthy volunteers. In our previous studies we have shown that apoptotic bodies can confer pro-survival signals to cardiomyocytes during myocardiopathia. Based on the experimental results of this current study we believe that the release of CD31+/Annexin+ EMPs during hypoxia might act as an endogenous survival signal. However, future studies are warranted to further explore this cellular signaling mechanism.

**P6302 | BENCH**

**Exacerbated aging of cerebral arteries is mediated by the adaptor protein p66Shc**

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1 University of Zurich, Center for Molecular Cardiology, Zurich, Switzerland; 2 Dept. of Advanced Biomedical Sciences, Federico II University, Naples, Italy

**Background:** Aging is an independent risk factor for cardiovascular and cerebrovascular disease which, due to the currently aging of western populations, may soon represent a major healthcare challenge. To date, little is known about the mechanisms of aging of cerebral arteries and whether the aging gene p66Shc is implicated in it. The present study was designed to assess age-induced vascular dysfunction in mice cerebral and systemic arteries in wild type (wt) and p66Shc−/− mice.

**Methods:** Basilar arteries and size matched second order femoral arteries of 3-months (3M), 6-months (6M) and 2-years old (2Y) mice were studied. Arterial rings were perfused with KRBv (118 mM NaCl, 5 mM KCl, 25.5 mM HCO3−, 1.2 mM CaCl2, 1.25 mM MgCl2, 2.5 mM glucose) and were subjected to an increasing concentrations of acetylcholine and sodium nitroprusside (SNP). O2−-generation was assessed in femoral and basilar arteries using the spin trap 1-hydroxy-3-methoxycarbonyl-2,2,5,5-tetramethyl-pyrrolidine.

**Results:** Endothelium-dependent, acetylcholine-induced relaxations were assessed in femoral and basilar arteries of 3M, 6M and 2Y of wt and p66Shc−/− mice. In wt mice, endothelial function of the femoral artery was not affected by age unlike in the basilar artery where an age-dependent dysfunction was observed. In the femoral artery, the dysfunction observed in the basilar artery was blunted as compared to wt. SNP-induced relaxations were comparable in femoral and basilar arteries of 3M, 6M and 2Y and p66Shc+/− mice. Electron spin resonance measurements of O2−-indicated comparable levels of ROS in the femoral arteries of 3M and 2Y of wt and p66Shc−/− mice. Differently, O2− levels in the basilar artery of wt mice were strongly increased by age unlike in p66Shc−/− mice where they remained comparable. Additionally, 2Y but not 3M wt mice presented significant higher levels of O2− compared to p66Shc+/− age-paired mice.

**Conclusion:** Endothelial function of cerebral arteries, but not of size-matched systemic ones is impaired by aging. This process appears to be paralleled by an increased ROS production mediated by the p66Shc−/− gene.

**P6303 | BENCH**

**Lipocalin 2 (Lcn-2) is a 25-kDA secreted acute phase protein, implicated in it. The present study was designed to assess age-induced vasodilation of O2− compared to wt. SNP-induced relaxations were comparable in femoral and basilar arteries of 3M, 6M and 2Y and p66Shc+/− mice. Electron spin resonance measurements of O2−-indicated comparable levels of ROS in the femoral arteries of 3M and 2Y of wt and p66Shc−/− mice. Differently, O2− levels in the basilar artery of wt mice were strongly increased by age unlike in p66Shc−/− mice where they remained comparable. Additionally, 2Y but not 3M wt mice presented significant higher levels of O2− compared to p66Shc+/− age-paired mice.

**Conclusion:** Endothelial function of cerebral arteries, but not of size-matched systemic ones is impaired by aging. This process appears to be paralleled by an increased ROS production mediated by the p66Shc−/− gene.

**P6304 | BENCH**

**Shock waves induce postnatal vasculogenesis in infarcted myocardium by recruitment of bone marrow derived endothelial progenitors**

J. Holfeld1, C. Tepekoyu1, M. Theurl2, W. Mathes1, D. Lobenwein1, R. Kozaryn1, P. Paulus3, R. Kirchmair2, M. Grimm1, 1 Insbruck Medical University, Department of Cardiac Surgery, Innsbruck, Austria; 2 Innsbruck Medical University, Department of Internal Medicine I, Innsbruck, Austria; 3 Johann Wolfgang Goethe-University Hosp., Frankfurt am Main, Germany

**Purpose:** Recent shock waves at low energy levels were described to induce angiogenesis and regression in ischemic tissue. Improvement of myocardial perfusion and relief of angina symptoms in human patients with severe coronary artery disease have been shown. We hypothesized that the recruitment of progenitor cells from bone marrow to infarcted myocardium is involved as well.

**Methods:** Sub-lethally irradiated C57Bl/6 wild-type mice received bone marrow transplantation (Bmtx) from transgenic GFP mice (C57Bl/6tg (CAG-EGFP) 1 Osbiu) (n=6 per group). 4 weeks after Bmx, myocardial infarction was induced by coronary artery ligation. Treatment group (SWT) received shock wave therapy (0.38mJ/mm², 200 impulses, 3Hz) 3 weeks after infarction, whereas control animals (CTR) underwent sham treatment. Hearts were harvested 3 weeks after therapy. GFP positive bone marrow derived cells in the heart were detected by double immunofluorescence microscopy. Lectin counterstaining revealed endothelial progenitor cells (EPCs). Gene expression of pivotal factors SDF-1, CXCR4, VEGF receptors and others was performed. Functional outcome was measured with a pressure catheter inserted into the left ventricle. For further mechanistic findings an in-vitro migration assay using human umbilical vein endothelial cells (HUEVOCs) was performed.

**Results:** Higher numbers of bone marrow derived endothelial progenitor cells per high power field had been found in the treatment group (CTR 3.98±0.6 vs. SWT 17.89±1.16, p<0.0001). The main chemotactant for EPC recruitment SDF-1 mRNA, was increased (CTR 1.86±0.68 vs. SWT 5.19±1.18, p<0.02). Migration assay revealed higher migration rates (CTR 171.9±15.89 vs. SWT 234.5±25.9, p<0.04). Functional outcome as assessed by pressure catheter showed an increase in dP/dtmax (CTR 1967±343 vs. SWT 3007±617, p<0.059), a decrease in dP/dtmin (CTR -1532±251.3 vs. SWT -2603±346.7, p<0.03) and an increase in Tau (CTR 33.68±5.99 vs SWT 124.7±42.15, p<0.09) indicating functional improvement after SWT.

**Conclusions:** Low energy shock waves induce postnatal vasculogenesis in infarcted myocardium by recruitment of bone marrow derived endothelial progenitor cells. Shock wave treatment may develop a regenerative adjunct or alternative treatment option to state of the art revascularization in myocardial infarction. Notably, it has already been applied in angina patients without causing any severe side effects.

**P6305 | BENCH**

**Peroxisome proliferator-activated receptor (PPAR)-alpha/gamma agonism enhances arteriogenesis in mice**

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**Background:** Agonism of the peroxisome proliferator-activated receptor (PPAR)-α shows lipid-modifying effects and PPAR-γ agonists enhance insulin-sensitivity. The vascular effects of combined PPAR-α/γ agonism are unknown. The aim of this study was to characterize the impact of the dual PPAR-α/γ agonist aleglitazar in endothelial function, neoangiogenesis and arteriogenesis.

**Methods and results:** Male C57Bl/6 wild-type (WT, normal chow) and alopoxprotein E-deficient (apoE−/−) mice on Western-type diet were treated with aleglitazar (10 mg/kg i.p.) or vehicle by daily injection. Endothelium-dependent vasodilation was quantitated in WT mice (n=6) by subcutaneously implanting discs covered with cell-impermeable nitrocellulose filters. The vascularized area of the discs was quantified after 14 days by perfusion of the animals with space-filling fluorescent microspheres. Aleglitazar treatment increased endothelium-dependent vasodilation by 178±18% compared to vehicle (p<0.05).

Endothelium-dependent vasorelaxation of aortic rings in response to carbachol was impaired in apoE−/− mice fed with WT for 6 weeks (relaxation 52±5% of max. contraction; n=6) compared to WT animals (relaxation 18±5% of max. contraction; n=3; p<0.001). Concomitant aleglitazar treatment partially restored endothelial function (relaxation 39±5% of max. contraction; n=6; p<0.05). After hindlimb ischemia induced by right femoral artery ligation (FAL), apoE−/− mice on WT diet treated with aleglitazar for 5 weeks before FAL were characterized
by an improvement of endothelial-dependent laser Doppler perfusion (right/left foot ratio 0.40±0.03) 1 week after FAL compared to control animals (right/left foot ratio 0.24±0.01; p < 0.001). Collateral-dependent perfusion measurements under conditions of maximal vasodilatation 1 week after FAL using fluorescent microspheres demonstrated that compared to WT mice (2 weeks aleglitazar prior to FAL), which control mice had an impaired perfusion restoration (RI leg ratio in WT 78±13 vs. apleo-/- 56±6; p < 0.001), which was normalized by aleglitazar treatment (RI leg ratio 79±5; p < 0.001).

Molecular analysis showed improved function of endothelial progenitor cells (EPC) with increased expression of phospho-eNOS and phospho-Akt. The effects of aleglitazar on EPC migration and colony forming units were mediated by both PPAR-α and -γ signaling and Akt.

Conclusion: The dual PPAR-γ agonist aleglitazar augments neangiogenesis, endothelial function and arteriogenesis. The study provides evidence for beneficial effects of combined PPAR-γ/α agonism on vascular function mediated by or in addition to its metabolic actions.

ATHEROSCLEROSIS AND INFLAMMATION

P6307 | BENCH oxLDL decreases wnt1 which promotes CD36 through b-catenin and PPAR-γ signaling pathway in macrophage

H. Yan, S. Wang, T. Chen, J.H. Zhu. First Affiliated Hospital of College of Medicine, Zhejiang University, Institute of Cardiology, Hangzhou, China, People’s Republic of China

Aims: Many present researches show wnt signaling plays important role in the initiation of atherosclerosis. Wnt1 participates in the migration of macrophages, our group want to further investigate the role of wnt1 in the formation of macrophage foam cell which promotes atherosclerosis, so we study the relationship between wnt1 and scavenger receptors in macrophages.

Methods and results: First we found that oxLDL suppress the expression of wnt1 in THP-1 cells, then THP-1 cells were treated with siRNA or overexpression plasmid of wnt1, CD36 was decreased or increased respectively. We also got the similar results in GM-CSF stimulated human peripheral blood monocytes. We then used inhibitors of β-catenin, protein kinase C (PKC) and PPAR-γ to demonstrate wnt1 regulates the expression of CD36 through β-catenin pathway and PPK-PPAR-γ signaling, furthermore co-immunoprecipitation was used to find β-catenin pathway is dependent on PPAR-γ. Existing data show oxLDL activates CD36 through PKC-PPAR-γ pathway. Meanwhile, we also found oxLDL can regulates CD36 production through ERK-β-catenin signaling.

Figure 1. oxLDL decreases wnt1 then increased CD36.

Conclusions: In the differentiation process from PBMCs to macrophages, oxLDL inhibit the expression of wnt1 but induce the CD36 production by activation of both β-catenin and PPAR-γ. Wnt1 induces the expression of CD36 through β-catenin pathway and protein kinase C-PPAR-γ signaling. This vicious circle promotes macrophage foam cell formation which contributes atherosclerosis ultimately.

P6308 | BENCH Combined administration of eicosapentaenoic acid and docosahexaenoic acid reduces atherosclerotic lesion in apolipoprotein E-deficient mice

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Background: Recent studies demonstrated that macrophages play an important role in the progression of atherosclerosis by promoting inflammatory response and lesion formation, and that highly purified eicosapentaenoic acid (EPA) reduces and stabilizes atherosclerotic lesions in apolipoprotein E-deficient (ApoE-deficient) mice by inhibiting activation of macrophages. However, effects of docosahexaenoic acid (DHA), one of the major n-3 PUFAs, on the development of atherosclerosis is still under debate. In this study, we examined whether additional dosage of DHA to EPA presents more effective anti-atherosclerotic properties in ApoE-deficient mice.

Method and result: Eight-week-old ApoE-deficient mice were fed on western-type diet supplemented with 2.5% (w/w) EPA, 5% (w/w) omega-3 acid ethyl esters which includes 2.3% (w/w) EPA and 1.9% (w/w) DHA (EPA + DHA), or none of n-3 PUFAs (control group) for 20 weeks. There were no significant differences in blood pressure and the levels of total cholesterol and free fatty acid in these groups. In EPA group, the level of triglyceride was significantly higher than control group. There were no significant differences in abdominal aorta compared with control group (p < 0.01). In vitro experiment using RAW264.7, a murine macrophage cell line, demonstrated that pretreatment with EPA or DHA attenuated the up-regulation of MMP-9 and MCP-1 induced by LPS. Conclusion: Combined administration of EPA and DHA showed better anti-atherosclerotic effect compared with EPA treatment in ApoE-deficient mice. Combination therapy of n-3 PUFAs may provide a new therapeutic option.

P6309 | BENCH A newly developed apoA-I mimetic peptide with a D-amino acid promotes HDL via ABCA1-mediated cholesterol efflux

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Apolipoprotein (apo)-A1 stimulates cholesterol efflux via the ATP-binding cassette transporter A1 (ABCA1), which generates HDL and reverses the macrophase cholesterol load. Despite these anti-atherogenic roles, the impact of specifically promoting ABCA1 cholesterol efflux on atherosclerosis development is not well understood. We previously developed an apoA-I mimetic peptide, FAMP (Fukukoto University ApoA-I Mimetic Peptide – type 5; ALE HLF TLY EKA LKA LED LKL KL LKL), which had ABCA1-mediated pathway. Therefore, a novel synthetic apoA-I mimetic peptide with a D-amino acid was newly developed (FAMP-D1).

The FAMP-D1 was added d-alanine at its C-terminus end to the FAMP consists of 25 amino acids (ALE HLF TLY EKA LKA LED LKL KL LKL d-ALA). Serum apoA-I from apoA-I plasma could take up cholesterol. After stimulation with LXR/RXR-agonists, FAMP-D1-mediated cholesterol efflux were increased, as well as with serum apoA-I, in addition specific cholesterol efflux with FAMP-D1 was much higher than those with FAMP and apoA-I (13.6% increasing of FAMP-D1, p < 0.01). Furthermore, after incubation of FAMP-D1 with human serum, FAMP-D1 was significantly elevated the efflux capacity of HDL. In conclusion, a newly developed apoA-I mimetic peptide with a D-amino acid remarkably removes cholesterol and forms HDL via an ABCA1 specific pathway.

P6310 | BENCH Chlamydia pneumoniae infection promotes vascular endothelial cell migration and angiogenesis through IQGAP1 related signaling pathway

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Purposes: Pathological angiogenesis is associated with unstable vulnerable atherosclerotic plaques and contribute to plaque rupture. Vascular endothelial cell (VEC) migration is a key step in angiogenesis. Multiple reports have demonstrated an association between Chlamydia pneumoniae infection and plaque vulnerability. However, how C. pneumoniae infection can result in plaque instability remains unclear. C. pneumoniae infection has been shown to promote cell migration. Whether C. pneumoniae infection might cause plaque destabilization through enhancing VEC migration and angiogenesis is unknown. IQGAP1 has been implicated as a regulator of cell motility and angiogenesis. In this study, we attempt to observe the effects of C. pneumoniae infection on VEC migration and angiogenesis, to investigate the role of IQGAP1 related signaling pathway in this process.

Methods and results: VEC migration by wound healing assay and tube formation by tube formation assay were both significantly enhanced after C. pneumoniae infection compared to the control group (P <.05). Co-immunoprecipitation (Co-IP) results revealed that C. pneumoniae infection of VECs significantly stimulated IQGAP1 phosphorylation. Then, we found C. pneumoniae infection significantly increased Src activity rather than PKC activity, and PP2, a selective Src tyrosine kinase inhibitor, but not the PKC inhibitor chelerythrine or GF 109203X, markedly decreased the level of IQGAP1 phosphorylation stimulated by C. pneumoniae infection, and suppressed the infection-induced VEC migration and tube formation (P <.05). Moreover, C. pneumoniae infection also induced recruitment of IQGAP1 to lamellipodia required for cell migration and angiogenesis. These data imply that IQGAP1 phosphorylation mediated by Src but not PKC plays an important role in C. pneumoniae infection-induced VEC migration and angiogenesis.

In addition, the infection-induced VEC migration and tube formation were also inhibited by wiskostatin, an N-WASP inhibitor (P <.05), and N-WASP was found to be recruited to lamellipodia after the infection, suggesting a possible role of N-
Atherosclerosis and inflammation

P6311 | BENCH
Repetitive treatment of percutaneous carbon dioxide mist prevents high fat diet-induced arteriosclerosis in extremely small size minipigs
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Methods: Male MMPs, weighing approximately 6 kg were used. Atherosclerosis model was induced using a high cholesterol diet (HFCD) for 5 weeks. The plaque volume, plaque volume index (PVI), mean plaque thickness, in situ plaque macrophage area, and serum concentrations of lipids, lipoproteins, and apolipoproteins were measured. The plaque volume index and mean plaque thickness were determined using a histological scoring system. Serum apoA1, apoB, apoCIII, and apoE levels were measured using ELISA assays. The apoB/apoA1 ratio was calculated.

Results: HFCD significantly increased serum total cholesterol (T-cho) and LDL levels at 2 weeks respectively. These levels in the normal diet group were 131±8 mg/dL and 8±3 mg/dL, respectively. At 8 weeks, serum T-cho and LDL levels were 346±28 mg/dL and 20±4 mg/dL, respectively. Treatment with CO2 mist slightly depressed these lipid levels (T-cho, 334±17 mg/dL; LDL, 235±19 mg/dL), whereas HFCD significantly increased these levels (T-cho, 346±28 mg/dL; LDL, 20±4 mg/dL). High fat and high cholesterol diet increased the plaque volume index and mean plaque thickness, whereas CO2 mist significantly decreased these parameters.

Conclusion: Treatment with percutaneous CO2 mist may be potentially useful for preventing arteriosclerosis. Beneficial effects of CO2 mist may be partially mediated via upregulation of PGR120 in perivascular adipose tissue.
**P6315 | BENCH**

Inhibition of DPP-4 attenuates monocyte inflammatory response through suppression of MAPK phosphorylation and ameliorates the development of CaCl2-induced abdominal aortic aneurysm in mice

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**Purpose:** Abdominal aortic aneurysm (AAA) is characterized by the destruction of tissue architecture due to chronic inflammation of unknown etiology. Recent studies showed that a dipeptidyl peptidase-4 (DPP4) inhibitor directly inhibits smooth muscle cell proliferation and monocyte inflammation independent of the increase in circulating glucagon-like peptide-1 level. We investigated the potential effect of a DPP4 inhibitor, vildagliptin, on the formation of abdominal aortic aneurysm (AAA) in mice.

**Methods:** For induction of AAA, we applied 0.5 mM CaCl2 to the infrarenal aorta, then mice received vildagliptin (30mg/kg/day, n=10) or a vehicle (n=10) with oral administration for 6 weeks. Saline-treated mice were served as controls (n=10). Incidence of AAA was defined as external diameter > 1.5 fold of the average of the control group. The expressions of mRNA were analyzed by real-time quantitative PCR using aortic tissue after one week CaCl2 treatment. The effects of vildagliptin were investigated in a monocyte cell line, RAW 264.7 cells.

**Results:** The expression of DPP-4 in abdominal aorta was strikingly increased at 6 weeks after application of CaCl2. Then, vildagliptin significantly attenuated AAA formation (external diameters; 1.1±0.06 mm [CaCl2] vs. 0.9±0.05 mm [CaCl2+vildagliptin]) at 0.64±0.02 mm [Saline], p=0.05. Respectively, (n=10). Histological analysis showed that the recruitment of macrophages into AAA lesion in CaCl2 treated group was significantly greater than that in vildagliptin group (3.3±2.0 cell/μm² vs 1.2±2.2 cell/μm², p=0.05). Quantitative PCR demonstrated that the elevated expressions of MMP-2, -9, -12 and monocyte chemotactic protein-1 in vildagliptin treated group at 1 week after CaCl2 treatment were significantly decreased in the vildagliptin group. In addition, mRNA expression of Hspa5 as a marker of Endoplasmic reticulum (ER) stress and p47phox as a marker of oxidative stress were also reduced in the vildagliptin group. In vitro experiments, induction of interleukin-6 from RAW cells in response to lipopolysaccharide was directed suppressed by vildagliptin alone (20M-2uM), accompanied by suppression of MAPK phosphorylation (JNK and ERK) and NF-κB activation.

**Conclusion:** Vildagliptin attenuated the development of CaCl2-induced AAA in mice. Anti-inflammatory effects through suppressing MAPK activation in macrophages may contribute to the protection of AAA.

**ENDOTHELIAL FUNCTION: CLINICAL**

**P6317 | BEDSIDE**

Changes in shear stress are major determinants of flow-mediated dilation and constriction: two complementary markers of endothelial function

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**Introduction:** Mediated dilation (FMD) measures the endothelium-dependent vasodilator response to a short-term increase in local shear stress. Complementary to this, flow-mediated vasoconstriction (L-FMC) measures autacoids responses in response to a decrease in local shear stress. Like FMD, L-FMC is mediated by endothelial autacoids, and it is abrogated by removal of the endothelium. No study has tested yet whether a relationship exists between decrease in blood flow/shear stress and the corresponding L-FMC.

**Materials and methods:** We evaluated radial artery FMD and L-FMC along with the changes in blood flow and shear rate/stress in 586 participants (79.6% men, mean age 67±13 years) using high-resolution ultrasound and Doppler. In models adjusted by age, sex and presence of cardiovascular disease, baseline and hyperemic shear stress were related to radial artery FMD and L-FMC. Stepwise multiple analyses examining clinical correlates of endothelial function parameters showed that age, sex and a history of hypertension are related to L-FMC (R2=0.07, P=0.001). Differences in FMD was associated with age and sex (R2=0.07, P=0.001). When resting shear was incorporated, this association was strengthened for both L-FMC and FMD (respectively, R2=0.14 and R2=0.07). Similar results were obtained when the corresponding changes in shear rate were considered (R2=0.14 for L-FMC and R2=0.07 for FMD), but the relationships between L-FMC and FMD were attenuated.

**Discussion:** Like for FMD, we show that changes in blood flow/shear stress are major correlates of L-FMC. These observations support the concept that FMD and L-FMC measure two complementary aspects of endothelium-dependent, shear-induced, vasomotion.

**P6318 | BEDSIDE**

Allopurinol and endothelial function

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**Background:** Uric acid levels are associated with endothelial dysfunction (ED) and atherosclerosis. Xanthine oxidase inhibition with allopurinol decreases uric acid levels and oxidative stress and improves endothelial function.

**Purpose:** This study investigated the effect of high-dose allopurinol therapy on endothelial function in hyperuricemic asymptomatic patients without any overt cardiovascular disease.

**Methods:** 60 subjects with uric acid (UA) >5 mg/dl, all non-smokers without any known cardiovascular disease were studied. They were divided in two groups. Both treatment and placebo groups consisted of 30 patients. In the treatment group, daily oral 600 mg allopurinol was started after randomization and maintained for 12 weeks. Endothelium-dependent dilation was assessed by measuring flow mediated dilation (FMD) of the brachial artery and endothelium independent dilation was assessed by measuring changes in brachial artery diameter in response to sublingual nitrate administration (NMD). UA, FMD and NMD were measured at baseline and at the end of the therapy.

**Results:** At baseline there were no significant differences between groups regarding: age, blood pressure, body mass index, glucose, lipids and UA levels, FMD and NMD. FMD improved significantly after treatment in the allopurinol group 8,2±1,3 vs. 6,9±2,0, 95% (p=0.01), UA was significantly lower after treatment in the allopurinol group 5,63±0,71 vs. 7,19±0,87 mg/dl (p=0.003). NMD did not change significantly in the allopurinol group, 10,66±0,59 vs. 10,79±1,01 (p=0.72). There were no significant differences regarding UA levels in the placebo group after and before the treatment 7,35±0,76 mg/dl vs. 7,27±0,85 mg/dl. FMD improved significantly in the allopurinol group 7,2±1,01 vs. 10,81±0,66, 95% (p=0.00). However, NMD did not change significantly in the placebo group 10,38±0,63 vs. 10,48±0,99 (p=0.79). No significant correlation was found (r=0, 15, p=0, 56) between the variation of UA plasma levels (UA after treatment - UA at baseline) and the variation of FMD (FMD after treatment - FMD at baseline) in the allopurinol group.

**Conclusions:** These results suggest that allopurinol improves endothelium-dependent dilation, but the improvement was not correlated with uric acid levels. The mechanism of improvement is correlated with its ability to reduce vascular oxidative stress.

**P6319 | BEDSIDE**

Warfarin administration is associated with an increase in vascular calcification biomarker,RANKL

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**Purpose:** Over the past three decades, the utility of oral anticoagulation with warfarin in thromboembolic disease has been fully demonstrated. Although vitamin K deficiency can induce osteoporosis, patients who are taking warfarin must be prohibited their intake of vitamin K-rich foods, like as green vegetables and “natto”, a popular Japanese soybean food fermented with Bacillus subtilis, which contains vitamin K-dependent matrix Gla protein (MGP). MGP has been known as a potent inhibitor of the arterial calcification. We hypothesized that warfarin therapy affects both bone mineral metabolism and vascular calcification.

**Methods:** We prospectively included 40 consecutive atrial fibrillation (AF) patients high risk for arteriosclerosis (age 68±6; y: 6 female). Exclusion criteria include the following: the CHADS2 scores > 4, age > 80 years old, HbA1c<8.0%, BP>160/100 mmHg. Twenty-two patients had been treated with warfarin at least 6 months before the study. Vitamin K-depleted matrix Gla protein (MGP), was known to be known as a potent inhibitor of the arterial calcification. We hypothesized that warfarin therapy affects both bone mineral metabolism and vascular calcification.

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shown that Sar patients have impaired endothelial function, augmented arterial stiffness and increased inflammatory status. Ocular involvement occurs in 15-25% of Sar patients mainly in the form of uveitis. The study was designed to determine if uveitis as a manifestation of ocular Sarcoidosis is associated with an extensive vascular dysfunction, as a result of a stronger inflammatory process.

Methods: We enrolled 62 Sar patients and 62 age and sex matched, control subjects (CI). Sar patients were divided in those with ocular Sarcoidosis (OS) (23 patients) and in those without ocular Sarcoidosis (WOS) (39 patients). Endothelial function was evaluated by flow-mediated dilatation (FMD), Carotid-foemoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (Aix) as a measure of arterial wave reflections.

Results: There was no significant difference in sex, age and mean arterial pressure, patients with OS compared to WOS patients and CI subjects had impaired FMD (4.48±2.38% vs. 6.46±1.92% vs. 8.30±3.47%, p>0.001), increased Aix (25.00±8.79% vs. 17.99±10.99% vs. 13.76±10.76%, p=0.001) and increased PWV (8.48±2.25 m/sec vs. 7.01±1.12 m/sec vs. 6.85±1.51 m/sec, p<0.001). Logistic regression analysis, after adjustment for possible covariates (such as age, sex, smoking habits, the presence of arterial hypertension, diabetes mellitus, dyslipidemia and the treatment with corticosterone), revealed that impaired FMD in Sar patients was independently associated with increased Odds of ocular involvement [Odds ratio=0.64, 95%CI (0.43, 0.95), p=0.03]. More precisely ROC curve analysis revealed that FMD had a significant diagnostic ability for the detection of OS (AUC=0.73, p=0.005) and a FMD value below 4.95% has a modest sensitivity (61%) and a significant specificity (80%).

Conclusions: In the present study we have shown that Sar patients with ocular Sarcoidosis have impaired endothelial function and increased arterial stiffness compared to Sar patients without ocular involvement. These results strengthen the vascular theory considers uveitis a consequence of vascular dysfunction in Sar patients.

P6321 | BEDSIDE
CD-144 positive endothelial microparticles are increased in patients with systemic inflammatory response syndrome after TAVI
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Background: The development of a systemic inflammatory response syndrome (SIRS) after TAVI is associated with peri-procedural complications such as major bleedings and vascular complications. Microparticles are proinflammatory, procoagulant membrane vesicles released from various cells and may have a key role in the endothelial and hemostatic response to SIRS. We assessed the association of CD144 positive endothelial microparticles (EMP) with the development of SIRS in patients undergoing TAVI.

Methods and results: We measured EMP, white blood cell count, interleukin 6 (IL-6), IL-8, and procalcitonin (PCT) before and 4 h, 24 h, and 48 h after transcutaneous TAVI in 51 consecutive patients (57% male, age 81.4±6.6 years, left-ventricular ejection fraction 50.4±12.7%; logistic EuroSCORE 27.0±16.6). The occurrence of SIRS was defined as fulfilling two of the following criteria during the first 48 h: fever, tachycardia, hyperventilation, and leukocyte count > 12 or < 4 (10^9/L).

CD144 positive EMP level at baseline was 3152.8 (1305.7 to 5064.2) per μL. Patients with uneventful course showed a significant EMP decline at 4 h after the procedure (from 3152.8 to 1553.0; p=0.02) and 2.06% of patients with SIRS showed a significant increase. Furthermore, the development of SIRS was associated with an elevation of IL-6 (p<0.001) and IL-8 (p=0.001) and a leukocyte increase (p=0.008) but not detectable by PCT elevation (p=0.11) during the first 4 hours.

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P6322 | BEDSIDE
The impact 25-hydroxyvitamin D3 and D2 serum levels on vascular function in patients with coronary artery disease

Vitamin D deficiency is highly prevalent worldwide and is associated with the presence of coronary artery disease (CAD). There are two major forms, 25-hydroxyvitamin D3 (cholecalciferol) and D2 (ergocalciferol). Endothelial dysfunction and arterial stiffness are key players in the pathophysiology of atherosclerotic disease. We study the effect of the different vitamin D fractions (D3/D2) on arterial wall properties in CAD patients.

Methods: We included 252 (mean aged 62±11 years) patients with stable CAD, one month after percutaneous coronary intervention. Endothelial function was evaluated by flow mediated dilatation (FMD). Carotid femoral pulse wave velocity (PWV) was measured as an index of arterial stiffness and augmentation index (AI) as a measure of reflected waves. Measures for 25(OH)D2/D3 were performed using Liquid Chromatography Mass Spectrometry technology. Subjects with vitamin D levels below 20, between 20 to 30 and above 30ng/ml were characterized as having deficiency, insufficiency and sufficiency respectively.

Results: From the study population, 155 (62%), 66 (26%) and 31 (12%) were characterized as having deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D deficiency and/or insufficiency had significantly higher D2 to D3 ratio compared to subjects with vitamin D sufficiency [0.029 (0.007-0.039) vs. 0.013 (0.012-0.021) vs. 0.009 (0.008-0.012), p<0.001]. There was no difference in the serum vitamin D levels with vitamin D deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D deficiency and/or insufficiency had significantly higher 2D vs. 2D ratio compared to subjects with vitamin D sufficiency [0.092 (0.07-0.13) vs. 0.015 (0.014-0.016) vs. 0.009 (0.008-0.012), p<0.001]. There was no different mean SUA levels between subjects with vitamin D deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D levels below 20, between 20 to 30 and above 30ng/ml were characterized as having deficiency, insufficiency and sufficiency respectively.

Conclusions: Vitamin D insufficiency/deficiency is highly prevalent in CAD subjects. Although vitamin D status is not associated with arterial stiffness and endothelial function, D2 concentrations are positively associated with endothelial function. These findings may suggest a beneficial role of vitamin D2 levels in vascular health.

P6323 | BEDSIDE
Depletion of Uric Acid due to URAT1 loss-of-function mutation causes endothelial dysfunction in hypouricemic patients
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Introduction: Uric acid (UA) has been reported to provide an antioxidant defense and preserves endothelial function. This suggests that the low level of serum UA (SUA), hypouricemia, might cause endothelial dysfunction. Uric acid transporter (URA T) 1 is expressed in the kidney and vessels and is the major determinant of SUA. Depletion of Uric Acid due to URAT -1 loss-of-function mutation causes renal hypouricemia with high urinary excretion of UA (FEUA), which is often associated with acute renal failure.

Methods: We examined whether the decrease of SUA associated with endothelial dysfunction in patients with hypouricemia carrying URAT1 mutations.

Results: From the study population, 155 (62%), 66 (26%) and 31 (12%) were characterized as having deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D deficiency and/or insufficiency had significantly higher D2 vs. D3 ratio compared to subjects with vitamin D sufficiency [0.029 (0.007-0.039) vs. 0.013 (0.012-0.021) vs. 0.009 (0.008-0.012), p<0.001]. There was no difference in the serum vitamin D levels with vitamin D deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D deficiency and/or insufficiency had significantly higher 2D vs. 2D ratio compared to subjects with vitamin D sufficiency [0.092 (0.07-0.13) vs. 0.015 (0.014-0.016) vs. 0.009 (0.008-0.012), p<0.001]. There was no different mean SUA levels between subjects with vitamin D deficiency, insufficiency and sufficiency respectively. Subjects with vitamin D levels below 20, between 20 to 30 and above 30ng/ml were characterized as having deficiency, insufficiency and sufficiency respectively.

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Effects of atorvastatin treatment on endothelial function and inflammatory status of ischemic heart failure patients: The impact of renal function


Purpose: Ischemic heart failure (HF) is characterized by increased inflammatory state and impaired endothelial function which further deteriorates exercise tolerance and outcomes. Impaired renal function is a major determinant of adverse prognosis in HF. Stains, beyond their lipid lowering role, exert beneficial effect on endothelial function in patients with atherosclerosis. Aim of the present study was to examine the impact of atorvastatin treatment and renal function on endothelial function and biomarkers of inflammation and cardiac remodeling in HF patients. Materials and methods: In a 4 weeks, an open-label, parallel, single-blind, randomized controlled study, 23 patients with ischemic HF. The study was carried out on two separate arms, one with atorvastatin 40mg/d and one with atorvastatin 10mg/d (randomized, double-blind, cross-over design). Endothelial function was evaluated by flow-mediated dilatation of the brachial artery. Cardiac remodeling was assessed based on MDRD formula. Serum levels of tumor necrosis factor alpha (TNFa), of brain natriuretic peptide (BNP) and of matrix metalloproteinase-9 (MMP9) levels were measured by ELISA as indices of inflammatory status, left ventricle loading conditions and remodeling respectively. Total cholesterol (TC) was measured based on common biochemistry techniques.

Results: Compared to baseline, treatment with 40 mg of atorvastatin improved FMD (3.1±0.29% vs. 6.0±1.45%, p<0.001), TNFa (p<0.01) and MMP9 levels (p<0.04) while there was no impact in BNP levels (p>0.68). Moreover, compared to baseline, treatment with atorvastatin 10mg/d also improved FMD (3.2±4.12% vs. 4.20±0.09%, p>0.08) and TNFa (p<0.01) but had no impact on MMP9 (p>0.76) and BNP levels (p>0.40). The increase in FMD was greater with the dose of 40mg/d (p<0.001). Importantly, only in the 40mg/d treatment group the increase in FMD was significantly associated with baseline TC levels (r>0.57, p=0.004) and with creatinine clearance (r=0.61, p=0.002). Finally, only in the 40mg/d treatment group the association between creatinine clearance and FMD was significant and further adjustment for confounders such as TC, age, ejection fraction smoking habits, the presence of diabetes mellitus and hypertension [b>0.09, 95% CI (0.02-0.16), p=0.01].

Conclusions: In ischemic HF subjects both high and low dose atorvastatin treatment can improve inflammatory status and endothelial function. Importantly, the greatest improvement in endothelial function is observed in patients receiving high dose atorvastatin treatment with elevated baseline TC levels and preserved renal function.

Constrictive pericarditis: a different perspective of the disease in cardiac magnetic resonance imaging era

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The aim of this study was to assess the progression of constrictive pericarditis (CP) based on the degree of pericardial inflammation as seen on Cardiac Magnetic Resonance (CMR) with Late Gadolinium Enhancement (LGE). Between 2011-12, we identified 42 patients with echocardiographic & CMR evidence of CP who were treated with anti-inflammatory therapy. CMR LGE was graded qualitatively based on the intensity of LGE. We subdivided our patients based on their CMR LGE intensity as shown in Table 1. Clinical resolution was defined as improvement in NYHA class by 1.

**Table 1**

<table>
<thead>
<tr>
<th>None-Mild LGE (N=24)</th>
<th>Moderate Severe LGE (N=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD, years)</td>
<td>60±13</td>
</tr>
<tr>
<td>Male %</td>
<td>19 (79%)</td>
</tr>
<tr>
<td>NYHA class median (10% to 90%)</td>
<td>3 (1–4)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>16 (71%)</td>
</tr>
<tr>
<td>JVD</td>
<td>17 (71%)</td>
</tr>
<tr>
<td>Segmentation</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>WAIR (mean±SD, mm/hr)</td>
<td>16±6</td>
</tr>
<tr>
<td>US CRP (mean±SD, mg/L)</td>
<td>22±2</td>
</tr>
</tbody>
</table>

*Follow up echocardiogram was available for 21 & 15 patient in both groups respectively.

24 (57%) patients had None-Mild LGE (weak LGE) while 18 (43%) had Moderate-Severe LGE (Intense LGE). Patients with weak LGE tended to be worse clinically
on initial evaluation with a higher NHV class, more pedal edema & JVD. Baseline inflammatory biomarkers tended to be higher in the intense LGE group. Clinical & echocardiographic resolution of CP after anti-inflammatory therapy was higher in the intense LGE group (83% vs 21%, P < 0.001) at a mean follow up of 3.6±2 months. Percardectomy was done frequently in the weak LGE group (46% vs 17%, P = 0.047). Multivariate analysis found intense LGE to be significantly associated with clinical/echocardiographic resolution of CP after adjusting for age (p=0.007).

Moderate to severe CMR LGE & high inflammatory markers are associated with milder clinical CP and responds to anti-inflammatory therapy.

### P6329 | BEDSIDE

**Association of aortic pulse wave velocity with NT-pro-BNP levels 12 months after acute STEMI**

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**Objectives:** We have previously shown that aortic pulse wave velocity (PWV) is associated with biomarkers of myocardial wall stress measured 4 months after acute STEMI. We speculated that vascular-ventricular coupling might be responsible for these results. In the present study, we prospectively investigated the relationship of increased aortic stiffness with N-terminal pro-B type natriuretic peptide (NT-pro-BNP) levels 12 months after STEMI.

**Materials and methods:** We enrolled 50 STEMI patients who were treated with primary coronary angioplasty and followed up to determine NT-proBNP levels. PWV and NT-pro-BNP levels were encoding, phase-contrast CMR. Blood samples were routinely drawn at baseline and follow-up to determine NT-proBNP levels. PWV and NT-pro-BNP levels were log-transformed for correlation analysis to achieve normal distribution.

**Results:** The mean age of the study population was 57±12 years and median baseline PWV was 7.0 m/s (IQR: 5.8 – 8.4). After 12 months mean infant size was 11.1±1.5 m/s. PWV was significantly higher in the LGE group compared with the non-LGE group at 12 months (9.1±1.8 vs 7.5±1.0 m/s, P=0.001). The median NT-proBNP level after 12 months was 169 ng/L (IQR: 97 – 335). In univariate analysis NT-proBNP levels after 12 months correlated with PWV (r: 0.415, P=0.003), age (r: 0.427, P=0.002), end-systolic volume (r: 0.291, P=0.040) and heart rate (r: 0.460, P=0.001). After multivariate analysis PWV remained an independent predictor of NT-proBNP levels 12 months after STEMI (model: r: 0.742, P<0.001).

**Conclusion:** Aortic stiffness, as determined by PWV, is associated with NT-pro-BNP levels 12 months after reperfused STEMI. This association remains significant after correction for infant size, age and end-systolic volume. Our data suggest a role for aortic stiffness in chronic left ventricular remodeling after STEMI.

### P6330 | SPOTLIGHT

**Deriving benefit from exercise-induced ischaemia in coronary artery disease patients? Investigation of warm-up angina with transmural perfusion gradients using high-resolution CMR perfusion**

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**Purpose:** Warm-up angiograms describe a reduction in ischaemia, angina and arrhythmias on second exercise in patients with coronary artery disease, after “warm-up”. The exact mechanism underlying this cardio-protection remains uncharacterised.

Cardiac magnetic resonance (CMR) compatible ergometers permit quantification of exercise-induced ischaemia, which is the most physiological method of inducing myocardial stress. Previous studies have demonstrated that transmural perfusion gradients (TPG) using high-resolution CMR allow discrimination between the subendocardial and subepicardial.

The purpose of this study was to test whether there is preferential redistribution of perfusion towards the vulnerable subendocardial layer on second exercise.

**Materials and methods:** 60 CHD patients underwent cardiovascular magnetic resonance (CMR) at baseline and follow-up to determine NT-proBNP levels. PWV and NT-pro-BNP levels were log-transformed for correlation analysis to achieve normal distribution.

**Results:** The mean age of the study population was 57±12 years and median baseline PWV was 7.0 m/s (IQR: 5.8 – 8.4). After 12 months mean infant size was 11.1±1.5 m/s. PWV was significantly higher in the LGE group compared with the non-LGE group at 12 months (9.1±1.8 vs 7.5±1.0 m/s, P=0.001). The median NT-proBNP level after 12 months was 169 ng/L (IQR: 97 – 335). In univariate analysis NT-proBNP levels after 12 months correlated with PWV (r: 0.415, P=0.003), age (r: 0.427, P=0.002), end-systolic volume (r: 0.291, P=0.040) and heart rate (r: 0.460, P=0.001). After multivariate analysis PWV remained an independent predictor of NT-proBNP levels 12 months after STEMI (model: r: 0.742, P<0.001).

**Conclusion:** Aortic stiffness, as determined by PWV, is associated with NT-pro-BNP levels 12 months after reperfused STEMI. This association remains significant after correction for infant size, age and end-systolic volume. Our data suggest a role for aortic stiffness in chronic left ventricular remodeling after STEMI.

### P6331 | BEDSIDE

**Reduced coronary flow reserve evaluated by phase contrast cine magnetic resonance imaging in patients with heart failure with preserved ejection fraction**

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**Background:** Previous studies demonstrated that approximately 50% of patients with the clinical symptom of heart failure have preserved systolic left ventricular function, commonly recognized as a heart failure with preserved ejection fraction (HFpEF). As the precise mechanism underlying HFpEF is unclear, effective treatments have not been established in patients with HFpEF. Phase contrast (PC) cine magnetic resonance (MR) imaging allows for the assessment of coronary flow reserve (CFR) noninvasively. Although impairment of CFR is observed in various pathophysiological conditions, CFR of HFpEF has not been fully investigated. The aim of this study was to assess the CFR in patients with HFpEF by PC cine MR imaging.

**Materials and methods:** We studied 20 HFpEF patients (mean age: 75±6 years), 20 left ventricular hypertrophy (LVH) (mean age: 73±5 years) and 20 controls (mean age: 74±5 years). Coronary artery disease was not observed in all study subjects.

By using 1.5T MR scanner and 32 channel cardiac coils, cine MR images of left ventricle were acquired to assess the left ventricular (LV) systolic function. Breath-hold PC cine MR images of coronary sinus (CS) were obtained to assess the blood flow of CS both at rest and during adenosine triphosphate (ATP) infusion. CFR was calculated as CS blood flow during ATP infusion divided by CS blood flow at rest.

**Results:** LV ejection fraction was preserved in all subjects. (HFpEF: 60±4±8%, LVH: 60±3±0%, controls: 61±0±8%). CFR was significantly reduced in patients with HFpEF compared with LVH patients (2.40±0.23 vs 2.58±0.15, P=0.006) and control subjects (2.40±0.23 vs 3.21±0.23, P<0.001). Significant negative correlation was observed between CFR by MRI and the ratio of early transmural flow velocity to tissue Doppler early blood flow at rest.

**Conclusion:** In patients HFpEF, CFR was significantly reduced in comparison to patients with LVH and controls. Decreased CFR was associated with the severity of diastolic dysfunction by echocardiography. The results in the current study indicated that the dysfunction of left ventricular microcirculation plays an important role for the pathophysiology in patients with HFpEF.

### P6332 | BEDSIDE

**Prognostic value of deformation analysis by speckle-tracking echocardiography and late gadolinium enhancement cardiac magnetic resonance in patients with acute myocardial infarction**

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**Aim:** This study evaluated the prognostic value of 2-dimensional speckle-tracking echocardiography and late gadolinium enhancement cardiac magnetic resonance (LGE) in patients with acute myocardial infarction (AMI) in comparison with transmural perfusion gradients cardiac magnetic resonance (LGE).

**Background:** Myocardial deformation analysis by STE has been shown to predict left ventricular (LV) functional recovery and remodeling after AMI.

**Methods:** A total of 96 patients (61±11 years) with first AMI (54 with ST-segment elevation myocardial infarction (STEMI) and 42 with Non-STEMI (NSTEAMI)), all treated by primary percutaneous coronary intervention, were included. STE and LGE were performed within 48 hours after AMI. Peak global longitudinal strain was determined by STE and LGE were performed to define the amount of global myocardial scar. At 18 months follow-up the primary endpoint was assessed as a composite of all-cause mortality, revascularization, reinfarction and hospitalization for heart failure.

**Results:** During follow-up 24 patients reached the primary endpoint. Among patients with STEMI, a peak global longitudinal strain < -17.2% had a sensitivity of 62.5% and a specificity of 76.1%, LGE had a sensitivity of 62.5% and a specificity of 73.9% considering a cut-off point of 8.5% to predict a primary event at 18 months follow-up. The accuracy to predict a primary endpoint was similar for STE compared with LGE (AUC=0.707 vs. 0.693, P=0.8913).
In patients with NSTEMI, a peak global longitudinal strain < -15.3% had a sensi-
tivity of 87.5% and a specificity of 84.6%, LGE > -13.6% had a sensitivity of 62.5% and a specificity of 88.5% to predict a primary endpoint at 18 months follow-up. The accuracy to predict a primary endpoint was also similar for STE compared with LGE (AUC=0.879 vs. 0.793, p=0.3021).

Conclusion: In patients with AMI, accuracy to predict a composite of all-cause mortality, revascularization, reinfection and hospitalization for heart failure was comparable between STE and LGE.

P6333 | BENCH
Comparison of NOGA endocardial mapping with cardiac magnetic resonance imaging for determination of infarct size and infarct transmurality for intramyocardial injection therapy
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Introduction: Cardiac magnetic resonance imaging (cMRI) with late enhance-
ment (LE) is the gold standard for the assessment of infarct size, infarct transmu-
rality and left ventricular (LV) function. The NOGA® electromechanical mapping system is currently used for online evaluation of myocardial viability, segmental wall motion and to define the zone of reversibility for targeted catheter-
based intramyocardial drug, gene and cell therapies.

Methods: Sixty domestic pigs underwent diagnostic NOGA endocardial mapping and cMRI with LE at a time difference between the two 3D images of 2±1 days after a 60 day period of closed chest reperfused myocardial infarction (MI). The in-
farc size was compared between the two images by LE of cMRI and delineating the infarcted core of the unipolar voltage polar map. The sizes of transmural and non-transmural infarction were calculated from the cMRI transmurality and NOGA bipolar voltage maps. Significant association between the transmural and non-transmural areas were calculated.

Results: Significant correlation between the 3D cMRI-LE and 2D NOGA unipo-
lar voltage polar map-derived infarct size was found (r=0.905, p=0.040.105) with a mean difference of 2.62% of the LV surface. Significant association between the transmural and non-transmural voltage polar maps of cMRI and NOGA could be proven with an overlap ratio of 91.3% regarding transmural infarction (r=0.727, p<0.105). The extent of the non-transmural infarction showed also strong correlation (r=0.555, p=0.232x105) between the two images. NOGA overestimated the transmural scar size with 6.81% of the LV surface, but slightly underestimated the size of non-
transmural infarction (3.04% of the LV).

Conclusions: Combining unipolar and bipolar voltage maps, NOGA endocardial mapping is useful to delineate the targeted zone of intramyocardial therapy and may predict accurately the size of transmural and non-transmural infarction, comparable to the gold-standard cMRI. This might be particularly useful in patients with contraindication for cMRI and designated for targeted intramyocardial regen-
erative therapy.

P6334 | BENCH
Value of the diffusion-weighted magnetic resonance imaging and calculation of the apparent diffusion coefficient in differential diagnostics of the primary and secondary renoparenchymal hypertension
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Objectives: Recently, diffusion-weighted magnetic resonance imaging (DW-MRI) has emerged as a reliable method to differentiate between various functional re-
nal abnormalities. There is a growing necessity to differentiate between primary and secondary causes of hypertension, especially in elderly patients who might have multiple co-morbidities. The purpose of our study was to assess the value of the DW-MRI and consecutive calculation of the apparent diffusion coefficient in differential diagnostics of the primary (essential) and secondary renoparenchy-
mal hypertension by long-standing chronic glomerulonephritis.

Materials and methods: The study included 32 consecutive patients (17 women and 15 men) with hypertension. The patients were divided into 2 groups de-
pending on the presence or absence of known chronic kidney disease, namely chronic glomerulonephritis, comparable by age, sex and level of the blood pres-
sure. 1st group consisted of hypertensive patients with known chronic dis-
 ease; 2nd group – of hypertensive patients without any indications of kidney dis-
ease. 11 healthy volunteers entered the group of comparison. All patients under-
went diffusion-weighted multi-section echo-planar MRI (b value=600 s/mm2), in the axial ADC maps, regions of interest were placed in the cortex of each kidney. The ADCs of the kidneys were calculated. In addition, magnetic res-
 onance angiographic technique (without the use of a contrast enhancement) was used to exclude the presence of renovascular hypertension (renal artery steno-
sis).

Results: There was a statistically significant difference between the ADC values of both kidneys in the 1st and 2nd group (2.65±0.21 vs 3.31±0.31; P<0.05), as well as between 1st group and the group of comparison (3.35±0.34; P<0.05) respectively. There was no statistically significant difference between the ADC values of both kidneys in the 2nd group and group of comparison (P>0.05).

Conclusion: Presence of secondary renoparenchymal cause of hypertension, namely chronic glomerulonephritis result in significant decrease of the ADC val-
ues calculated on DW-MRI in comparison with healthy volunteers as well as pa-
tients with primary or essential hypertension. DW-MRI and consecutive calcu-
lalion of the apparent diffusion coefficient can be a valuable tool in differential diagnosis of primary essential and secondary renoparenchymal hypertension caused by long-standing glomerulonephritis as well as to determine the extent of target organ damage in patients with hypertension and underlying chronic kidney disease.

P6335 | BEDSIDE
Correlation between left ventricular diastolic pressures and E/E’ ratio- a simultaneous Doppler and catheterization study in 190 unselected patients: Are there gender differences?
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Purpose: Mitral E/E’ ratio is recommended for detecting elevated left ventricu-
lar filling pressures. More recently, gender specific differences in E/E’ratios have been demonstrated. However, the influence of haemodynamic measurements is not clear. The aim of our prospective study was (1) to assess the usefulness of mitral E/E’ ratio for predicting left ventricular filling pressures in an unselected group of patients undergoing cardiac catheterization and (2) to assess gender differences.

Methods: 203 unselected patients were chosen for simultaneous echocardio-
 graphic examination and cardiac catheterization. E/E’ ratio was correlated with left ventricular enddiastolic pressures (LVEDP) pre and post laevocardiography. 190 patients had sufficient echocohgicity to allow complete assessment of Doppler and tissue Doppler parameters.

Results: Overall, there was only a moderate significant correlation between E/E’ ratio and LVEDP pre laevocardiography (R= 0.24). In patients with ejection fraction (EF) >50% there was no significant correlation. Female patients had higher baseline E/E’ ratios than male patients. An E/E’ ratio >15 for predicting an elevated LVEDP was only significant in male but not in female patients. Irre-
sp ective of gender, a stratification of E/E’ ratio <8, 8.1-15 and >15 did not allow better prediction of LVEDP.

Conclusions: In an unselected group of patients undergoing catheterization, E/E’ ratio is only moderately correlated with LVEDP. There are significant gender differ-
ences and an E/E’ ratio >15 predicted an elevated LVEDP only in male patients.

P6336 | BEDSIDE
Long-term prognostic impact of basal thinning of the interventricular septum in patients: With cardiac sarcoidosis
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Purpose: Basal thinning of the interventricular septum (IVS) is one of the key findings for diagnosing cardiac sarcoidosis (CS). However, the long-term prog-
 nostic significance of the basal IVS thinning in CS remains unclear.

Methods: We examined 74 consecutive patients diagnosed as CS by clinical and/or pathological findings and clearly evaluated basal IVS by echocardiography. We measured the thickness A which was 10 mm distant from the aortic annulus on the IVS and the thickness B which was the one-third point nearby the annulus, and calculated the ratio A/B. Patients were divided into two groups according to the presence or absence of basal IVS thinning, defined as thickness A ≤ 4 mm and/or ratio A/B ≤ 0.6, as previously reported.

Results: Basal IVS thinning was observed in 21 patients. Age, gender, LVEF, angiotensin converting enzyme, lysozyme activity and BNP levels, use of and dose of corticosteroid therapy were comparable between the two groups. During the follow-up (5.1±2.5 years), the presence of basal IVS thinning was associated with higher long-term adverse events including all-cause death, symptomatic ar-
 rhythmias, and heart failure admission (P=0.006, Fig. 1A). Multivariate analysis showed the presence of basal IVS thinning (HR 2.86, 95% CI 1.31–6.14) and use of corticosteroid therapy (HR 0.29, 95% CI 0.13–0.66) were independent determinants for long-term adverse events. Furthermore, patients with basal IVS thinning
had larger extent of late gadolinium enhancement (LGE) than those without (27% vs 14%, P=0.0003, Fig. 1B).

Conclusions: Presence of basal IVS thinning was an independent determinant for poor long-term clinical outcomes with the larger extent of LGE, suggesting the basal IVS thinning could be a novel prognostic indicator in patients with CS.

P6337 | BENCH
Ultrasound diagnosis of pulmonary congestion in heart failure; simplified approach

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Pulmonary edema (PE), due to fluid retention and redistribution is the cardinal manifestations of heart failure (HF). The aim of this investigation was to study the effectiveness of simplified thoracic sonography in diagnosis of PE

Material and methods: 400 patients with II-IV NYHA functional class HF were evaluated (105 patients with diastolic and 295 with systolic HF). The control group consisted of 160 patients with different heart diseases (CHD, Hypertension, Aortic valve diseases), but without HF. Sonographic examination of a lung was done with 3.0-4.0 MHz convex or sector probe, from 10 points on thoracic wall (cross points of midclavicular line with II, IV and V intercostal spaces and anterior axillary line with IV and V intercostal spaces), which corresponded to the projection of lower, middle and upper lobes of right lung and upper and lower lobes of left lung.

Results: During ultrasound examination 94.5% of patients with HF had “Comet tail phenomenon” (CTPh), which was registered only in 35.5% patients without HF. The difference was found to be statistically significant (p=0.0001) and in systolic HF group in 95.9% patients. In 91% of patients with HF CTPh was registered from 3 and more registration points. In control group CTPh was registered from more than 3 points only in 2 (1.3%) patients. The best results in diagnosis of DHF can be achieved if we take “3 and more registration points” as a reference point for diagnosis of pulmonary congestion (sensitivity - 0.911, specificity - 0.942, positive predictive value 0.975). The time of examination by simplified method for evaluation of CTPh and pleural space took 3-4 minutes.

Conclusion: In patients with HF during pulmonary ultrasound examination significantly often was registered CTPh. The count of registration points from the thoracic wall of CTPh 3 and > is sensitive and specific sign of HF. The simplified thoracic ultrasound is highly effective in diagnosis of PE in patients with HF.

P6338 | BENCH
Tissue engineered pulmonary valve stent implantation in sheep: transnathoracoscopic echocardiographic evaluation (TTE)

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Purpose: Implanted tissue valves are prone to degeneration particularly in the adolescent. Tissue engineered valves in minimally invasively implanted stents may improve the durability. Thus implanted animals were followed up by transthoracic echocardiography to use for long-term follow up of up to six months.

Methods: Porcine pulmonary heart valves were decellularized, sutured into a cone shaped nitinol stent and seeded with autologous CD133+cells derived from the bone marrow of n=10 sheep (38.55 ± 2.60 mmHg). The valved stents were implanted in sheep with orthotopic position for six months. The implantation was completed in eight of ten animals with orthotopic position. This study was composed of 218 patients who underwent left heart catheterization and Echo-Doppler exam at the same day. The pre-a LVEDP was considered normal. LVEDP at the nadir of “a”-wave before the rapid onset of isovolumetric LV pressure by automatically mechanical measurement. A pre-a LVEDP < 10 mmHg and a LVEDP < 15 mmHg were considered normal. LV systolic dysfunction was defined as a ≤55% ejection fraction (EF).

Results: The E/A ratio was well correlated with the pre-a LVEDP and the LVEDP at the nadir of “a”-wave before the rapid onset of isovolumetric LV pressure by automatically mechanical measurement. A pre-a LVEDP < 10 mmHg and a LVEDP < 15 mmHg were considered normal. LV systolic dysfunction was defined as a ≤55% ejection fraction (EF).

Conclusion: TTE was an effective method for long-term follow-up of tissue engineered implants. The E/A ratio was well correlated with the pre-a LVEDP and the LVEDP at the nadir of “a”-wave before the rapid onset of isovolumetric LV pressure by automatically mechanical measurement. A pre-a LVEDP < 10 mmHg and a LVEDP < 15 mmHg were considered normal. LV systolic dysfunction was defined as a ≤55% ejection fraction (EF).

Conclusion: Coronary microvascular function was severely impaired in patients with stress hyperglycaemia after AMI.

MONITORING LEFT VENTRICULAR FUNCTION

P6341 | BEDSIDE
What does the mitral E/e’ ratio represent in parameters of LV hemodynamics?

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Background: Conflicting evidence exists as to whether the mitral E/e’ ratio can be a reliable predictor of the left ventricular end-diastolic pressure (LVEDP). Moreover, recently some study reported that the mitral E/e’ ratio was better correlated with the pre-a diastolic pressure (LVEDP) than LV end-diastolic pressure (LVEDP) in patients without heart failure (HF). Therefore, this study was aimed to investigate whether the value of the mitral E/e’ ratio is a reliable predictor for the LVEDP estimation.

Methods: This study was composed of 218 patients who underwent left heart catheterization and Echo-Doppler exam at the same day. The pre-a LVEDP was measured at the onset of the a-wave and the LVEDP at the nadir of “a”-wave before the rapid onset of isovolumetric LV pressure by automatically mechanical measurement. A pre-a LVEDP < 10 mmHg and a LVEDP < 15 mmHg were considered normal. LV systolic dysfunction was defined as a ≤55% ejection fraction (EF).

Results: The E/A ratio was well correlated with the pre-a LVEDP and the LVEDP. The septal E/e’ ratio was better correlated with the LVEDP than with pre-a LVEDP, irrespective of the LVEDP level or EF value. The septal E/e’ ratio was significantly higher in decreased EF and in the dilated left ventricular (LV) geometry. No significant difference in mean LVEDP was found among the three groups with E/e’ ratios of < 8, 8-15, and > 15. The sensitivity of septal E/e’ ratios > 15 for predicting a > 15 mmHg LVEDP were 42% and the specificity of was 71%. Also the septal E/e’ ratios > 8 had sensitivity of 12% and specificity of 87% for predicting a < 15 mmHg LVEDP.

Conclusion: Our study showed that the mitral E/e’ ratio is better correlated with the LVEDP than with pre-a LVEDP, irrespective of the presence of heart failure. However, as the mitral E/e’ had low sensitivity and specificity for predicting increased LVEDP, the clinical value of mitral E/e’ ratio is limited as a predictor of LVEDP.
Recovery of left ventricular systolic function after acute myocardial infarction: a comparative study between emergency percutaneous coronary intervention and fibrinolytic therapy

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Background: Myocardial injury after AMI is known to be a regional and heterogeneous process, so regional functional evaluation has been shown to provide additional important diagnostic and prognostic information to global function assessments.

Objectives: Quantitative assessment of the recovery of the regional and global left ventricular systolic function after reperfusion in acute myocardial infarction.

Methods: The study included 60 patients with first-time acute myocardial infarction, thirty were treated with fibrinolytic therapy and 30 treated with emergency PCI. Evaluation was performed at 1 week and after 30 days by conventional echo (2D, MM, color and PW Doppler), by tissue Doppler image (mitral annular systolic velocity, Sa) and 2D strain (Global longitudinal peak systolic strain, GLPSS). Results: 47% of the study populations were considered as having a significant recovery in systolic function by one month (60% of invasive subgroup, and 40% of those who had fibrinolysis). Conventional echo parameters showed insignificant difference neither from 1 week to 1month, nor between the two subgroups. There was a significant improvement in Sa from 5cm/sec ± 0.4 at 1 week to 7cm/sec ± 0.8 at one month, and was higher in invasive subgroup compared to pharmacological subgroup (8 cm/sec ± 2 versus 5 cm/sec ± 2, p=0.02).GLPSS showed significant improvement from -13.5% ± 7at one month to -15% ± 6at one month. GLPSS was best in invasive group in pharmacological one at baseline (-12.5% ± 5 versus -11.9% ± 4, p=0.04). At one month, GLPSS improved to -12%±4%, -16%±3 in the pharmacological and invasive subgroups respectively (p=0.04).

Conclusion: GLPSS and TDI parameters detected the recovery of LV systolic function after AMI.

P6343 | BEDSIDE
Estimation of the global peak left atrial longitudinal strain and peak left atrial longitudinal strain rate in patients with recurrent atrial fibrillation

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Purpose: To compare indices of the global peak left atrial longitudinal strain (globP ALS) and peak left atrial longitudinal strain rate (P ALSR) in chronic heart disease (CHD) patients, healthy volunteers and patients with atrial fibrillation (AF).

Materials and methods: A total of 48 patients with the history of myocardial infarction (MI) (mean age 65±6.6 years, ejection fraction (EF) 58±8%) were divided into 2 groups: paroxysmal (n=22) and persistent (n=26) AF. Apical four- and two-chamber views of 6 myocardial segments in the filling phase were obtained to assess globP ALS and LA volume index (LAVI) was calculated at baseline and after 4 months of treatment, we measured a) the carotid-femoral pulse wave velocity (PWV), b) carotid-femoral intima-media thickness (CF-IMT) and c) flow-mediated dilation of the brachial artery (FMD) and carotid intima-media thickness in patients with type 2 diabetes mellitus (T2DM).

Results: Both systolic and diastolic performance, as assessed by TDI, are strong predictors of an adverse outcome in patients with atrial fibrillation and are superior to conventional echocardiographic measurements of both systolic and diastolic function, that is, LVF and E/e'.

Conclusion: Both systolic and diastolic performance, as assessed by TDI, are strong predictors of an adverse outcome in patients with atrial fibrillation and are superior to conventional echocardiographic measurements of both systolic and diastolic function, that is, LVF and E/e'.

P6344 | BENCH
Systolic and diastolic function by tissue Doppler imaging predicts adverse outcome in patients with atrial fibrillation

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Purpose: This study evaluates the prognostic value of TDI in patients with atrial fibrillation.

Methods: Echocardiograms from 313 patients with AF during examination were analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke. Longitudinal systolic velocity (s') and early diastolic velocity (e') were measured by color TDI in six mitral annular sites and analyzed offline. The combined end-point was all-cause mortality, acute myocardial infarction, heart failure or stroke.
ness (IMT); e) E’/A’ ratio of mitral annular velocities, LV longitudinal (GLS), strain, twisting (Tw, deg), peak twisting (Tw, deg/sec) velocity, untwisting at mitral valve opening (unTw) and untwisting (unTw) velocity using speckle tracking echocardiography; d) coronary flow reserve (CFR). Forty normal subjects (N) served as controls.

Results: At baseline patients with psoriasis had higher PWVc, PWVb, AI, IMT, Tw velocity, unTw velocity and lower CFR, E’/A’, GLS than normals (p<0.05). Risk factors age and sex were similar between the treatment groups. Four months post-treatment, patients treated with biological agents (n=83) had higher FMD (11.2±4.1% vs. 5.1±4%); CFR (3.3±1.4 vs. 2.6±1.1); E/A (0.94±0.3 vs. 0.74±0.3) and reduced E/E’ (8.3±3.9 vs. 4.3±3.9); Tw (15.6±6 vs. 17.1±9.9); T velocity (97.4±5 vs. 110±48), untwisting at mitral valve opening (8.3±3.9 vs. 4.1±3.9) and unTw velocity (100±44 vs. 120±60) (p<0.05 for all comparisons) showing values similar to those in controls (n=39). No differences between anti-TNFα and anti-IL-12/23 were detected. Conversely, after treatment, patients on cyclosporine and methotrexate had no change in FMD (6.6±6 vs. 6.3±4); CFR (2.7±1.4 vs. 2.9±1); E’/A’ (0.89±0.3 vs. 0.91±0.3) but an increase in AI (34±19 vs. 26±22); cSBP (135±22 vs. 128±15), Tw (15.5±5 vs. 13.6) and unTw velocity (110±59 vs. 98±55) (p<0.05 for all comparisons). PASI was similarly improved in all treatment arms

Conclusion: Treatment with biological agents improves endothelial and coronary microcirculatory function leading to improved LV myocardial deformation and twisting.

P6347 | BEDSIDE
Intra myocardial adiposity is associated with left ventricular diastolic dysfunction without history of coronary artery disease

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Background: Ectopic fat appositions such as visceral adipose tissue and epicardial adipose tissue are shown to be associated with left ventricular diastolic dysfunction (LVDD). In this study we evaluated the association between intra left ventricular myocardial fat (ILVMF) and LVDD in patients without history of coronary artery disease (CAD).

Methods: We retrospectively evaluated 1214 consecutive patients >20 years with coronary computed tomography (CT). Patients with LV ejection fraction <50%, severe valvular disease and history of CAD were excluded. Finally a total of 988 (age 64±13 years; 57% male) were included in the analysis. ILVMF was evaluated on unenhanced CT.

Results: Of 988 patients, 42 (4.3%) had ILVMF. The patients with ILVMF were elder (p<0.01), and had more prevalence of dyslipidemia (p<0.01), diabetes mellitus (p<0.01), metabolic syndrome (p<0.03), higher triglyceride (p<0.01), and great use of statin (p<0.01) than patients without ILVMF. In echocardiographic parameters, e’ as left ventricular diastolic parameter was significantly lower in patients with ILVMF than in patients without ILVMF (5.5±1.9 VS. 6.3±3.3, p<0.02), but no significant difference was found in LV mass index, LAVI. Multivariate logistic analysis revealed that ILVMF was independently associated with e’ (Table).

Multivariate logistic analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio (95% CI)</td>
<td>p</td>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td>e’</td>
<td>0.82 (0.69-0.96)</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &gt;65 yo</td>
<td>1.42 (0.75-2.70)</td>
<td>0.26</td>
</tr>
<tr>
<td>Gender</td>
<td>0.75 (0.40-1.39)</td>
<td>0.35</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.72 (0.85-3.45)</td>
<td>0.13</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>2.51 (1.31-4.89) &lt;0.01</td>
<td>2.00 (1.12-4.32)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.20 (1.18-4.17)</td>
<td>0.03</td>
</tr>
<tr>
<td>Visceral adipose tissue (cm²)</td>
<td>1.01 (1.00-2.01)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

After adjustment for dyslipidemia, diabetes mellitus and visceral adipose tissue area, e’ was significantly associated with existence of intra left ventricular myocardial fat.

Conclusion: ILVMF was associated with LVDD in without history of CAD, suggesting that evaluation of ILVMF may be involved in a pathogenesis of heart failure with preserved ejection fraction.

P6348 | BEDSIDE
The missing links in missed transmissions of remotely monitored cardiovascular devices

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Introduction: Remote monitoring (RM) has become the standard of care for cardiovascular implantable electronic devices (CIED) follow up, promising time and remote monitoring is a unique tool to monitor and detect low CRT periods with one day delay and thus allows to take urgent measures to regain the optimal biventricular pacing.

Methods: We retrospectively evaluated 1214 consecutive patients who were implanted with cardiac resynchronization devices (CRT-D) devices and subsequently monitored on a daily basis via remote monitoring for the median follow-up (FU) of 30.5 months. Low CRT pacing was defined as <95% CRT% within 24h. Patients have been stratified to 4 groups, according to quartile of cumulative time spent in low CRT%: quartile 1 (0 to 7 days), 2 (8 to 17 days), 3 (18 to 64 days) and quartile 4 (>65 days).

Results: Long-term mortality and mean CRT% for the whole study population was 13.1% and 95.22% respectively. During the FU 63.2% of patients had at least one episode of low CRT pacing. None of the patients died, if the cumulative duration of low CRT% was within the range of 0-7 days (quartile 1). However, mortality rates for higher quartiles of low CRT% were significantly higher: 17.3 vs 14.0 vs 28.6% (quartile 2-4 respectively, all P<0.05 vs quartile 1). The prolongation of low CRT period (quartile 3 and 4) did not further increase mortality (both p>NS versus quartile 2). Adjusting for baseline confoundings, the cumulative low CRT pacing burden was not duration of the longest episode of low CRT% was the independent risk factor for death. One additional day of low CRT% increased the risk of future death by 0.3% [HR 1.003; 95% CI 1.0001-1.006; p<0.05].

Conclusions: Cumulative low CRT% is an independent risk factor for death in CRT recipients. The cumulative low CRT% lasting more than 7 days increase long-term mortality. Remote monitoring is a unique tool to monitor and detect low CRT periods with one day delay and thus allows to take urgent measures to regain the optimal biventricular stimulation.

P6350 | BEDSIDE
The clinical impact of telemonitoring for chronic heart failure: the RENEWING HEALTH project

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Purpose: To compare the clinical impact of remote monitoring (RM) with usual care (UC) of patients with chronic heart failure (HF).

Methods: The European RENEWING HEALTH Project aims to evaluate the clinical, organisational and economic effectiveness of RM in patients with diabetes, chronic obstructive pulmonary disease, implantable devices and HF in 9 European Countries. The patients were randomly assigned to RM or UC in multi-centre trial in the Veneto Region (Italy) and Central Greece. Inclusion criteria were: age >65 years and hospital discharge after acute heart failure in the previous three months and ejection fraction (EF) <40% or >40% plus BNP >400

The table exhibits that ILRs were the worst in compliance, while ICDSs were the best.

Conclusions: Even in centers practicing remote management as standard of care and maintaining excellent scheduling practice, failed evaluations occur frequently. Causes were technology related (wireless superior), device related (IRLS worst, ICDS best) and patient related. Attention to these factors may facilitate compliance with transmission, efficient workflow & timely resolution of actionable data.

Trend of missed transmissions in CIEDs

| Number who transmitted as per schedule | 197 | 53 | 18 |
| Number who failed scheduled transmission | 110 (35%) | 54 (50%) | 29 (61.7%) |
pp/ml (or plus NT-proBNP >1500 pp/ml) during hospitalization. The primary outcome was the combined end-point of all-cause mortality and hospitalizations for heart failure during the 12 month follow-up. Considering a 0.80 statistical power to demonstrate a 38% reduction of the primary end-point in RM group the sample size was 284 patients for the RM group and 142 for the UC group. The RM group was equipped to monitor blood pressure, heart rate, 1-lead ECG, pulse oximetry and weight with triggers set according to individuals’ personalised plan. Veneto sites have completed the predefined 9-months follow-up and we present these results.

Results: 188 (RM) and 97 (UC) patients were enrolled in Veneto. Baseline characteristics were similar in RM and UC group, except for some comorbidities, more frequent in the RM group: cerebrovascular disease in 18.6% vs 8.9% (p<0.04), diabetes in 38.8% vs 28.8% (p=0.04), atrial fibrillation was more frequent in UC group, 48% vs 43% (p=0.04). In both groups median age was 80 y, male gender was > 60%, ischemic heart disease was most frequent in cardiac disease, more than 70% were enrolled because of elevated proBNP or BNP and other because of reduced EF, > 53% were on diuretics, 70% on ACE-I or ARB, >65% on betablockers. >50% on aldosterone antagonists, 26% on digitalis, 48% on antiplatelets and 55% on anticoagulants. At the 9-month follow-up the primary end-point was reached in 34.8% and 48.4% (p=0.04) of patients in RM and UC groups, respectively.

Conclusion: Although the results are preliminary, we have observed a significant reduction in the combined end-point of all cause death and hospitalizations at 9 months in patients with HF randomized to telemonitoring service when compared to usual care. More data will be available in the next months when the clinical trial is completed.

P6352 | SPOTLIGHT
Increased rate of very low isotope-dose stress-only myocardial perfusion SPECT using CZT technology and quantitative analysis

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Purpose: To evaluate the feasibility and rate of very low isotope-dose (<2mSv) stress-only (SO) myocardial perfusion SPECT (MPS) using CZT technology and quantitative analysis (QA) compared to conventional MPS.

Methods: We identified 4852 patients (2392 males, 49.3%) without CAD history, who underwent stress first Tc-99m sestamibi MPS between Feb 24 and Dec 25 2013. Acquisition was performed using a fast CZT camera (3255 patients 67.1%) and a conventional camera (1597 patients). Stress acquisition time of CZT and conventional was 5-7 and 16-20 minutes, respectively. CZT Tc-99m doses ranged 5-10 mCi stress/15-25 rest weight adjusted. Conventional doses were 10-13 mCi stress/20-34 rest weight adjusted. QPS, CSMC utilized custom normal limits for the CZT and commercial for conventional camera. Total perfusion deficit (TPD) was derived. SO was based on visual analysis and QA.

Results: Stress dose of CZT MPS was 5-7 mCi (<2 mSv) in 2757/3255 patients (84.7%) and <10 mCi (<3 mSv) in 99.9%. Stress dose in the conventional MPS was 9-13 (3-4 mSv) in 1597 patients (100%). SO was more frequent among women than men, 1353/2460 (55%) vs. 691/2392 (28.9%), respectively, p<0.001. Among 2460 women, SO rates were higher in CZT vs. conventional MPS, 958/999 (95.5%) vs. 275/354 (77.6%), respectively, p<0.001. Rate of TPD <5% among men performing SO was more frequent in CZT compared to conventional, 499/1556 (32.1%) vs. 192/836 (22.9%), respectively p<0.001. Normal TPD (<5%) among women having SO was more frequent in the CZT compared to conventional MPS, 479/499 (96%) vs. 165/192 (85.9%), respectively, p<0.001. Analysis by gender + BMI demonstrated higher rates of SO in the CZT vs. conventional in men and women with BMI<30 or >30, with higher rates in women vs. men among BMI groups (Table).

Conclusion: Very low-dose (<2 mSv stress) CZT MPS provided higher rates of stress-only compared to conventional MPS in women and men across BMI groups, highly supported by normal quantitative analysis.

P6353 | BEDSIDE
The relationship between 99mTc-sestamibi washout and mitochondrial morphological changes in cardiomyopathy patients
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Background: Impaired myocardial retention of myocardial 99mTc-sestamibi (MIBI) scintigraphy reportedly reflects mitochondrial damage in various cardiac diseases. We investigated the relationship between the MIBI washout rate (WR) and mitochondrial morphological changes in comparison with the expression of messenger ribonucleic acid (mRNA) of mitochondrial electron transport-related enzymes in cardiomyopathy patients.

Methods: Forty cardiomyopathy patients, consisting of 20 hypertrophic cardiomyopathy (HCM) and 20 dilated cardiomyopathy (DCM) patients, were enrolled in this study. Resting myocardial MIBI scintigraphy was performed during overnight fast. Planar and single-photon emission computed tomography (SPECT) images were acquired. Quantitative MIBI WR was calculated on the early and delayed planar images. Biventricular cardiac catheter was conducted, and endomyocardial biopsy specimens were subsequently obtained for the expression of mRNA using reverse transcription-polymerase chain reaction (RT-PCR) analysis and electron microscopic analyses.

Results: A significant reduction in the mRNA expression of mitochondrial electron transport-related enzymes [cytochrome c oxidase subunit 5B (COX5B), nicotinamide adenine dinucleotide dehydrogenase (ubiquinone) flavoprotein 3 (NDUFB3), α-ketoglutarate dehydrogenase (α-KGDH)] was found in both cardiomyopathy patients with an increased MIBI WR than in those without it. In electron microscopic analysis, a greater variation of mitochondrial size and more disorganized mitochondria were observed in HCM patients with an increased MIBI WR compared with those without it. Severe damaged mitochondria and glycogen deposition were more frequently observed in DCM patients with an increased MIBI WR than in those without it.

Conclusions: MIBI WR is associated with the severity of mitochondrial functional and morphological damage. Our results indicate that myocardial MIBI scintigraphy is a useful modality for assessing disease severity in cardiomyopathy patients.

P6354 | BEDSIDE
Diagnostic accuracy of the cadmium-zinc-telluride SPECT system using low-dose protocol with a short-scan time
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Background: Although low-dose stress myocardial perfusion imaging (MPI) using the cadmium-zinc-telluride (CZT) ultrastart camera system is reported to show adequate image quality, an optimal scan time has not been elucidated.

Methods: One hundred thirty patients underwent both low-dose stress/rest (185MBq/370MBq) 99mTc-tetrofosmin MPI using a Discovery NM 530c (46 patients with exercise stress, 84 with ATP stress) and coronary angiography (CAG) within 3 months. Image scan time was 10-min for stress and 6-min for at rest (Image-1). Subsequently, images were reconstructed to evaluate a shorter scan time (Image-2: 6-min for stress and 4-min for at rest), using a list mode on a Xeleris workstation. Sensitivity, specificity and accuracy of both Image-1 and Image-2 in detecting coronary artery disease (CAD) (~50% luminal narrowing) were analyzed on a per-vessel basis.

Results: CAG revealed significant CAD in 106 patients. Image-1 showed that respective sensitivity, specificity and accuracy were 68%, 78% and 72% for LAD stenosis, 73%, 76% and 75% for LCX stenosis, 70%, 76% and 73% for RCA stenosis, whereas Image-2 had higher sensitivity and accuracy without significant loss of specificity than Image-1 (respectively sensitivity, specificity and accuracy were 80%, 82% and 80% for an LAD, 81%, 76% and 79% for an LCx, 78%, 74% and 76% for an RCA stenosis).

Conclusion: These results suggest that further reduction of either scan time or tracer dose may be possible for the CZT ultrastart camera system, even with the low dose protocol using 555 MBq of 99mTc-tetrofosmin.
P6355 | BEDSIDE
Real-time respiratory triggered SPECT myocardial perfusion imaging using CZT technology: impact of respiratory phase on CT attenuation correction
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Purpose: To assess the impact of the respiratory phase of real-time respiratory triggered SPECT acquisition on CT attenuation correction (CT-AC).
Methods: 40 patients underwent 1-day 99mTc-tetrofosmin pharmacological stress/rest myocardial perfusion SPECT imaging on a novel CZT gamma camera. SPECT was performed with free-breathing acquisition (unmatched) and with real-time respiratory triggering by intermittent acquisition confined to deep inspiration so as to match the respiratory phase of low-dose CT acquired for attenuation correction (phase-matched). Unmatched and phase-matched CT-AC SPECT were compared regarding visual diagnosis (scar and/or ischemia), segmental tracer uptake and image quality.
Results: Compared to unmatched CT-AC SPECT, applying CT-AC to respiratory phase-matched SPECT led to normalization (Fig. 1A) of presumed ischemia (Fig. 1B) in 3 patients and of scar in 1 patient. Thus, a change in diagnosis was observed in 4 patients (10%). Furthermore, phase-matched CT-AC SPECT showed a significant increase of relative segmental tracer uptake in inferobasal segments (mean difference ± SD: stress +3.2±1.6% vs. -0.05%, rest +3.6±1.2% vs. -0.01) and significant reduction in apical and anteroseptal segments (ranging from -2.5±1.0 to -4.4±1.2, all p<0.05). Image quality scores improved significantly with phase-matched CT-AC SPECT (mean difference ± SD: ±0.5±0.7, p<0.001).
Conclusions: Compared to unmatched CT-AC SPECT, respiratory phase-matched CT-AC SPECT showed significant regional changes in tracer uptake, leading to a change in diagnosis in a significant amount of patients. Furthermore, image quality improved significantly, hinting at the potential of respiratory triggered myocardial perfusion SPECT in combination with phase-matched CT-AC.

P6356 | BEDSIDE
RETI CARD SPECT sub-study: correlation between heart muscle perfusion and severity of hypertensive, diabetic or atherosclerotic retinopathy in patients with suspected stable coronary artery disease
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Purpose: To assess the impact of the respiratory phase of real-time respiratory triggered SPECT acquisition on CT attenuation correction (CT-AC).
Methods: 40 patients underwent 1-day 99mTc-tetrofosmin pharmacological stress/rest myocardial perfusion SPECT imaging on a novel CZT gamma camera. SPECT was performed with free-breathing acquisition (unmatched) and with real-time respiratory triggering by intermittent acquisition confined to deep inspiration so as to match the respiratory phase of low-dose CT acquired for attenuation correction (phase-matched). Unmatched and phase-matched CT-AC SPECT were compared regarding visual diagnosis (scar and/or ischemia), segmental tracer uptake and image quality.
Results: Compared to unmatched CT-AC SPECT, applying CT-AC to respiratory phase-matched SPECT led to normalization (Fig. 1A) of presumed ischemia (Fig. 1B) in 3 patients and of scar in 1 patient. Thus, a change in diagnosis was observed in 4 patients (10%). Furthermore, phase-matched CT-AC SPECT showed a significant increase of relative segmental tracer uptake in inferobasal segments (mean difference ± SD: stress +3.2±1.6% vs. -0.05%, rest +3.6±1.2% vs. -0.01) and significant reduction in apical and anteroseptal segments (ranging from -2.5±1.0 to -4.4±1.2, all p<0.05). Image quality scores improved significantly with phase-matched CT-AC SPECT (mean difference ± SD: ±0.5±0.7, p<0.001).
Conclusions: Compared to unmatched CT-AC SPECT, respiratory phase-matched CT-AC SPECT showed significant regional changes in tracer uptake, leading to a change in diagnosis in a significant amount of patients. Furthermore, image quality improved significantly, hinting at the potential of respiratory triggered myocardial perfusion SPECT in combination with phase-matched CT-AC.

P6357 | BEDSIDE
Very low isotope-dose stress-first myocardial perfusion imaging using fast SPECT technology: correlation to invasive coronary angiography
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Purpose: To assess the diagnostic value of very low isotope-dose stress-first my-ocardial perfusion SPECT (MPS) in identifying significant coronary artery disease (CAD) using invasive coronary angiography (ICA) as gold standard.
Methods: We identified 118 consecutive patient (98 males, 83.1%) who under- went a very low isotope-dose stress-first Tc-99m sestamibi myocardial perfusion SPECT (MPS) using fast CZT technology, and were referred to invasive coro-nary angiography within 60 days following nuclear testing. Of these 87 (71 males, 81.6%) did not have history of myocardial infarction or coronary bypass surgery and were included in the final analysis. Tc-99m doses ranged 5-10 mCi stress/15-22 rest, weight adjusted. All patients underwent stress supine/rest supine and rest supine 5-7, 3-2 and 2-3 minutes, respectively. Quantitative ana-lysis (QPS, CSMC) of MPS utilized custom developed normal limits specific for the CBT camera. Summed stress score (SSS%) supine, SSS% supine, total per-fusion deficit (TPD) supine, TPD prone and %ischemia (change from QPS) were automatically derived. Significant coronary disease by ICA was defined as ≤70% stenosis.
Results: Stress dose of Tc-99m was ≤6 mCi (≤1.8 mSv) in 61 patients (74.4%). Maximal stress dose was 10 mCi (3 mSv) injected to 5 patients with BMI 32-39. Significant coronary disease in ICA was found in 61/ 87 patients (70.1%). ROC analysis demonstrated area under the curve (AUC) higher than 0.8 for all quanti-tative parameters (Table). Prone variables SSS% prone and TPD stress prone yielded slightly larger AUC. A threshold for abnormality ≥4.5 yielded Sensitive/ specificity for SSS% supine 75/47.3, TPD supine 75/64.2, change% 82/76.9, SSS% prone 78.9/ 78.3, and TPD prone 82.5/ 73.9.
Conclusions: Very low isotope-dose stress-first MPS using fast CZT technology provided high diagnostic value with reduced patient radiation exposure.

P6358 | BEDSIDE
Myocardial perfusion SPECT imaging versus invasive fractional flow reserve: a comparison between conventional SPECT and cadmium-zinc telluride-based CZT SPECT
Purpose: Recently introduced cardiac SPECT cameras with cadmium zinc telluride-based (CZT) detectors may provide superior image quality allowing faster acquisition with reduced radiation doses. Although concordance between SPECT and invasive fractional flow reserve (FFR) measurement has been stud-ied, concordance of conventional and CZT-based SPECT with FFR has not been compared. Therefore, we prospectively assessed the level of agreement for con-ventional and CZT SPECT with FFR in patients with stable coronary artery dis-ease.
Methods: Both invasive FFR and myocardial perfusion imaging using conven-tional and CZT SPECT were performed in 100 patients with stable angina and intermediate grade stenosis at invasive coronary angiography. A cut-off value of <0.75 was used to define abnormal FFR.
Results: Mean age was 64±11 years, 64% were male. Thirty-one percent had intermediate coronary stenoses; 33% had FFR <0.75. On a per-patient basis the concordance with FFR was 70% for conventional SPECT and 73% for CZT SPECT (p=0.627).
Conclusions: Only 20%-30% of patients with intermediate coronary stenoses have significant coronary artery disease by SPECT or invasive FFR. The agree-ment between SPECT and FFR is modest and is similar for conventional and CZT SPECT. Further investigations are particularly necessary in patients with dis-crepant SPECT and FFR results, especially to determine whether these patients should undergo revascularisation.
P6359 | BEDSIDE
Progressive reduction in positive ischemic gated-SPECT studies in the last years
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Purpose: Different studies have shown a progressive reduction in the number of positive ischemic gated-SPECT studies. Our objective was to analyze the evolution of the gated-SPECT results performed in our Hospital.
Methods: During a period of 11 years, 10,529 gated-SPET of myocardial perfusion were performed in our Nuclear Cardiology Unit. We evaluated the number of rest tests and stress-rest tests, and the presence of myocardial ischemia (differential stress score > 2) in intervals of years according to the population age.
Results: Stress–rest (%) 1132 (93.3) 1752 (88) 2369 (91.7) 2.234 (95.1) 2.257 (94.4) Rest studies (%) 81 (6.7) 238 (12) 215 (8.3) 116 (4.9) 135 (5.6)
Conclusions: The proportion of rest and stress-rest-gated-SPECT studies along the last years did not change, while the number of studies with myocardial ischemia has been reduced significantly although the population age evaluated has increased.

P6360 | BEDSIDE
Myocardial perfusion imaging is low yield to assess for occult ischemia in patients with atrial fibrillation
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Purpose: The value of myocardial perfusion imaging (MPI) to evaluate for myocardial ischemia in patients with atrial fibrillation is uncertain. These patients often routinely undergo stress MPI. We hypothesize that MPI is low yield in this setting.
Methods: We identified 942 consecutive patients with atrial fibrillation who were referred for MPI for arrhythmia evaluation from October 2006 through June 2012. As outcomes, we assessed MPI results, revascularization within 6 months of MPI, and all cause mortality. MPI was considered abnormal if ejection fraction was less than 45% or if there were perfusion defects at rest or stress not attributed to artifact.
Results: Our patients were elderly (69±10.1 years), mostly male (63.1%), and all cause mortality. MPI was considered abnormal if ejection fraction was less than 45% or if there were perfusion defects at rest or stress not attributed to artifact. Rates of obstructive CAD and revascularization were also low with only 7% patients receiving percutaneous coronary interventions (Fig. 1). Of these patients who had known CAD. After a follow-up of 2.9±1.7 years, there were 62 deaths (6.6%). Reversible perfusion defects did not predict mortality (univariable HR 0.49, 95% CI 0.12 to 1.32). Utilizing Cox proportional hazard modelling, only age (HR 1.05, 95% CI 1.02 to 1.08) and abnormal ejection fraction (HR 2.62, 95% CI 1.39 to 4.62) predicted mortality.
Conclusions: MPI offers low yield and failed to risk stratify these patients. MPI should thus be considered rarely appropriate as part of a routine evaluation in patients with atrial fibrillation. Testing should be reserved for patients with chest pain or other symptoms considered an ischemic equivalent.

P6361 | BEDSIDE
Novel baseline correction method for quantitative analysis of myocardial perfusion from dce-cmr data using steady state T1 enhancement relaxation
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MR perfusion imaging enables quantitative estimation of myocardial blood flow (MBF). However the time interval between stress and rest imaging is insufficient for complete wash out of the first dose of contrast agent resulting in increase of the baseline signal intensity (SI) in the second data acquisition round and reducing quantification accuracy. Baseline correction usually is performed by using the pre contrast baseline SI level (MBFPC). Here we introduce a novel inter subject T1 baseline correction method.
Perfusion data were obtained from a hardware perfusion phantom with known perfusion values (1 and 2 mL/g/min). Images were acquired for different T1 baseline levels obtained by recirculating water and Gadolinium in the phantom after each of 4 consecutive injections. Images were acquired on a Philips Achieva 3T (TX) system. T1 mapping was performed using a MOLLI sequence. T1 weighted images are acquired before and after passage of the bolus of contrast to measure myocardial blood volume (MBV). MBF was estimated by Fermi deconvolution. A correction factor (CF) was calculated as CF=MBV1st/MBV th, i=2…4 and was used to correct MBF values (MBFCorr).
Figure 1 compares the MBFCorr with the MBFPC and the MBF before baseline correction. The MBFCorr values are in close agreement with the actual 1 and 2 mL/g/min perfusion rates (1.12±0.06 and 2.3±0.09 mL/g/min) compared with the non corrected MBF (1.5±0.4 and 2.6±0.3 mL/g/min) and MBFPCorr (0.8±0.07 and 2.3±0.3 mL/g/min). MBFCorr showed less variability (Coefficients of variation for 1 and 2 mL/g/min: MBFCorr 0.07 and 0.03; MBFPCorr 0.15 and 0.13). MBF estimates are strictly dependent on baseline SI values. T1 baseline correction allowed more precise perfusion estimation in comparison with pre contrast baseline correction.

MISCELLANEOUS – MIXED
P6363 | BENCH
Palpating the heart: in vivo cardiac time harmonic elastography under guidance of b-mode ultrasound with real time elastographic feedback
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Background: Cardiac MR elastography (cMRE) was recently shown sensitive to diastolic dysfunction. cMRE measures the periodic alteration of the myocardial shear modulus based on externally induced low-frequency acoustic vibrations produced by a loudspeaker. It was demonstrated that shear wave amplitudes are reduced in patients with pathologically increased myocardial stiffness (Fig. 1a). Purpose of this feasibility study is to adopt the principles of cMRE by fast and cost-efficient echocardiography.
Methods: Cardiac time harmonic elastography (cTHE) was implemented into a commercial ultrasound B-mode scanner connected to a vibration bed designed to introduce 30-Hz continuous vibrations into the patient’s chest (Fig. 1b). The alteration of shear wave amplitudes was displayed in real time after placement of the elastographic processing window of 1–2 cm width by B-mode guidance. In a group of 9 healthy volunteers, we focused on three different regions of the heart – the lateral wall of the left ventricle (LV), the right ventricle’s wall (RV wall) and the blood pool of the right ventricle (RV lumen, Fig. 1c).
The extent of target organ damage in patients with hypertension and underlying diabetic chronic kidney disease significantly affect the ADC values calculated. Diffusion-weighted magnetic resonance imaging and consecutive calculation of the apparent diffusion coefficient can be a valuable tool to determine vulnerability to even moderate blood pressure elevations. Recently, diffusion-weighted magnetic resonance imaging (DW-MRI) was used to differentiate various functional renal abnormalities. The reproducibility and feasibility of the DW-MRI of the kidneys in healthy volunteers and in patients with renal abnormalities has been reported. The purpose of our study was to assess the value of the diffusion magnetic resonance imaging of the kidneys and consecutive calculation of apparent diffusion coefficient in patients with arterial hypertension and known diabetic kidney disease.

Materials and methods: The study included 37 consecutive patients (19 men and 18 women) with hypertension. The patients were divided into 2 groups depending on the presence or absence of known diabetic kidney disease, comparable by age, sex and level of the blood pressure. 1st group consisted of hypertensive patients with known diabetic chronic kidney disease; 2nd group — of hypertensive patients without known diabetes mellitus. 11 healthy volunteers entered the group of comparison. All patients underwent transverse diffusion-weighted multi-section echo-planar MRI (b value=600 s/mm²). The ADCs of the kidneys were calculated. Results: There was a statistically significant difference between the ADC values of both kidneys in the 1st and 2nd group (3.01 ±0.19 vs 3.28 ±0.24; P<0.05), as well as between 1st group and the group of comparison (3.37 ±0.38 vs P<0.05) respectively. There was no statistically significant difference between the ADC values of both kidneys in the 2nd group and group of comparison (P>0.05). In addition, the ADC values of patients with microalbuminuria did not differ from those of the other patients (P>0.05).

Conclusion: Target-organ damage caused by hypertension on the background of underlying diabetic chronic kidney disease significantly affect the ADC values calculated on diffusion-weighted magnetic resonance imaging in patients with known diabetic kidney disease. Despite the target-organ damage caused by hypertension, it did not affect the ADC values in patients without known diabetic kidney disease. Diffusion-weighted magnetic resonance imaging and consecutive calculation of the apparent diffusion coefficient can be a valuable tool to determine the extent of target organ damage in patients with hypertension and underlying diabetic chronic kidney disease.

Diffusion-weighted magnetic resonance imaging in patients with arterial hypertension and known diabetic kidney disease: value of the apparent diffusion coefficient calculation

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Objectives: Unlike the majority of patients with uncomplicated hypertension in whom minimal renal damage develops in the absence of severe blood pressure elevations, patients with diabetic chronic kidney disease exhibit an increased vulnerability to even moderate blood pressure elevations. Recently, diffusion-weighted magnetic resonance imaging (DW-MRI) was used to differentiate various functional renal abnormalities. The reproducibility and feasibility of the DW-MRI of the kidneys in healthy volunteers and in patients with renal abnormalities has been reported. The purpose of our study was to assess the value of the diffusion magnetic resonance imaging of the kidneys and consecutive calculation of apparent diffusion coefficient in patients with arterial hypertension and known diabetic kidney disease.

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Conclusion: Target-organ damage caused by hypertension on the background of underlying diabetic chronic kidney disease significantly affect the ADC values calculated on diffusion-weighted magnetic resonance imaging in patients with known diabetic kidney disease. Despite the target-organ damage caused by hypertension, it did not affect the ADC values in patients without known diabetic kidney disease. Diffusion-weighted magnetic resonance imaging and consecutive calculation of the apparent diffusion coefficient can be a valuable tool to determine the extent of target organ damage in patients with hypertension and underlying diabetic chronic kidney disease.

F. Kondo³, T. Fukusato², K. Kozuma¹, T. Isshiki¹.

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P6367 | BEDSIDE
The volume of left atrium measured by multi-detector computed tomography can predict of long term outcome in catheter ablation of atrial fibrillation
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Background: This study aimed to identify the volume left atrium (LA) and left atrial appendage (LAA) calculated by multidetector computed tomography (MDCT) is related to the long term outcome of radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF).
Methods: We analyzed data from 99 consecutive patients who referred for RFCA due to drug-refractory symptomatic AF (age 56±10 years; 74% men; 64% paroxysmal AF). Prior to the procedure, all patients underwent ECG-gated 128 channels MDCT scan for assessment for PV anatomy, LA and LAA volume estimation, and electro-anatomical mapping intervention.
Results: The volume of LA and LAA calculated by CT was 142.6±32.2 mL and 14.7±6.0 mL respectively. LA volume was smaller in paroxysmal AF (PAF) than persistent AF (PeAF) (133.9±29.3 mL vs. 158.0±31.4 mL, p<0.0001) but LAA volume was not significantly different between PAF and PeAF (13.9±5.0 mL vs. 16.3±7.3 mL, p>0.05). Patients were classified into 2 groups by the LA volume of 160mL; group 1 (LA volume <160mL, n=73) and group 2 (LA volume ≥160mL, n=26). After a mean follow up 12.6±5.3 months, 78.8% of the patients maintained sinus rhythm after the index ablation. AF free survival was significantly greater in group 1 than group 2 (84.9% vs. 61.5%, p<0.01). No relationship was found between LAA volume and the outcome of RFCA. Multivariate analysis showed that the LA volume >160mL was an independent predictor of arrhythmia-free after ablation (Hazard ration 2.55, 95% confidential interval 1.02-6.35, p=0.045).
Conclusion: Higher LA volume is independent risk factor for AF recurrence after RFCA but not LAA volume. The LA volume quickly assessed by MDCT could be a good predictor of long term recurrence after AF ablation.

P6369 | BEDSIDE
Lateral myocardial infarction generates prominent R wave in V1
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Purpose: The correct location of the necrosis in cases of Q wave MI, is important not only from the academic point of view but also for its clinical implications. Because of this, it is necessary to clarify if the presence of prominent R wave in V1, as a mirror image of an infarction zone, is due to involvement of posterior wall or lateral wall.
Methods: In a total of 155 patients that has presented MI with infero-lateral zone involvement ( Inferior, lateral and infero-lateral MI; proved by CE-CMR) the following ECG parameters were evaluated: R in V1 >3 mm, R/S ratio in V1 >1 (classic criteria for posterior MI), and R/S ratio in V1 <0.5 and correlated with MI location according CE-CMR.
Results: R ≥3 mm criteria: Present in 30 cases: 5 cases of IM lateral, 23 cases of inferior-lateral MI, 2 cases of inferior MI. Absent in 125 cases, 73 lateral/infero-lateral MI (26/47), 52 inferior MI. (SE 27.7%, SP 96.4%). R/S ≥1 criteria: Present in 20 cases: 3 cases of lateral MI, 17 cases of infero-lateral MI, 0 cases of inferior MI. Absent in 135 cases, 81 cases of lateral/infero-lateral MI (28/53), 54 cases of inferior MI (SE 19.8%, SP 100%), R/S >0.5 criteria: Present in 47 cases: 6 cases of lateral MI, 39 cases of infero-lateral MI, 2 cases of inferior MI. Absent in 108 cases, 56 cases of lateral/infero-lateral MI (25/31), 52 cases of inferior MI (SE 44.8%, SP 96.4%).
Conclusion: The criteria R >3 mm in V1 and R/S in V1 >1 are very specific but with low sensitivity for diagnosis of lateral MI. The criteria R/S >0.5 has greater sensitivity with no significant reduction in specificity. The prominent R wave in V1 according the exposed criteria (including the classic criteria for posterior MI), is due to lateral MI and not to involvement of infero-basal segment of inferior wall (old posterior wall)

P6370 | BEDSIDE
Cardiac sympathetic denervation is related with microvascular dysfunction in non-infarcted myocardium in patients with ischemic cardiomyopathy
M.T. Rijnierse1, S. De Haan1, H.J. Harms2, A.C. Van Rossum1, A.A. Lammertsma2, C.P. Allaart1, P. Knaapen1. 1VU University Medical Center, Department of Radiology, Amsterdam, Netherlands; 2VU University Medical Center, Department of Nuclear Medicine & PET, Amsterdam, Netherlands
Purpose: Myocardial infarction (MI) results in sympathetic innervation injury of the scar and adjacent areas, which is associated with sudden cardiac death. Sympathetic denervation has also been observed in patients with chronic multi-vessel coronary artery disease but without MI, suggesting that perfusion abnormalities lead to sympathetic nerve injury. Impaired hyperemic myocardial blood flow (MBF), reflecting subtle perfusion abnormalities may therefore be associated with sympathetic nerve injury in non-infarcted myocardium. The aim of this study was to assess the relation of positron emission tomography (PET) assessed sympathetic innervation and hyperemic MBF in non-infarcted myocardium.

P6368 | BEDSIDE
The economic results of the CAPP study
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Purpose: To determine the most cost-effective diagnostic pathway for stable chest pain patients between cardiac computerised tomography (CT) and exercise stress electrocardiography testing (EST).
Method: A UK prospective randomised controlled trial of 500 troponin negative, stable chest pain patients without known coronary artery disease. Patient healthcare resource use (GP & nurse visits, emergency department (ED) visits, hospital investigations, hospital admissions and outpatient visits) was collected over the 12 month study period and total costs calculated per patient. Patient health related quality of life was measured using the EQ-5D administered at baseline, 3, 6 & 12 months and converted to utility scores for the calculation of Quality Adjusted Life Years (QALYs).
Results: 12 patients withdrew, resulting in 245 in the EST cohort and 243 in the CT cohort, with no significant difference in baseline demographics. There were increased revascularisation in the CT arm, but increased ED attendances with more associated admissions in the EST. Mean (95% CI) total costs per patient for the CT and EST groups were €2304.80 (1951.81 to 2477.80) and €2303.60 (€1522.21 to 2540.99) respectively. The small difference in total mean costs was not statistically significant (p=0.992). Mean (95% CI) QALYs for CT and EST were 0.81 (0.70 to 0.84) and 0.79 (0.76 to 0.83) respectively. The small difference in QALYs of 0.02 (bootstrapmed 95% CI -0.02 to 0.06) was not statistically significant (p=0.443). A complete case analysis using linear regression to adjust costs and QALYs for age, sex, type of pain (non anginal/typical/atypical) and baseline health related qual-

P6366 | BEDSIDE
Cardiac sympathetic denervation is related with microvascular dysfunction in non-infarcted myocardium in patients with ischemic cardiomyopathy
M.T. Rijnierse1, S. De Haan1, H.J. Harms2, A.C. Van Rossum1, A.A. Lammertsma2, C.P. Allaart1, P. Knaapen1. 1VU University Medical Center, Department of Radiology, Amsterdam, Netherlands; 2VU University Medical Center, Department of Nuclear Medicine & PET, Amsterdam, Netherlands
Purpose: Myocardial infarction (MI) results in sympathetic innervation injury of the scar and adjacent areas, which is associated with sudden cardiac death. Sympathetic denervation has also been observed in patients with chronic multi-vessel coronary artery disease but without MI, suggesting that perfusion abnormalities lead to sympathetic nerve injury. Impaired hyperemic myocardial blood flow (MBF), reflecting subtle perfusion abnormalities may therefore be associated with sympathetic nerve injury in non-infarcted myocardium. The aim of this study was to assess the relation of positron emission tomography (PET) assessed sympathetic innervation and hyperemic MBF in non-infarcted myocardium.
Methods: Patients with ischemic cardiomyopathy, referred for primary prevention implantable cardioverter defibrillator therapy according to current guidelines were included. [15O]H2O- and [11C]Hydroxyephedrine (HED)-PET was performed to quantify resting MBI, hyperemic MBF, and sympathetic innervation. Late gadolinium enhanced-cardiac magnetic resonance (LGE-CMR) imaging was performed to assess left ventricular end-systolic (LVESV) and end-diastolic volumes (LVEDV), and scar size. HED retention index (RI) and MBF were assessed in remote segments without scar, selected on LGE-CMR results.

Results: 44 patients were included (38 men, age 67±8 years, LVEF 29±6%). In non-infarcted myocardium, HED RI positively correlated with hyperemic MBF (R=0.45, p<0.01), resting MBF (R=0.31, p=0.04), and negatively with LVEF (R=-0.32, p=0.03) and LVEDV (R=-0.36, p=0.02). Multivariate linear regression analysis revealed that hyperemic MBF (R=0.68 p<0.01), LVEDV (B=-0.05, p<0.01), and NTproBNP (R=0.24, p=0.04) were independently associated with HED RI in remote myocardium.

Conclusion: Impaired sympathetic innervation is associated with impaired hyperemic MBF in non-infarcted segments in patients with ischemic cardiomyopathy. Whether impaired hyperemic MBF is the primary cause of this relation remains uncertain.

P6371 | BEDSIDE
Characterization of coronary microvascular dysfunction in patients with suspected coronary artery disease
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Purpose: Coronary microvascular dysfunction (CMD) is defined as impaired myocardial perfusion in the absence of epicardial artery obstruction. This may cause chest pain, ECG abnormalities and stress perfusion results mimicking epicardial coronary artery disease (CAD). We evaluated CMD in symptomatic patients with intermediate probability of CAD with comprehensive anatomical and functional imaging tests.

Methods: We recruited prospectively 189 patients with intermediate pre-test probability of CAD. All patients underwent computed tomography coronary angiography (CTCA), quantitative positron emission tomography (PET) perfusion imaging with 15O-water during adenosine stress using a hybrid scanner, invasive coronary angiography (ICA) and fractional flow reserve (FFR) when feasible. CMD was defined as abnormal myocardial perfusion stress (MBF <25 mL/g/min) and absence of haemodynamically significant CAD (<50% stenosis or FFR >0.8).

Results: Significant obstructive CAD was found in 38%, non-obstructive in 40%, whereas 22% had no coronary atherosclerosis. Stress myocardial perfusion abnormalities were present in 72 patients (38%). These were explained by matching epicardial stenosis in 55, whereas 17 patients (9.0%) had CMD. Of these, 2 had globally reduced stress perfusion without any coronary atherosclerosis. Four patients had globally reduced stress perfusion in the absence of haemodynamically significant CAD, but non-obstructive atherosclerosis on CTCA. Eleven patients, with non-infarcted myocardium, had additional perfusion abnormalities in regions unmatched with the obstructive lesions. Of CMD patients 24% were female, 41% had diabetes or prediabetes, 71% dyslipidemia, 47% hypertension, 65% family history of CAD and 17% were currently smoking. Type of chest pain was typical in 5 (29%) and atypical in 10 (59%) patients and 2 patients had other symptoms.

Conclusions: In a patient population with intermediate probability of CAD, some features of CMD can be identified in 9% of the patients who have numerous risk factors. However, CMD without any coronary atherosclerosis is rare (1%). Coexistence of CMD with non-obstructive CAD (3%) and obstructive CAD (6%) is more common. Quantitation of myocardial perfusion combined with anatomical imaging provides comprehensive way to identify CMD.

P6372 | BEDSIDE
Increased hsCRP in patients with acute-onset chest pain and significant coronary artery stenosis assessed with MDCT despite normal ECG and plasma troponin
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Purpose: Plasma high-sensitivity C-reactive protein (hsCRP) is significantly elevated in patients with acute coronary syndrome (ACS), whereas the potential clinical value of hsCRP in patients with acute-onset chest pain but without ACS has not been fully established. The aim of this study was to evaluate the correlation between hsCRP and the presence of significant coronary artery stenosis assessed with 320-slice multidetector computed tomography (320-MDCT) in patients with acute-onset chest pain and subsequent normal plasma troponins and ECG.

Methods: We measured hsCRP in 473 patients with acute-onset chest pain referred to the emergency department, who turned out to have normal levels of plasma troponins and no significant changes in the 12-lead electrocardiogram during a 24-hour observation period. Coronary calcium score and measurement of luminal obstruction were evaluated with 320-MDCT angiography by independent observers. A significant coronary artery stenosis was defined as a diameter stenosis >50%.

Results: A significant coronary artery stenosis was found by 320-MDCT in 99 (21%) of the patients. The remaining 374 patients constituted the control group. The patient group with significant coronary artery stenosis was older (median age 60 vs. 54 years, p<0.0001), a larger percentage was men (73% vs. 53%, p=0.006), and the median coronary calcium score was considerably higher (304 vs. 27, p<0.0001) compared with the control group. In addition, hsCRP was significantly higher in patients with a significant coronary artery stenosis (2.2mg/L vs. 1.4mg/L compared with controls, p=0.003). In a multiple regression analysis including sex, age, smoking status, hypertension, hypercholesterolemia, presence of diabetes, family disposition and coronary calcium score, hsCRP was found to be an independent predictor of significant coronary artery disease (p=0.05).

Conclusion: In patients with acute-onset chest pain and subsequent normal plasma troponins and ECG, hsCRP is higher in patients with than in patients without significant coronary artery disease assessed with 320-MDCT.
rolled. Coronary flow velocity and pressure were measured distal to the stenotic lesion using a dual pressure-flow sensor guidewire under adenosine triphosphate infusion. The instantaneous hemodynamic diastolic pressure-velocity slope index (IHPVPS; interpreted as coronary conductance) and the extrapolated zero-flow pressure (Pz; interpreted as back pressure) were obtained from DVPVR plot. Wave intensity analysis was used to identify and quantify individual pressure and velocity waves. A consistent pattern of six predominating waves was identified, and all wave components were compared.

**Results:** Myocardial fractional flow reserve improved from 0.730 ± 0.161 to 0.898 ± 0.065 (P < 0.001) after the procedure. Wave intensity analysis revealed that PCI elevated DVPVR and significantly increased the forward-traveling waves and backward-traveling suction wave (table).

<table>
<thead>
<tr>
<th>Pressure Wave Component</th>
<th>Pre-PCI (mmHg)</th>
<th>Post-PCI (mmHg)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pz</td>
<td>2.13 ± 1.52</td>
<td>3.24 ± 2.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IPVPS (cm/s/mmHg)</td>
<td>20.12 ± 1.07</td>
<td>12.4 ± 7.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Estimated wave speed (m/s)</td>
<td>24.0 ± 18.9</td>
<td>10.3 ± 4.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Cumulative wave intensity</td>
<td>&lt;10^5 W/m^2</td>
<td>&lt;0.898</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dominant forward-traveling compression wave</td>
<td>5.9 ± 4.4</td>
<td>10.9 ± 7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Forward-traveling decompression wave</td>
<td>2.5 ± 1.6</td>
<td>3.5 ± 2.7</td>
<td>0.028</td>
</tr>
<tr>
<td>Late forward-traveling compression wave</td>
<td>0.8 ± 0.9</td>
<td>1.8 ± 1.6</td>
<td>0.017</td>
</tr>
<tr>
<td>Early backward-traveling compression wave</td>
<td>4.6 ± 3.8</td>
<td>7.4 ± 5.6</td>
<td>0.042</td>
</tr>
<tr>
<td>Late backward-traveling compression wave</td>
<td>2.7 ± 2.7</td>
<td>3.1 ± 3.5</td>
<td>0.581</td>
</tr>
<tr>
<td>Backward-traveling suction wave</td>
<td>8.1 ± 3.8</td>
<td>12.4 ± 7.9</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Values are shown in mean ± SD.

**Conclusions:** Pz was decreased and IPVPS was elevated in patients with significant coronary stenosis. PCI raised the dominant forward-traveling waves due to relieving stenosis as well as the backward-traveling suction wave. PCI may immediately improve the coronary microcirculation suction function.

**P6376 | BEDSIDE**

Relevance of index of microcirculatory resistance on fractional flow reserve in intermediate coronary artery stenosis


**Purpose:** We investigated the relevance of the index of microcirculatory resistance (IMR) and fractional flow reserve (FFR) of intermediate coronary lesion.

**Methods:** We enrolled patients who met the following criteria: stable angina with de novo coronary stenotic lesions of intermediate epicardial coronary stenosis (approximately 50–70% diameter stenosis) in the left anterior descending coronary artery. An intracoronary combined pressure-temperature sensor-tipped guidewire was used to measure the thermodilution-derived IMR and FFR.

**Results:** Sixty-seven intermediate coronary lesions (approximately 50–70% diameter stenosis) in the left anterior descending coronary artery. An intracoronary combined pressure-temperature sensor-tipped guidewire was used to measure the thermodilution-derived IMR and FFR.

**Conclusions:** The correlation of the index of microcirculatory resistance (IMR) with FFR after PCI was significant (R2=0.31; P=0.001). The correlation of the index of microcirculatory resistance (IMR) with FFR after PCI was significant (R2=0.31; P=0.001).

**P6377 | BEDSIDE**

Fractional flow reserve for the prediction of cardiac events after drug-eluting stent implantation

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**Background:** Previous studies have identified post-stent fractional flow reserve (FFR) >0.90 as a useful surrogate for favorable long-term clinical outcome after bare-metal stent implantation. In drug-eluting stent (DES) era, anti-proliferative DES have markedly reduced neointimal proliferation within stented segment and it is considered that the correlation between post-stent FFR and long-term outcome including target lesion revascularization (TLR) might be attenuated in lesions treated with DES. However, the prognostic value of post-stent FFR after DES implantation remains undetermined.

**Methods:** FFR measurements at maximum hyperemia were performed after elective percutaneous coronary intervention for coronary lesions treated with DES. Patients were followed up for at least one year. During one year follow-up period, TLR and major adverse cardiac events (MACE) were evaluated. MACE was defined as any death, myocardial infarction, stroke, or any revascularization.

**Results:** A total of 146 patients with DES implantation were enrolled. Pre intervention FFR increased from 0.68 ± 0.09 to 0.86 ± 0.07 after stent implantation (p < 0.001). During one year follow-up after stent implantation, TLR and MACE occurred in 11 and 33 patients (7.5% and 22.6%). There was no significant difference in post-stent FFR between patients with or without subsequent TLR (0.87 ± 0.05 vs. 0.86 ± 0.07, p = 0.67). After grading lesions to 3 categories according to the post-stent FFR (below 0.80, 0.81 to 0.90, and ≥ 0.90), TLR and MACE were increased. MACE was defined as any death, myocardial infarction, stroke, or any revascularization.

**Conclusion:** In patients treated with DES, post-stent FFR couldn’t predict subsequent TLR or MACE at one year.
Phasic coronary blood flow pattern and vasodilator reserve of the right ventricle


**Purpose:** Coronary blood flow in the left ventricle has been extensively studied in health and disease. However, what little is known about right ventricular myocardial perfusion is from experimental animal studies. The purpose of our study was to assess phasic coronary blood flow pattern and flow reserve of the right ventricle.

**Methods:** Nine patients underwent coronary blood flow velocity measurements, using a 0.014 inches Doppler guidewire in the right ventricular branch (RVC) and in the right coronary artery (RCA) distal to the origin of RVC. Measurements were recorded at baseline (b) and at maximal hyperemia (h) after adenosine administration. Coronary flow reserve (CFR) was calculated as the ratio of the time-averaged peak coronary flow velocity (APV) at maximal hyperemia (h-APV) to the APV at baseline (b-APV).

**Results:** Results are shown in the table and the figure.

**Table 1**

<table>
<thead>
<tr>
<th>Diameter</th>
<th>b-APV</th>
<th>b-DSVR</th>
<th>h-APV</th>
<th>h-DSVR</th>
<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCA</td>
<td>23.8±0.7</td>
<td>23.8±9.5</td>
<td>1.25±0.33</td>
<td>53.1±11.3</td>
<td>1.2±0.21</td>
</tr>
<tr>
<td>RVC</td>
<td>1.33±0.5</td>
<td>17.8±9.5</td>
<td>0.89±0.21</td>
<td>41.3±16.8</td>
<td>0.83±0.09</td>
</tr>
</tbody>
</table>

**DSVR:** diastolic to systolic velocity ratio.

**Conclusions:** Coronary blood flow in the RV is out of phase with that in the left ventricular myocardium, showing a systolic predominant pattern. Although a small proportion of the right coronary blood flow is directed to the right ventricle, there was no significant difference in resting CFR between left and right ventricular myocardium.

**P6380 | BEDSIDE**

Impact of coronary plaque burden and composition on peri-procedural myocardial infarction and coronary flow reserve after percutaneous coronary intervention

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**Background:** Peri-procedural myocardial infarction (PMI) is one of the major complications of percutaneous coronary intervention (PCI). We investigated the influence of coronary plaque burden and characteristics on PMI using intravascular ultrasound (IVUS) with radiofrequency-based tissue characterization technology (iMAP).

**Methods and results:** The study population consisted of 33 consecutive patients with stable angina pectoris who underwent PCI. IVUS images were recorded before and after PCI for offline analysis, and coronary flow reserve (CFR) was measured after PCI. PMI was defined as a post-PCI cardiac troponin T elevation >3 times the upper reference limit (0.014 ng/ml). The overall plaque volume in patients with PMI (n=12) was significantly greater than that in patients without PMI (n=21) (240.4±106.0 mm³ vs. 152.1±76.9 mm³, p=0.0096).

The iMAP-IVUS analysis demonstrated that the fibrotic, lipidic, and necrotic tissue volume within culprit lesions was also greater in patients with PMI than in patients without PMI (129.4±52.2 mm³ vs. 94.6±40.8 mm³, p=0.041; 26.8±10.5 mm³ vs. 15.8±11.5 mm³, p=0.011; and 81.3±48.4 mm³ vs. 40.2±33.6 mm³, p=0.0071, respectively). Multivariate logistic analysis demonstrated that necrotic tissue volume was the only independent predictor of PMI. Multiple regression analysis demonstrated that the post-PCI CFR values significantly correlated with overall plaque volume (R²=0.21, p=0.0099), and there were no correlations with the percent tissue burden of each plaque component.

**Conclusions:** The iMAP-IVUS analyses demonstrate that necrotic tissue volume is a potent predictor of PMI. Microcirculatory disturbance after PCI is significantly influenced by overall plaque volume, regardless of plaque compositions.

**P6381 | BEDSIDE**

Supplemental oxygen does not affect coronary physiologic indices measured during elective percutaneous coronary intervention


**Purpose:** Supplemental oxygen is frequently used during coronary interventional procedures. Existing scientific evidence however, provide little support for routine use in normoxic patients. In experimental patients, hyperoxemia has been associated with a reduction of coronary blood flow as well as an increase in coronary microvascular resistance, implying potential detrimental effects in patients with coronary artery disease. We studied the effects of supplemental oxygen on coronary physiologic indices such as fractional flow reserve (FFR), coronary flow reserve (CFR) and the index of microcirculatory resistance (IMR), all dependent on maximum coronary flow and minimal coronary microvascular resistance.

**Methods:** In 18 patients (mean age 69 y.) with stable coronary artery disease and a 40-80% diameter stenosis in the proximal or mid part of a major coronary artery, intracoronary pressure- and thermodilution-derived flow indices were recorded using a pressure-temperature sensor-tipped guidewire at baseline and during maximum hyperemia induced by i.v. infusion of adenosine (140μg/kg/min). Patients were then randomly assigned in a double-blind fashion to mask inhalation of either oxygen 6 l/min (group 1, n=9) or room air (group 2, n=9) for ten minutes followed by repeated measurements of FFR, CFR and IMR. Coronary wedge pressure was recorded during balloon inflation allowing correction for collateral flow. Statistical analysis was performed using repeated measures ANOVA.

**Results:** Baseline FFR, CFR and IMR were 0.79, 3.0 and 13 for group 1 and 0.73, 3.4 and 12 for group 2. No significant changes in the indices were seen after 10 minutes of mask inhalation (mean differences for FFR, CFR and IMR 0.05 vs 0.1, 0.05 vs 0.01, 0.53 vs 1.8 for group 2).

**Conclusions:** In patients undergoing elective percutaneous intervention supplemental oxygen did not significantly influence coronary physiologic indices. This may reflect that vasocostrictive effects of hyperoxemia are outweighed by the endothelium-independent mechanisms mediating vasodilation during adenosine- induced hyperemia.

**P6382 | BEDSIDE**

Intermediate-term within-subject reproducibility of instantaneous wave-free ratio and its hemodynamic dependence in comparison with fractional flow reserve


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**Background:** The instantaneous wave-free ratio (iFR) is a novel pressure-derived index of coronary physiological stenosis severity without vasodilator drugs. Intermediate-term within-subject variability of iFR and its hemodynamic dependence or the relationship with microvascular resistance has not been fully investigated.

**Methods and results:** Fractional flow reserve (FFR), iFR, and the index of microcirculatory resistance (IMR) were measured twice, in 37 coronary arteries from 37 patients (65±9.6 y) with an average interval of 43±22 days. Hemodynamic status including aortic pressure, distal coronary artery pressure, and heart rate were similar between the 2 measurements. There were no significant difference in FFR, iFR and IMR between the 2 measurements (FR: 0.88±0.08 vs 0.85±0.06; FFR: 0.77±0.06 vs 0.78±0.07; IMR: 21.7±1.04 vs 19.9±1.93, respectively). Regression analysis showed significant relationship between the 2 measurements for all three indices (FFR: R²=0.65, p<0.001, FFR: R²=0.65, p<0.001, and IMR: R²=0.31, p<0.001, respectively). The repeatability coefficients and relative repeatability coefficients of FFR, iFR and IMR were 0.08 (10.2%), 0.08 (10.4%), and 18.2 (87.5%), respectively. Coefficients of variation of iFR, FFR, and IMR were 3.7%, 3.9%, and 31.8%, respectively. Reproducibility of iFR significantly correlated with heart rate (p<0.008). FFR and iFR showed a significant relationship (R²=0.46, p<0.001), whereas there was no association between FFR and IMR, nor between iFR and IMR.

**Conclusion:** FFR showed good reproducibility similar to FFR and independence of hyperemic microvascular resistance, although less independent of hemodynamic status.
Lesion characteristics as a predictor of optimal post-stent fractional flow reserve

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Background: Previous studies have identified post-stent fractional flow reserve (FFR) >0.90 as a useful surrogate for favorable long-term clinical outcome after percutaneous coronary intervention. Higher value of post-stent FFR should be pursued for optimal percutaneous coronary intervention. However, there is little information regarding factors that influence post-stent FFR. The purpose of this study was to determine the impact of patient and lesion characteristics on post-stent FFR.

Methods: FFR measurements at maximum hyperemia were performed before and after elective percutaneous coronary intervention. Lesions with pre-interventional FFR <0.80, lesions with bypass graft and patients with acute myocardial infarction were excluded. If final value of FFR after stent implantation was >0.90, this post-stent FFR was considered as optimal post-stent FFR. For lesion characteristics, pressure drop pattern of FFR was assessed and classified into “abrupt pattern” and “gradual pattern” according to the pullback curve of FFR. The effect of patient and lesion characteristics including pressure drop pattern on post-stent FFR was evaluated.

Results: A total of 205 lesions with stent implantation were evaluated. Pre-interventional FFR ranged from 0.67 ± 0.10 to 0.87 ± 0.07 after stent implantation (p < 0.0001). Optimal post-stent FFR was attained in 75 lesions (36.6%). On logistic regession analysis, optimal post-stent FFR was positively correlated with abrupt pressure drop pattern (HR, 2.1; 95%CI, 1.1-4.2; p=0.03) and pre-stent FFR per 0.1 increase (HR, 1.5; 95%CI, 1.0-2.1; p=0.03), and negatively correlated with lesion location in left anterior descending artery (HR, 0.8; 95%CI, 0.08-0.39; p < 0.0001).

Conclusion: Abrupt pressure drop pattern, pre-stent FFR and lesion location of left anterior descending artery were independent predictors of optimal post-stent fractional flow reserve. Utilization of such information might help to optimize percutaneous coronary intervention.

Whole blood viscosity is an overlooked parameter in evaluation of Fractional Flow Reserve (FFR)

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Purpose: Although Fractional Flow Reserve (FFR) is considered as the gold standard tool for functional assessment of coronary artery stenosis, this prominent technique may have some limitations. As a pressure-dependent measurement, it may be affected from blood viscosity. Whole Blood Viscosity (WBV) can be computed with a validated equation only with hematocrit and total plasma protein concentration. In this study we aimed to evaluate the relationship between FFR and WBV.

Methods: We included 327 patients who were performed FFR after evaluating baseline coronary angiogram. According to the FFR cut-off value of 0.80, we divided the patients into two groups: 115 patients with critical stenosis as FFR(+) group (68.9% male, mean age 62.4±9.1) and 212 patients without critical stenosis as FFR(-) group (73.9% male, mean age 61.3±9.6). WBV was calculated for both low-shear rate (LSR) (0.5 sec-1) and high-shear rate (HSR) (208 sec-1) concentration. In this study we aimed to evaluate the relationship between FFR and WBV.

Results: WBV at LSR (OR: 1.021, 95%CI: 1.009-1.033; p=0.001) and at HSR (OR: 1.037, 95%CI: 1.025-1.050; p <0.0001). In multivariate logistic regression analysis, WBV at LSR (OR: 1.021, 95%CI: 1.009-1.033; p=0.001) and at HSR (OR: 1.037, 95%CI: 1.025-1.050; p <0.0001) were independent predictors of critical stenosis in FFR.

Conclusion: In our study, we have delineated that WBV has an important association with FFR values. While evaluating FFR results, WBV should not be overlooked.

Lesion characteristics in the interpretation of myocardial single photon emission computed tomography for detection of myocardial ischemia using fractional flow reserve


Background: Myocardial single photon emission computed tomography (SPECT) is an established noninvasive method for the assessment of the functional significance of coronary artery stenosis. However, myocardial SPECT was considered to have some limitations in patients with multi-vessel disease, acute myocardial infarction, non-culprit lesion. The aim of this study was to elucidate the consideration in the interpretation of myocardial SPECT for detection of myocardial ischemia by using fractional flow reserve (FFR).

Methods: We enrolled 124 patients (131 lesions) with significant coronary artery disease (CAD) who underwent myocardial SPECT followed by conventional coronary angiography (CAG) with FFR retrospectively. Significant CAD was defined as >50% diameter stenosis assessed by CCA. We compared the functional re- sults of each epicardial vessel assessed by FFR and the perfusion defects in each myocardial territory as detected by myocardial SPECT in patients with multi-vessel disease, acute myocardial infarction and non-culprit lesion. Function- ally significant stenosis was defined as FFR <0.8. Image analysis of myocardial SPECT was performed by two experienced cardiologists.

Results: In comparison with FFR, the sensitivity, specificity, negative and positive predictive value of myocardial SPECT being able to detect myocardial ischemia was 41%, 79%, 59% and 65%, respectively. The agreement between FFR and myocardial SPECT in the same territories was 61% in total (Kappa = 0.21). However, the agreement between FFR and myocardial SPECT was 65% in patients with non-myocardial infarction, 40% in patients with myocardial infarction, 79% in patients with single vessel disease, 51% in patients multi-vessel disease, 67% in culprit lesion, and 53% in non-culprit lesion, respectively.

Conclusions: The poor concordance between myocardial SPECT and FFR for the evaluation of myocardial ischemia especially in patients with myocardial infarction, multi-vessel disease, and non-culprit lesion. These factors must be considered to evaluate the functional significance of coronary artery stenosis by using myocardial SPECT.

Invasive Imaging of Coronary Disease

P6387 | BEDSIDE

Achievement of very low LDL-c level and plaque vulnerability at non-culprit plaques in patients with stable coronary artery disease: insights from frequency-domain optical coherence tomography analysis

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Purpose: Intensive lowering LDL-C with statins has been demonstrated to re- duce cardiovascular events and slow plaque progression. While statin use has been also reported to favourably modify fibrous cap thickness, the association between achieved LDL-C level and fibrous cap thickness under statin therapy has not been fully elucidated. Also, the benefit of achieving a very low LDL-C level to fibrous cap thickness remains unknown. As frequency-domain optical coherence tomography (FD-OCT) enables us to evaluate plaque microstructures, we sought to investigate plaque morphologies in patients having low LDL-C level by using FD-OCT.

Methods: 293 non-culprit lipid plaques in 280 stable CAD patients treated with statins were evaluated by FD-OCT imaging in the entire of target vessel requiring percutaneous coronary intervention. These plaques were stratified into 4 groups according to attained LDL-C level (<1.3, 1.3-1.8, 1.8-2.6, <2.6mmol/l). Clinical characteristics and FD-OCT derived plaque microstructures were compared.

Results: 23% and 7.9% of study subjects achieved LDL-C <1.8mmol/l and <1.3mmol/l, respectively. Patients who achieved LDL-C <1.3 mmol/l were more likely to be older (p=0.02) and receive high-dose statin (p <0.001). FD-OCT imaging demonstrated that achieving lower LDL-C level was associated with thicker fibrous cap at non-culprit plaques (p <0.001). The thickest fibrous cap was ob- served in patients with LDL-C <1.3 mmol/l. After adjustment for clinical characteristics, plaques in patients achieved LDL-C <1.3mmol/l continued to demonstrate the thickness of fibrous cap (p=0.001).

Conclusions: Achievement of stricter LDL-C goal was beneficial to the thickness of fibrous cap at non-culprit plaques. Our findings may support more favourable effect of achieving very low LDL-C level to stabilizing non-culprit plaques in patients with stable CAD.

Flow in the coronary: What do you need more? / Invasive imaging of coronary disease 1141
P6389 | BEDSIDE
Long-term vascular response to biodegradable polymer sirolimus-eluting stents in comparison with durable polymer sirolimus-eluting stents and bare-metal stents
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Purpose: Long-term vessel response after biodegradable polymer biolimus-eluting stents (BES) implantation remains unclear. We sought to evaluate the vascular response of biodegradable polymer BES at 5 years after stent implantation using optical coherence tomography (OCT) as compared with that of durable polymer sirolimus-eluting stents (SES) and bare-metal stents (BMS).

Methods: Five-year follow-up OCT was performed in 30 patients with 33 stents (10 with 12 BES; 10 with 11 SES; 10 with 10 BMS). Quantitative parameters and qualitative characteristics of the neointima were evaluated.

Results: A total of 5,178 struts (BES, n=2,056; SES, n=1,410; BMS, n=1,712) were analyzed. The percentage of uncovered struts was 0.7% of the BES group, 0.2% of the SES group (<0.01), and 0.0% of the BMS group (P=0.3). The percentage of uncovered struts ratio (13.5% vs 21.8%; P=0.001) and the percentage of cross sections with uncovered struts ratio >0.3 (3.6% vs 7.9%; P=0.001) as well as the percentage of cross sections with at least one uncovered strut (13.5% vs 21.8%; P<0.001) and the percentage of cross sections with uncovered struts ratio >0.3 (3.6% vs 7.9%; P<0.001) were significantly lower in the BES group as compared to SES group and BMS group.

Conclusions: Although MLD by OCT was significantly correlated with the MLA by QCA, QCA underestimated the severity of side-branch after single stent crossover. There was no significant difference of luminal area (MLA) by 3D OCT. Although MLD by OCT was much smaller than MLA measured by OCT, there was no significant decrease of MLA during the follow-up (2.66±0.27 vs. 2.44±0.19 at 1 year after procedure, P=0.998). Shapes of side-branch ostium were almost vertical ellipse. Only about 10% of side-branch ostium had a circular shape and there was no horizontal ellipse shape.
P6392 | BEDSIDE
Prognostic impact of tissue protrusion after stenting in patients with acute coronary syndrome: an optical coherence tomography study
B. Bonnet, P. Plastaras, J.F. Huang, M.F. Seronde, R. Chopard, F. Schiele, N. Meneveau. University Hospital of Besancon - Hospital Jean Minjoz, Besancon, France

Background: Optical Coherence Tomography (OCT) has been extensively studied in stent implantation to assess post-procedural results, with a view to optimizing outcomes. However, the real clinical impact of various OCT-defined abnormalities remains unknown. We investigated the prognostic impact of tissue protrusion between stent struts after stent implantation in patients with non-ST elevation acute coronary syndromes (NSTEMI).

Methods: Prospective study of consecutive pts with NSTEMI (<72 h) undergoing PCI for an infarct-related artery presenting a single lesion without diffuse disease on the culprit artery. Patients were treated at the operator’s discretion according to current guidelines. OCT was performed after initial coronary angiography and at the end of the angioplasty procedure. Tissue prolapse was defined as the projection of tissue (plaque or thrombus) into the lumen between stent struts after implantation. The primary endpoint of procedural complications associated with no flow, and PCI-related myocardial infarction (MI) as defined by an increase in troponin over baseline levels at 24 hours according to the Universal Definition of MI 2012. Secondary endpoint was the functional result of angioplasty as assessed by fractional flow reserve (FFR) measured at the end of the procedure.

Results: 43 patients were included, mean age 63 ± 11 yrs, 90% were men. Tissue protrusion was observed in 35 (81%), with this tissue taking up a median of 3.5% of the stent lumen area. By visual inspection, tissue protrusion was more frequent in patients with late stent thrombosis (6.8% vs 2.1%; p < 0.001), comparison between Groups A1 and A2 revealed that DES struts protruding outside the BMS edges (A2) were more often uncovered (5.0% vs 1.9%; p < 0.001) and malapposed (4.1% vs 2.1%; p = 0.0001) as compared to overlapped struts (A1).

Conclusions: This OCT study demonstrates that, at six-month follow-up, struts coverage is more complete in DES implanted for BMS restenosis as compared to DES deployed to treat atherosclerosis lesions, suggesting a lower risk of late stent thrombosis in the first group of patients.

P6393 | BEDSIDE
Impact of optical coherence tomography-versus intravascular ultrasound-guided percutaneous coronary intervention on mid-term clinical outcomes
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Background: Intravascular ultrasound (IVUS)-guided percutaneous coronary intervention (PCI) can provide stent optimization and has impact on favorable clinical outcomes. Although optical coherence tomography (OCT) shows superior spatial resolution when compared to IVUS, the aim of this study was to evaluate whether OCT guided PCI can be a substitution for IVUS guided PCI in the real world population.

Methods: Patients treated with stent implantation under OCT or IVUS guidance were enrolled from an university medical center and an university hospital OCT and IVUS image databases. A total of 306 patients were included (129 with OCT guidance and 177 with IVUS guidance). Patients with left main disease were excluded. OCT and IVUS-guided PCI were defined as 1) a final minimum stent area ≥90% of the distal reference lumen area or MSA ≤5 mm² 2) requiring additional pullbacks were analyzed, distributed equally between MF and PF groups. No difference was found in image quality, defined as the number of perfect or acceptable frames per pullback [246 (178; 282) vs 230 (192; 269) out the total of 272, respectively; p = 0.986; Figure A]. Comparing the methods on millimeter level, and defining quality as the worst frame of the given millimeter, we found no difference at any section of the total length either in perfect clearance (p = 0.419) or in perfect and acceptable clearance (p = 0.676). Amount of contrast used was significantly lower with MF compared to PF [12 mL (11; 13) versus 20 mL (17; 25), respectively; p = 0.031; Figure B]. Considering target vessel, lesion localization, vessel diameter and procedural phase, guiding size, flushing method, none of the anatomical or procedural factors were found to have an individual direct impact on image quality.

P6394 | BEDSIDE
Incidence of acute coronary syndrome from in-stent neoatherosclerosis in patients with drug eluting stent evaluated by optical coherence tomography
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Objective: We investigate to clarify the role and frequency of neoatherosclerosis evaluated by optical coherence tomography (OCT) at long-term follow-up in patients with previous drug eluting stent (DES) implantation and acute coronary syndrome (ACS). Furthermore, all of the patients who show ACS with neoatherosclerosis were treated by SES.

Methods and results: Forty-nine consecutive patients showed recurrent ischemia due to late phase (≥6 month) restenosis of DES evaluated by coronary angiogram and OCT between August 2009 and August 2013 (18 with sirolimus eluting stent [SES], 12 with paclitaxel eluting stent [PES], 8 with zotarolimus eluting stent [ZES], and 11 with everolimus eluting stent [EES]). A lesion with features of Neoatherosclerosis (Lipid-laden intima, thin-cap fibroatheroma, thrombus, disrupted intima) was found in 15 stents with SES, 2 stents with PES, no stents with ZES, and 1 stent with EES (83.3%, 16.7%, 0%, and 9.1% respectively, p < 0.05). Nine of 18 patients (50.0%) with features of neoatherosclerosis showed history of acute cardiac syndrome (ACS). Furthermore, all of the patients who show ACS with neoatherosclerosis were treated by SES.

Conclusion: These results suggested that neoatherosclerosis might be possible mechanism for late phase occurrence of ACS in patients with DES, and frequency of neoatherosclerosis depends on the kind of DES.

P6395 | BEDSIDE
Prognostic impact of tissue protrusion after stenting in patients with acute coronary syndrome: an optical coherence tomography study
B. Bonnet, P. Plastaras, J.F. Huang, M.F. Seronde, R. Chopard, F. Schiele, N. Meneveau. University Hospital of Besancon - Hospital Jean Minjoz, Besancon, France

Background: Optical Coherence Tomography (OCT) has been extensively studied in stent implantation to assess post-procedural results, with a view to optimizing outcomes. However, the real clinical impact of various OCT-defined abnormalities remains unknown. We investigated the prognostic impact of tissue protrusion between stent struts after stent implantation in patients with non-ST elevation acute coronary syndromes (NSTEMI).

Methods: Prospective study of consecutive pts with NSTEMI (<72 h) undergoing PCI for an infarct-related artery presenting a single lesion without diffuse disease on the culprit artery. Patients were treated at the operator’s discretion according to current guidelines. OCT was performed after initial coronary angiography and at the end of the angioplasty procedure. Tissue prolapse was defined as the projection of tissue (plaque or thrombus) into the lumen between stent struts after implantation. The primary endpoint of procedural complications associated with no flow, and PCI-related myocardial infarction (MI) as defined by an increase in troponin over baseline levels at 24 hours according to the Universal Definition of MI 2012. Secondary endpoint was the functional result of angioplasty as assessed by fractional flow reserve (FFR) measured at the end of the procedure.

Results: 43 patients were included, mean age 63 ± 11 yrs, 90% were men. Tissue protrusion was observed in 35 (81%), with this tissue taking up a median of 3.5% of the stent lumen area. By visual inspection, tissue protrusion was more frequent in patients with late stent thrombosis (6.8% vs 2.1%; p < 0.001), comparison between Groups A1 and A2 revealed that DES struts protruding outside the BMS edges (A2) were more often uncovered (5.0% vs 1.9%; p < 0.001) and malapposed (4.1% vs 2.1%; p = 0.0001) as compared to overlapped struts (A1).

Conclusions: This OCT study demonstrates that, at six-month follow-up, struts coverage is more complete in DES implanted for BMS restenosis as compared to DES deployed to treat atherosclerosis lesions, suggesting a lower risk of late stent thrombosis in the first group of patients.
interventions based on the OCT or IVUS findings immediately after stent implanta-
tion. The primary endpoint was a cumulative incidence of major adverse cardiac
events (MACE) including cardiac death, myocardial infarction (MI) and target
lesion revascularization (TLR) at 1-year follow-up period. Definite or probable stent
thrombosis (ST) rate was also evaluated.

Results: In the OCT-guided group, 111 of 129 patients (85.5%) received additional
interventions whereas 23 of 177 patients (14.7%) were treated in the IVUS-guided
group. The incidences of MACE rate between OCT-guided and IVUS-guided
groups at 1-year follow-up was not different (4.7% vs. 5.6%, p=NS). ST was devel-
oped in 1 patient in IVUS-guided group, but not developed in OCT-guided group
(p=NS).

Conclusions: OCT-guided PCI was comparable to IVUS-guided PCI in terms of
MACE and ST rates, suggesting that OCT guidance may be an alternative
strategy for stent optimization.

P6396 | BENCH
Usefulness of optical frequency domain imaging for vasa vasorum
visualization in stented coronary arteries in pigs and humans
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Purpose: Vasa vasorum (VV), nutrient microvessels of the vessel wall, is known
to be involved in the pathological progression of atherosclerosis. However, its
role in the natural course of the non-significant plaque (NCRP) is unclear.

Methods: Sirolimus-eluting (n=6), biolimus A9-eluting (n=6) and bare metal
stents (n=6) were implanted in the left coronary arteries in pigs for 1 month. Af-
ter euthanization, the area of VV was measured using the OFDI system. The
area of VV was compared between the two groups.

Results: The area of VV was significantly larger in the sirolimus-eluting stent
than the biolimus A9-eluting stent (P<0.01, n=36 sections).

Conclusions: OFDI clearly visualized micro-lumen structures in the adventitia of
coronary arteries in pigs.

IMPACT OF OPTICAL COHERENCE TOMOGRAPHY ON
CORONARY MORPHOLOGY
P6400 | BEDSIDE
Impact of optical coherence imaging on different culprit lesion morphology
in acute coronary syndrome
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Background: Previous studies have reported that plaque rupture and erosion were
the most common causes of acute coronary syndrome (ACS) and spotty calcifi-
cations were identified as markers of plaque rupture. Optical coherence tomogra-
phy (OCT) offers a high-resolution imaging to assess the plaque morphology and
coronary calcification.

Purpose: The aim of this study was to evaluate the relationship between the
distribution of coronary calcification and the culprit lesion morphology in patients
with ACS.

Methods: We enrolled consecutive 183 patients with ACS (mean age: 68±11
years, 148 males). Culprit lesion was assessed by OCT and patients were divided
into the rupture and non-rupture group according to the OCT findings. Maximum
radial thickness, cross-sectional area of calcification and radial depth from the
lumen and longitudinal length of calcification were compared between 2 groups.

Results: Plaque rupture was detected at culprit site in 105 patients and coronary
calcification was identified in 58 patients. There were no significant differences in
age and gender between 2 groups.

Maximum thickness, area and longitudinal length of calcification were smaller in
rupture group (457.4±384.1 μm vs. 722.1±384.1 μm, p<0.01, 0.7±0.4 mm² vs.
1.8±1.4 mm², p<0.01, 2.2±1.1 mm vs. 5.6±5.3 mm, p<0.01, respectively).
Radial depth of calcification from the lumen was significantly greater in rupture
group (150.0±65.3 μm vs. 83.1±63.3 μm, p<0.001).

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Conclusions: Distribution of coronary calcification could be associated with morphological etiology of ACS.

P6401 | BEDSIDE

A novel method to assess coronary artery bifurcations by OCT: Cut-plane analysis for side-branch ostial assessment from a main vessel pullback

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Background: In the assessment of coronary bifurcations, evaluation of side branch (SB) ostia by an optical coherence tomography (OCT) pullback performed in the main branch (MB) could speed up lesion evaluation. Dedicated software that reconstructs the cross-sections perpendicular to the SB centerline could improve assessment of SB ostia. We aimed to validate a new method (cut-plane analysis) for assessing the SB ostium from a MB OCT pullback.

Methods: Thirty-one sets of frequency-domain OCT pullbacks, obtained from 28 patients, from both the MB and the SB of a coronary artery bifurcation were analyzed. Measurements of the SB ostium from the MB pullback were then performed by 1) conventional analysis and 2) cut-plane analysis, and the measurement error for each analysis was estimated.

Results: Correlations of measurements of the SB ostium, acquired from the MB pullback, with in coronary arteries, were high with conventional analysis, albeit not reaching significance (area: Rcutplane=0.927 vs. Rconventional=0.870, p=0.256; mean diameter: Rcutplane=0.918 vs. Rconventional=0.788, p=0.056; maximum diameter: Rcutplane=0.841 vs. Rconventional=0.812, p=0.734; maximum diameter: Rcutplane=0.770 vs. Rconventional=0.635, p=0.316). Cut-plane analysis was associated with lower absolute error for SB ostium measurements than conventional analysis (area: 1.50±0.31mm2 vs. 0.56±0.45mm2, p=0.001; mean diameter: 0.44±0.30mm vs. 0.18±0.14mm, p=0.001; minimum diameter: 0.39±0.29mm vs. 0.22±0.27mm, p=0.007; maximum diameter: 0.59±0.37mm vs. 0.30±0.26mm, p=0.001). Intra- and inter-observer agreement for cut-plane analysis was high.

Conclusions: Area measurements of SB ostium performed by cut-plane analysis of an OCT pullback performed in the MB have high correlation with reference measurements performed from a SB OCT pullback and lower error compared to conventional analysis. This approach could alleviate the need for SB instrumentation and potentially reduce procedural complexity in assessment of coronary bifurcations.

P6402 | BEDSIDE

Relationship between thin-cap fibroatheroma and plaque progression in patients with coronary artery disease—an intravascular ultrasound and optical coherence tomography study


Background: Intensive lipid lowering therapy using statin has been reported to cause coronary artery plaque regression in patients with coronary artery disease (CAD). However, morphological characteristics of non-culprit coronary plaques that progress subsequently have not been elucidated. The aim of this study was to clarify the morphological characteristics of non-culprit coronary plaques in patients with CAD using intravascular ultrasound (IVUS) and optical coherence tomography (OCT).

Methods and results: A total of forty-nine CAD patients (acute coronary syndrome (ACS); n=38, non-ACS; n=11) undergoing percutaneous coronary intervention (PCI) were studied by both IVUS and OCT during acute phase, and IVUS examination at 10-month follow-up. Non-culprit 10mm segment with mild to moderate plaque in the target vessels at least 5mm proximal or distal to the stent edge were analyzed. Baseline characteristics of those plaques were evaluated by OCT and IVUS, and change of plaque volume between baseline and follow-up period was quantified by IVUS. Volumetric IVUS analysis was performed at 1mm intervals for each 10mm segment, and plaque progression/regression was evaluated. Patients were divided into 2 groups; progression group (n=38) and regression group (n=38). All patients received statin treatment during follow-up. Baseline low density lipoprotein cholesterol (LDL-C) [132±47 vs. 130±34mg/dl] and reduction of LDL-C during follow-up ([35±34 vs. ±35±22%]) were similar between the groups, whereas no IVUS parameters including plaque burden (p=0.11), plaque volume (p=0.35) and vessel volume (p=0.35) were correlated with plaque progression. Those with plaque progression showed a significantly higher incidence of thin-cap fibroatheroma (TCFA) (63 vs. 21%, p=0.01), and calcification (73 vs. 37%, p=0.04), compared with patients without plaque progression. Multivariate regression analysis showed that only TCFA (OR 9.82, p=0.05) was a predictor of plaque progression.

Conclusions: Non-culprit plaques with TCFA showed plaque progression as assessed by IVUS, indicating that intensive lipid lowering therapy and complete revascularization should be considered in patients with TCFA.

P6403 | BEDSIDE

Size discrepancy of frequency domain optical coherence tomography versus intravascular ultrasound in human coronary artery and phantom in vitro coronary model

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Background: In the real practice, frequency domain-optical coherence tomography (FD-OCT) is believed to depict smaller image than intravascular ultrasound (IVUS). But there are various results regarding their size discrepancy. The aim of the study was to compare the size discrepancy of FD-OCT and IVUS and investigate the mechanism of the size discrepancy.

Methods: FD-OCT and IVUS were performed in a stent implanted phantom cylindrical coronary model and 57 stented human coronary arteries. Total of 11 matched FD-OCT and IVUS images from in-stent phantom model were measured. Meanwhile, total of 285 matched images at in-stent and distal reference segment from the 57 coronary lesions were measured in human coronary artery.

Result: In phantom model, FD-OCT showed similar lumen diameter as actual phantom diameter. IVUS overestimated lumen diameter by 5.9% (p=0.001) in reference segment and 2.5% (p=0.001) in stented segment. In human coronary artery, IVUS depicted larger diameter than FD-OCT in reference segment (2.57±0.60 mm vs. 2.77±0.49 mm, p=0.001) and in stented segment (2.99±0.49 mm vs. 3.05±0.45 mm, p=0.003). The difference of mean diameter was more prominent in reference segment (7.8%) than in stented segment (2.0%). Furthermore, correlation between FD-OCT and IVUS measurements were higher in stented segment than in reference segment (stented segment diameter R2=0.8670, reference segment diameter R2=0.7351; stented segment area R2=0.8663, reference segment area R2=0.7806).

P6404 | BEDSIDE

Prediction of late neointimal regression after drug-eluting stent implantation by optical coherence tomography

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Background: Repaired intervention for mild to intermediate in-stent lesion after drug-eluting stent (DES) implantation may be safely deferred if late neointimal regression (LNR) could be predicted. Neointimal tissue characteristics may be related to the late neointimal progression or regression late after DES implantation.

Purpose: The aim of this study was to predict LNR after DES implantation by optical coherence tomography (OCT).

Methods: Serial (12 and 18 months after DES implantation) OCT imaging was performed in 42 stented lesions from 26 patients. LNR was defined as [neointimal area (NIA) at 18 months - NIA at 12 months -0]. Clinical, lesion and OCT characteratics (both morphological and morphometrical) were compared between lesions with LNR and those without.

Results: LNR was observed in 24 of 42 (57%) lesions. Clinical, lesion and procedural characteristics were similar between lesions with and without LNR. By OCT, lesions with LNR had similar baseline neointimal area (2.2±1.5 vs. 2.2±1.5 mm2, p=0.96). On the other hand, lesions with LNR had significantly higher prevalence of “homogenous” neointima (77 vs. 23%, F<0.0001) than those without LNR, where “heterogenous” neointima was the predominant neointimal tissue by OCT. “Homogenous” neointima was the only OCT predictor of LNR (F<0.004).

Conclusions: LNR was observed in about 60% of the mild to intermediate in-stent lesions. Presence of “homogenous” neointima may predict LNR.
The association between tissue morphology assessed with optical coherence tomography and mid-term results after paclitaxel-coated balloon dilatation

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Purpose: The morphological assessment of neointimal tissue using optical coherence tomography (OCT) is highly significant to clarify the pathophysiology of in-stent restenosis (ISR) lesions. Mid-term results after paclitaxel-coated balloon dilatation (PCB) might affect the occurrence of long-term stent events such as stent thrombosis or restenosis in patients with coronary artery disease. However, the relationship between the extent of plaque calcification and stent expansion after PCB has not been fully investigated. We sought to assess the relationship between plaque morphology and OCT findings on recurrence of ISR after PCB.

Methods: Between October 2008 and August 2013, we performed PCI for 201 ISR lesions using PCB (161 men, mean age 68±9.8 years). The morphological assessment of neointimal tissue at the minimum lumen area site as to restenotic tissue structure (homogeneous, heterogeneous, or layered type) using OCT was performed. We examined the association between tissue structure and mid-term (6-8 months) results including ISR and target lesion revascularization (TLR) rates.

Results: The mean follow-up period was 195±36 days. The association of tissue structure with ISR and TLR rates is shown in the figure. The ISR rate of lesions with homogeneous structure tended to be lower than that with heterogeneous structure (20.2% vs. 38.5%, p=0.071), whereas the TLR rate of lesions with homogeneous structure was significantly lower than that with heterogeneous structure (11.7% vs. 34.6%, p=0.014).

Conclusions: The tissue morphology of ISR lesion assessed with OCT may have an impact on the mid-term efficacy of PCB.

P6406 | BEDSIDE

Serial FD-OCT assessment of complex calcified coronary plaque formation following rotational atherectomy

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Background: Target lesion calcification is known to influence the results of percutaneous coronary intervention (PCI). Rotational atherectomy (RA) plays an important role in facilitating the dilatation or stenting of these lesions. The aim of this study was to assess the incidence of calcium crack after balloon angioplasty following RA and its impact on the results of PCI by serial FD-OCT evaluation.

Methods: From October 2011 to May 2013, a total of 21 calcified lesions requiring RA in patients with CAD were interrogated by FD-OCT. In all patients, serial OCT images just after RA, after balloon angioplasty, and after stent implantation were analyzed at 1-mm intervals. The arc, thickness of the calcium component, and the lumen area in each segment were measured after RA. Final stent area and incidence of incomplete stent apposition (ISA) in each segment were analyzed. Lumen gain was calculated as: ('final stent area')-'lumen area after RA'. The incidence of calcium cracks after balloon angioplasty following RA was also assessed by OCT.

Results: A total of 398 segments in 21 lesions were analyzed. Calcium cracks after balloon angioplasty following RA and ISA after stent implantation were observed in 164 segments (41%) and 196 segments (49%), respectively. The segment with calcium cracks after angioplasty had smaller lumen area (3.73±1.66 mm2 vs. 2.52±0.66 mm2, P<0.001), larger calcium arc (290±78 vs. 161±62 degree, P<0.001), and thinner calcium thickness (0.60±0.32 vs. 1.05±0.42 mm, P<0.001) than those without cracks. The presence of calcium cracks after angioplasty was associated with larger lumen gain and fewer incidence of ISA after stent implantation (3.99±1.71 vs. 3.28±1.61 mm2, P<0.01, 40.5 vs 59.7%, P=0.01, respectively).

Conclusion: FD-OCT is effective for evaluating plaque characteristics in calcified coronary lesions. The presence of calcium cracks after rotational atherectomy and subsequent balloon angioplasty was the important manifestation to achieve optimal result after final stent implantation.
Conclusions: 3D-OCT could evaluate the configuration of overhanging struts in front of side branch orifice. The ostial diameter was decreased in the SB jailed by main vessel stent without KBI. The jailing configuration and compartment could affect the reduction of SB ostial diameter due to tissue attachment.

P6409 | BEDSIDE
Difference of vessel healings between Sirolimus- and Everolimus-eluting stent Implantation in bifurcation lesions: from J-REVERSE OCT Sub-study
D. Terashti1, T. Shinkie1, H. Otake1, Y. Murasato2, Y. Kinoshita2, K. Fujii2, Y. Takeda3, H. Takahashi1, H. Kinutani1, H. Hariki1 on behalf of J-REVERSE investigators. 1Department of Preventive Medicine, Graduate School of Health Sciences Kobe University, Kobe, Japan; 2Shin-Yukihashi hospital, Yukihashi, Japan; 3Toyohashi Heart Center, Toyohashi, Japan; 4Hyogo Medical University, Nishinomiya, Japan; 5Rinku General Medical Center, Izumisano, Japan.

Purpose: We aimed to clarify the differences of vessel healings after stenting in the bifurcation lesions between those treated with sirolimus-eluting stent (SES) or everolimus-eluting stent (EES).

Methods: J-REVERSE is a prospective multicenter registry of cases treated with provisional stenting to bifurcation lesions using SES (n=18) and EES (n=46) with or without final kissing inflation (FKI). The first 64 lesions at selected study sites were predefined for inclusion in the optical coherence tomography (OCT) sub-study and underwent 9-month follow-up OCT. In addition to standard OCT parameters, stent eccentric index (SEI; minimum divided by maximum stent diameter), neointimal unevenness score (NUS; maximum neointimal thickness in the cross-section (CS) divided by the average NIT of the same CS; to assess the uniformity of neointima suppression), and the frequency of uncovered and malapposed struts were averaged for each segment (proximal, bifurcal, and distal segment).

Results: The rate of patients treated with FKI were similar between EES and SES (p=0.39). Overall, the average stent and lumen area, average NIT, and the frequency of uncovered struts were similar. Although EES tended to have a smaller SEI than SES, the frequency of malapposed struts and average NUS in EES group were smaller than those in SES group, indicating more uniform vessel healing observed in EES. In the detailed segmental analysis, the disparities of the frequency of malapposed struts and SEI were observed in all the segment with a statistical significance in bifurcation segment. EES had significantly smaller NUS in the entire segment (Table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>EES (n=46)</th>
<th>SES (n=18)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average NUS (over all)</td>
<td>2.0±0.3</td>
<td>2.3±0.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Average NUS (proximal segment)</td>
<td>2.4±1.6</td>
<td>2.9±0.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Average NUS (distal segment)</td>
<td>2.1±1.6</td>
<td>2.9±1.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Average SEI (over all)</td>
<td>0.86±0.05</td>
<td>0.88±0.03</td>
<td>0.08</td>
</tr>
<tr>
<td>Average SEI (proximal segment)</td>
<td>0.86±0.06</td>
<td>0.87±0.04</td>
<td>0.40</td>
</tr>
<tr>
<td>Average SEI (distal segment)</td>
<td>0.85±0.07</td>
<td>0.88±0.06</td>
<td>0.05</td>
</tr>
<tr>
<td>% malapposed struts, (%) (over all)</td>
<td>0.2±0.6</td>
<td>1.3±2.8</td>
<td>0.01</td>
</tr>
<tr>
<td>% malapposed struts, (%) (proximal segment)</td>
<td>0.63±1.7</td>
<td>1.1±2.4</td>
<td>0.44</td>
</tr>
<tr>
<td>% malapposed struts, (%) (distal segment)</td>
<td>0.3±0.6</td>
<td>0.8±2.4</td>
<td>0.01</td>
</tr>
</tbody>
</table>

P6411 | BEDSIDE
Impact of underneath plaque characteristics on the fate of acute incomplete stent apposition: serial optical coherence tomography sub-study of Japan-drug eluting stents evaluation; a randomized trial
M. Nakagawa1, T. Shinkie1, T. Kubo2, H. Okura3, K. Mizuno4, T. Akasaka5, H. Yokoi6, T. Muramats8, M. Nakamura2, S. Nanto7 on behalf of J-DESERT investigators. 1Kobe University, Division of Cardiovascular Medicine, Kobe, Japan; 2Kakayama Medical University, Division of Cardiovascular Medicine, Kakayama, Japan; 3Kawasaki Medical School, Department of Cardiology, Kurashiki, Japan; 4Nippon Medical School, Department of Cardiovascular Medicine, Tokyo, Japan; 5Fukuoka Sanno Hospital, Cardiovascular Medicine Center, Fukuoka, Japan; 6Saiseikai Yokohama City Eastern Hospital, Division of Cardiology, Yokohama, Japan; 7Toho University Ohashi Medical Center, Department of Cardiovascular Medicine, Tokyo, Japan; 8Osaka University Hospital, Advanced Cardiovascular Therapeutics, Suita, Japan.

Background: Little is known about the impacts of plaque characteristics on vascular response to incomplete stent apposition observed immediately after stent placement (acute ISA).

Methods: In the Japan-Drug Eluting Stents Evaluation; a Randomized Trial (J-DESERT), 42 patients (47 stents) treated with either sirolimus (SES) or paclitaxel (PES) eluting coronary stent underwent serial OCT examination before and after implantation and at 8-month follow-up. Acute ISA were surveyed from OCT cross-sections post stenting and sum of acute ISA area was measured as well as plaque characteristics underneath acute ISA were assessed from matched OCT cross section before stenting. The fate of acute ISA was evaluated at 8-month.

Results: A total of 241 cross-sections with acute ISA were identified. Among those, 216 cross-sections (90.6%) were resolved- and 25 (10.4%) were persistent ISA. The mean ISA area of resolved ISA was significantly smaller than that of persistent ISA (0.25±0.20 mm2 vs. 0.39±0.33 mm2, p=0.048). Based on receiver operating curve analysis, the best cutoff value of acute ISA area for predicting resolved ISA was 0.175 mm2 (sensitivity: 64.3%; specificity: 86.4%; AUC=0.659). Acute ISA over fibrous plaque resolved more frequently than those over lipid or calcified plaque (Ratio of ISA resolution: 95.1% over fibrous, 78.9% over calcified, p<0.001). Multivariate logistic analysis revealed fibrous plaque over acute ISA was the independent predictor factor associated with resolved ISA (7.582; 95% CI: 2.882 to 19.944, p<0.001). Late-acquired ISA was identified 18 cross-sections at 8-month follow-up. Among those, lipid plaque underneath late-acquired ISA was more frequently observed than fibrous or calcified plaque (77.8% on lipid, 16.7% on fibrous, 5.5% on calcified).

Conclusions: Plaque character underneath ISA as well as ISA area affect the fate of acute ISA after SES / PES implantation.
CORONARY IMAGING AND CLINICAL OUTCOME

P6413 | BEDSIDE

Vessel shrinkage (negative remodeling) is the main mechanism of lumen compromise in intraluminal vasculopathy. A long-term serial intravascular ultrasound study

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Purpose: There is limited long-term data on the mechanism of lumen compromise in intraluminal vasculopathy (CAV).

Methods: We performed serial intravascular ultrasound (IVUS) evaluation of the LAD in 66 consecutive heart transplant recipients. Baseline and follow-up (mean duration=3.2 years) proximal LAD segments were matched; and a ≥20mm long proximal segment was analyzed every 1mm, and results normalized for analysis length and reported as mm/mm.

Results: Overall, the change of mean lumen area was well correlated to the change in mean vessel area (r=0.94, p<0.01), but not to the change in mean plaque area (p=0.16) (Figure). Twenty two pts (33.3%) had a history of cellular rejection. Clinical characteristics, baseline IVUS, and follow up IVUS were similar between pts with vs without rejection. During follow up, vessel area decreased in pts with and without rejection (-0.25±1.62 vs -0.08±1.17 mm²/mm, p=0.62). And plaque area increased in both groups (0.27±0.68 vs 0.09±0.33 mm²/mm, p=0.16). As a result, lumen area decreased in both groups, and there was no significant difference between them (-0.53±1.67 vs -0.16±1.12 mm²/mm, p=0.3). Furthermore, the correlations between mean lumen areas vs mean plaque or vessel areas were similar in pts with or without rejection.

Conclusions: Lumen loss occurs in long term follow up of CAV pts with and without rejection. Although plaque increase contributes to lumen loss, the main mechanism is vessel negative remodeling.

P6414 | BEDSIDE

Longitudinal stent deformation in the drug-eluting stent era: an intravascular ultrasound study


Background: Longitudinal stent deformation (LSD) in drug-eluting stents (DES) has been described as a disruption of stent structure. We aimed to assess the degree and rate of LAD via intravascular ultrasound (IVUS) across different DES platforms.

Methods: Patients with implanted DES for de novo lesions were divided into 5 groups according to sirolimus- (SES); paclitaxel- (PES); zotarolimus- (ZES); everolimus- (EES); and biolimus- (BES) eluting stents (PtCr-EES). Stent length was measured using automatic pullback of an IVUS catheter, and was compared to labeled length for calculation of absolute value of difference in length and relative difference (absolute value of difference divided by the labeled length).

Results: A total of 534 DES’s in 475 patients were included. The baseline characteristics were comparable between groups; highest calcification as seen in the SES group (p<0.003). The absolute and relative absolute value of difference in length showed the lowest degree in the SES group and the highest in the ZES group (p=0.05 and 0.05, respectively). The absolute relative difference of >5% was lowest in the SES group compared to the other groups (p=0.009), however, significant (>15%) absolute relative difference was similar among groups (p=0.97) (Table 1).

Conclusions: LSD was seen in all stent platforms. However, the degree of LSD was lowest in the SES group. Incidence of significant LSD was low, with no significant difference see among all stent platforms.

Abstract P6414 – Table 1. The degree and rate of LAD through IVUS

<table>
<thead>
<tr>
<th>Attenuation group</th>
<th>Ulceration group</th>
<th>Control group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=15)</td>
<td>(n=24)</td>
<td>(n=82)</td>
<td></td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>9 (60%)</td>
<td>14 (58%)</td>
<td>42 (51%)</td>
</tr>
<tr>
<td>Reference vessel diameter (mm)</td>
<td>3.07±0.58</td>
<td>3.41±0.58</td>
<td>3.15±0.51</td>
</tr>
<tr>
<td>The incidence of slow flow/no reflow after stenting</td>
<td>3 (20.0%)</td>
<td>5 (20.8%)</td>
<td>4 (1.9%)</td>
</tr>
<tr>
<td>Gray-scale IVUS characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumen CSA (mm²)</td>
<td>5.0±1.3</td>
<td>7.6±3.0</td>
<td>4.7±1.4</td>
</tr>
<tr>
<td>EEM CSA (mm²)</td>
<td>17.1±3.5</td>
<td>19.7±4.9</td>
<td>16.0±4.5</td>
</tr>
<tr>
<td>Plaque and Media CSA (mm²)</td>
<td>12.2±3.9</td>
<td>15.0±3.2</td>
<td>11.4±3.9</td>
</tr>
<tr>
<td>IVUS-IVUS characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrous (%)</td>
<td>55.7±9.5</td>
<td>56.9±10.0</td>
<td>61.7±9.9</td>
</tr>
<tr>
<td>Fibro-fatty (%)</td>
<td>27.5±9.5</td>
<td>10.4±5.8</td>
<td>13.8±8.2</td>
</tr>
<tr>
<td>Necrotic core (%)</td>
<td>12.2±6.1</td>
<td>20.7±9.0</td>
<td>15.9±9.0</td>
</tr>
<tr>
<td>Dense calcium (%)</td>
<td>4.6±3.0</td>
<td>12.3±6.4</td>
<td>8.3±7.1</td>
</tr>
<tr>
<td>Fibrous (mm²)</td>
<td>5.8±2.6</td>
<td>6.8±2.2</td>
<td>7.1±2.8</td>
</tr>
<tr>
<td>Fibro-fatty (mm²)</td>
<td>3.5±1.9</td>
<td>1.2±0.7</td>
<td>1.6±1.2</td>
</tr>
<tr>
<td>Necrotic core (mm²)</td>
<td>13.4±4.0</td>
<td>2.5±1.3</td>
<td>1.7±1.0</td>
</tr>
<tr>
<td>Dense calcium (mm²)</td>
<td>0.5±0.4</td>
<td>1.4±0.7</td>
<td>0.9±0.8</td>
</tr>
</tbody>
</table>

Conclusion: The attenuated plaque had significantly larger fibro-fatty tissue. The ulcerated plaque had significantly larger EEM CSA. The ulcerated plaque had significantly larger necrotic core and dense calcium. The ulcerated plaque in ACS had significantly larger necrotic core. The attenuated plaque and the ulcerated plaque showed higher frequency of slow flow/no reflow during PCI.

P6415 | BEDSIDE

The variable profile of endothelial shear stress and remodeling along the length of plaque determines the topography and natural history of coronary artery disease


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Purpose: Low endothelial shear stress (ESS) promotes atherosclerosis and expansive remodeling, leading to adverse vascular outcomes. However, the pattern of plaque progression in the longitudinal arterial axis and the corresponding pathobiologic mechanisms are not known. In this study, we assessed the hypothesis that the longitudinal variation of ESS and remodeling in plaque regions determine the topography and the natural history of coronary artery disease.

Methods: In the PREDICTION Study, we performed 3D coronary reconstruction by angiography/IVUS at baseline (BL) and at 6-12 months follow-up (FU). All discrete BL plaques (max thickness ≤0.5mm, length 9-30mm) were categorized as proximal, mid and distal 3mm-long segments. In these segments, we assessed BL remodeling index (RI) and ESS with computational fluid dynamics. At FU, we evaluated the plaque burden (PB) and lumen area change in the same locations.

Results: In 313 arteries from 220 patients, 371 plaques (length 16.6±4.0 mm) were identified. BL PB was higher in the mid plaque (45.8%) than in the proximal (43.8%) and distal plaque (43.5%, p<0.001). BL ESS was higher in the mid plaque (1.8 Pa) than in the proximal (1.7 Pa) and distal plaque (1.6 Pa, p<0.05). Remodeling was also non-uniform, as expansive remodeling was more frequent in proximal plaque (OR 1.7, 95%CI 1.3 to 2.3, p<0.001) and constructive remodeling in mid plaque (OR 1.6, 95%CI 1.2 to 2.2, p<0.001). At FU, plaque regression was evident in all plaque portions (PB change -0.3% in proximal, -1.2% in mid, 0.7% in distal segments).

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-0.9% in distal plaque, p<ns). Lumen area however increased only in the proximal and mid part while it decreased in the distal part of plaque (change 1.4%, 0.3% and -0.4% respectively, p<0.05). In the distal plaque region, 7% of segments exhibited a combination of low ESS and expansive remodeling at BL and both BL low ESS and expansive remodeling were independent predictors of lumen area narrowing at FU (beta = -1.5 mm²/Pa, 95% CI: -2.1 to -0.9, p<0.001 and beta = -2.6 mm²/unit increase in RL, 95% CI: -3.2 to -2.1, p<0.001 respectively).

**Conclusions:** Plaque, arterial remodeling and ESS are heterogeneously distributed along the length of individual coronary plaques. Despite universal plaque regression in this aggressively treated patient population, the distal part of lesions manifests progressive luminal narrowing, under the synergistic local effects of low ESS and expansive remodeling. The detailed characterization of remodeling and ESS profiles along the longitudinal aspect of lesions may enhance the early identification of plaques at highest risk for adverse outcomes.

**P6417 | BENCH**

High-resolution intravascular ultrasound using optical coherence tomography technique: basic study


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**Purpose:** Intravascular ultrasound (IVUS) provides visualization of the arterial wall with high penetration for the diagnosis of atherosclerosis. However, IVUS has an insufficient axial-resolution to measure the fibrous-cap thickness, and the assessment of the microstructure of the arterial surface layer requires the employment of optical coherence tomography (OCT). In this study, we applied the OCT technique to IVUS data to improve the axial-resolution of the IVUS image.

**Methods:** The OCT technique transforms the received signal in the time domain to that in the frequency domain. The technique compensates for the phase rotation of each frequency component of the signal in the frequency domain, where this procedure enables to form focal images at all depths from the data of a single transmit event. We applied the OCT technique with an adaptive beamforming method to IVUS data of a 40 MHz platform in a simulation study.

**Results:** Figure shows the IVUS image of an artery with and without the proposed method based on the OCT technique, where the fibrous-cap thickness is from 40 to 120 μm. The conventional IVUS depicted blurred interfaces caused by its insufficient axial-resolution. In contrast, IVUS with the proposed method based on the OCT technique depicted interfaces clearly including the fibrous cap. Because the proposed method is applied to IVUS data, the IVUS using the proposed method has the same penetration as the conventional IVUS.

**Conclusions:** This study reported that the proposed method based on the OCT technique has the high potential to improve the axial-resolution of IVUS to 40 μm using a 40 MHz platform. We believe that IVUS will acquire both penetration and resolution using the OCT technique in the near future.

**P6418 | BENCH**

Impact of patients’ characteristics, procedural, angiographic, and IVUS findings on neatherosclerosis after stent implantation: Insights from optical coherence tomography study

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**Purpose:** Recent studies have reported that the development of neatherosclerosis (NA) inside the stents is associated with late complications such as very late stent thrombosis and late catch up. However, few data exist regarding clinical characteristics, procedural, angiographic, and IVUS findings at stent implantation were compared.

**Results:** As for baseline characteristics, age and total cholesterol level were significantly higher in NA than in non-NA. As for procedural characteristics, duration since stent implantation, especially in BMS, was significantly longer in NA than in non-NA (60.5±44.8 vs. 23.4±24.1 months, P<0.001). Maximum balloon pressure was significantly higher in NA than in non-NA. Interestingly, by IVUS positive remodeling at pre-procedure was frequently observed in NA compared to non-NA. In multivariate analysis, duration since stent implantation and pre-interventional arterial remodeling by IVUS remained independent predictors for NA (Table).

**Predictors for neatherosclerosis**

<table>
<thead>
<tr>
<th>Univariate models</th>
<th>Multivariate model</th>
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<tbody>
<tr>
<td>Odds ratio</td>
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</tr>
<tr>
<td>Positive remodeling</td>
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<tr>
<td>Total cholesterol</td>
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<td>DES or BMS</td>
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**Conclusions:** These results demonstrate that in addition to the duration since stent implantation, pre-interventional arterial remodeling by IVUS may be related to the development of NA inside the stents.

**P6419 | BENCH**

Modification of plaque composition and improvement of plaque stability by glucagon-like peptide-1 agonist - In vivo findings using iMap IVUS in Watanabe heritable hyperlipidemic rabbits

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**Background:** Recent studies reported glucagon-like peptide-1 agonist (GLP-1A) may inhibit aortic atherosclerosis development and formation in ApoE knock-out mice. However, whether GLP-1A stabilizes the fully developed lesion of atherosclerosis or alters the complicated plaque composition is still unclarified.

**Methods:** Ten Watanabe Heritable Hyperlipidemic rabbits (10- to 12- month-old) were divided into GLP-1A treatment group and control group. After angiography and iMap™ intravascular ultrasound (IVUS) observations, 30 mmol/kg/day Lixisenatide was administered in GLP-1A group. Same volume of normal saline was administered in control group. After 12 weeks, evaluated by angiography and iMap™ IVUS, brachiocephalic arteries were harvested for pathological analysis.

**Results:** Although IVUS analysis showed no change of plaque burden between 2 groups, GLP-1A treatment indeed changed plaque composition. MAP IVUS analysis revealed higher %fibrosis (control vs. GLP-1A: 66.3±2.3% vs. 75.1±2.4%, p<0.01), lower %callus (23.9±3.8% vs. 16.2±1.1%, p=0.02), and lower %calcification (2.2±0.2% vs. 1.0±0.2%, p<0.01) in the plaque in GLP-1A group than that in control group. Pathological analysis confirmed iMap observations. Although the area of vessel, lumen, and plaque is comparable between GLP-1A and control group, GLP-1A treatment improved smooth muscle cell (SMC) rich plaque (%SME: 6.9±3.0% vs. 8.1±4.0%, p=0.2) with increased fibrotic contents (%fibrosis: 34.1±3.0% vs. 38.5±5.3%, p=0.02). Furthermore, plaque macrophage infiltration and calcification formation were significantly reduced by GLP-1A (%macrophage: 3.2±0.5% vs. 7.5±0.5%, p<0.02, %calcification: 2.0±1.1% vs. 1.3±0.2%, p<0.01).

**Conclusions:** GLP-1A modifies the plaque composition and then improves the stability of fully developed plaque lesions. iMap is feasible and reliable to identify the plaque characteristics in vivo.

**P6420 | BEDSIDE**

Assessment of the atherosclerotic plaque at nonculprit lesions with coronary computed tomography angiography in comparison to intravascular ultrasound

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**Background:** The composition of atherosclerotic plaque has an important influence on the risk of future coronary events. Plaque with attenuation on intravascular ultrasound (IVUS) is associated with decreased calcium content and increased fibrous tissue content which is related to the development of coronary artery disease (CAD). However, coronary computed tomography angiography (CTA) is the most reliable noninvasive method of evaluating plaque composition. This study aimed to compare detection of attenuated plaques at nonculprit lesions between CTA and IVUS, and to clarify the differences in the morphology and risk factors between CTA and IVUS.

**Methods and results:** We performed coronary CTA in 598 consecutive patients with suspected CAD, among whom 82 underwent coronary angiography and percutaneous coronary intervention. In these 82 patients, 210 plaques were evaluated by both coronary CTA and IVUS. Fifty-nine calcified plaques were excluded from analysis. The remaining 151 plaques comprised 50 soft plaques, 51 attenuated plaques, and 50 fibrous plaques. Attenuated plaques had a significantly higher CT density than soft plaques (P<0.001) and a significantly lower CT density than fibrous plaques (P<0.001). Macrolipoma combined with lipid pool-like changes were more frequent in attenuated plaques than in soft plaques (P<0.05). Patients with attenuated plaques had significantly lower levels of high-density lipoprotein (HDL) cholesterol than those without attenuated plaques (P<0.001).
On multivariate analysis, significant independent predictors of attenuated plaque were low HDL-cholesterol (odds ratio: 0.87, 95% confidence interval: 0.81 to 0.92, P < 0.001) and microcalcification combined with lipid pool-like changes (4.53, 1.66 to 12.3, P = 0.003).

Conclusions: Analysis of nonculprit lesions by coronary CTA would be useful for detecting the plaque associated with an increased risk of future coronary events.

**P6421 | BEDSIDE**

Different serial changes of neointimal condition between biodegradable-polymer coated biolimus A9-eluting stents and biocompatible durable-polymer coated everolimus-eluting stents


Background: First generation drug-eluting stents (DES) show delayed neoinimal coverage of stent struts due to chronic inflammation of durable-polymer, which may cause stent thrombosis. Recently, second generation DESs including biodegradable-polymer coated biolimus A9-eluting stents (BES) whose polymer will be completely absorbed within twelve months, and biocompatible durable-polymer coated everolimus-eluting stents (EES) were available. In this study, we performed serial evaluation of neointimal coverage after BES or EES implantation at eight-month and twenty-month by optical coherence tomography (OCT).

Methods: Serial OCT evaluations were performed in 11 patients with 14 BESs at eight-month and twenty-month by optical coherence tomography (OCT). We performed serial evaluation of neointimal coverage after BES or EES implantation. Polyurethane coated everolimus-eluting stents (EES) were available. In this study, we will be completely absorbed within twelve months, and biocompatible durable-polymer coated everolimus-eluting stents (EES) were available. In this study, we performed serial evaluation of neointimal coverage after BES or EES implantation at eight-month and twenty-month by optical coherence tomography (OCT).

Results: At eight-month, Ave-NHT of EES was significantly higher than BES. At twenty-month, %Uncovered of EES was significantly lower and Ave-NHT of EES was significantly higher than BES (Table).

Conclusions: Biocompatible durable-polymer coated EES showed accelerated neointimal healing compared to biodegradable-polymer coated BES, which may have the favorable effects against stent thrombosis.

**P6424 | BEDSIDE**

Assessment of microcirculatory resistances after successful angioplasty of obstructed coronary arteries supplying hibernated myocardium can predict functional recovery

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Purpose: To investigate whether assessment of microcirculatory resistances both before and after percutaneous coronary intervention (PCI) may help predicting functional recovery in patients with severe coronary artery disease (CAD) and left ventricular dysfunction due to hibernated myocardium.

Methods: 33 patients with CAD, left ventricular dysfunction and evidence of hibernated myocardium underwent PCI. Functional severity indexes (fractional flow reserve [FFR] and coronary flow reserve [CFR]) and resistance indexes (hyperemic stenosis resistance [HSR] and hyperemic microvascular resistance [HMR]) were measured before and after PCI using a dual sensor pressure-flow wire. Ejec- tion fraction (EF), wall motion score index (WMSI) by transthoracic echocardiography (TTE) and summed rest score (SRS) of myocardial perfusion by 99mTc Tetrofosmin SPECT were measured before PCI and after 3 months.

Results: Overall FFR, HSR and CFR improved significantly after PCI. However, 9 (27%) patients (Group A) showed significantly higher post PCI HMR values as compared to the remaining 24 patients (Group B) (0.01±0.8 vs. 1.35±0.3; P=0.001). From the analysis of the two groups, there were no significant differences in pre PCI FFR, HSR, HMR, CFR, EF, WMSI and SRS. Post PCI FFR, HSR and CFR were not significantly different, as well. At 3 months, TTE showed a significant improvement of EF (from 36±7% to 47±10%; P=0.01) and WMSI (from 2.08±0.40 to 1.71±0.40; P=0.001) only in group B, as compared to group A (from 39±6% to 42±10% and from 1.92±0.63 to 1.93±0.68; P=NS; P=NS). Similarly, SRS substantially improved only in group B (from 13.1±5.9 to 9.3±6.4; P=0.001), compared to group A (from 10.6±8.9 to 9.2±6.2; P=NS).

Conclusions: Persistently high HMR values measured after successful PCI can predict lack of improvement of left ventricular function and myocardial perfusion in patients with obstructive CAD and evidence of hibernated myocardium.

**P6422 | BEDSIDE**

Structural remodeling of human coronary vasa vasorum with plaque progression

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Purpose: Pathological studies have suggested that coronary vasa vasorum (VV) might involve the progression of coronary plaque. However, little is known about the relationship between in vivo VV and plaque characteristics. Frequency-domain optical coherence tomography (FD-OCT) has enough penetration depth and spa- tial resolution to look at both VV surrounding the adventitia (AVV) and intra-plaque VV (IPVV). The aim of this study was to investigate the relationship between coronary VV and plaque characteristics using FD-OCT.

Methods: This study consisted of consecutive 43 patients who underwent FD-OCT to explore the left anterior descending artery in 10mm length centered on the first major septal branch irrespective of culprit lesion site. We classified FD-OCT images into five groups: normal (n=10), non-obstructive fibrous plaque (NOFP n=6), obstructive fibrous plaque (OFP n=9), athematomatous plaque (AP n=7), and ruptured plaque (RP, n=11). AVV and IPVV were manually segmented and total volume of VV was quantified by Simpson’s method.

Result: Volume of IPVV was different among five groups (Normal 0.303±0.156mm3, NOFP 0.595±0.225mm3, OFP 0.401±0.230mm3, AP 0.250±0.149mm3, and RP 0.171±0.099mm3, p<0.01, IPVV: normal 0.00±0.00mm3, NOFP 0.00±0.00mm3, OFP 0.015±0.019mm3, AP 0.023±0.018mm3, and RP 0.035±0.019mm3, p<0.01, respectively, shown in the figure).

Conclusions: AVV is propagated in the beginning of plaque formation. According to change of plaque characteristics, IPVV emerges instead of AVV increase. Our results suggest that structural remodeling of VV closely accompanies with plaque progression.

**FUNCTIONAL ASSESSMENT FOR PERCUTANEOUS CORONARY INTERVENTION**

**P6425 | BEDSIDE**

Efficacy of contrast medium induced Pd/Pa ratio in predicting functional significance of intermediate coronary artery stenosis assessed by fractional flow reserve: the RINASCI study

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Purpose: A critical prerequisite for the assessment of the functional significance of coronary stenosis by Fractional Flow Reserve (FFR) is the achievement of maximal hyperemia using adenosine. Nevertheless, both the intra-venous (i.v.) and the coronary (i.c.) routes have several drawbacks that limit the widespread application of FFR in the real world. Radiographic contrast medium induces sub-maximal reactive hyperemia. We hypothesized that Pd/Pa ratio registered during sub-maximal reactive hyperemia induced by i.v. injection of conventional non-ionic radiographic contrast medium (Contrast Medium induced Pd/Pa Ratio: CMR) can be sufficient for the assessment of physiological severity of stenosis in the vast majority of cases. The aim of the present study was to test the accuracy of CMR in comparison to FFR.

Methods: Intermediate coronary stenoses were prospectively and consecu- tively enrolled. CMR was obtained after i.v. injection of 6 ml of radiographic contrast medium, while FFR was measured after i.c. (600 μg) or i.v. (140 μg/kg/min) administration of adenosine.

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Results: Despite CMR values were significantly higher than FFR values (0.88 [IR 0.80-0.92] vs 0.87 [IR 0.83-0.94], p < 0.001), a strong correlation between CMR and FFR values was observed (r=0.94, p<0.001) with an excellent agreement at the 2.0 clinical cut point of CFRflow. This could allow limiting use of adenosine to obtain FFR to doubtful cases. In particular, we suggest to consider significant a CMR value <0.83, not significant a CMR value ≥0.88 and to induce maximal hyperemia using adenosine for FFR assessment when CMR is between 0.84 and 0.87.

P6426 | BEDSIDE Pressure-derived coronary flow reserve cannot be used as an alternative for coronary flow velocity reserve
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Purpose: Calculation of CFR from coronary pressure measurements (CFRpres) has been proposed as an alternative to Doppler flow velocity derived CFR (CFRflow). CFRpres is defined as the ratio between the square root of the pressure drop across the stenosis during hyperaemia and at baseline. This simplified model neglects the effects of stenosis geometry on flow impediment, raising concerns on its validity. We sought to validate CFRpres against CFRflow in a large cohort of coronary stenoses of intermediate severity.

Methods and results: A total of 299 coronary stenoses from 228 patients were evaluated by means of intracoronary pressure and flow velocity measurements. CFRflow was calculated as the ratio of hyperaemic average peak flow velocity (APV) to APV during basal conditions and CFRpres as indicated above. CFRflow was higher than CFRpres [median 2.21 (Q1: 1.37; 2.76 vs 1.55 (Q1: 1.29, 1.91; p<0.001)]. There was a moderate overall linear correlation between CFRflow and CFRpres (r=0.428; p<0.001; R²=0.18). Blunt Altman analyses showed a mean bias of -0.56±0.39 with a proportional error of -0.30 (p<0.001) and significant heteroscedasticity (95% limit of agreement: -0.56 to 1.74). Moreover, categorical agreement at the 0.2 clinical cut point of CFRflow was low (k=0.171, p<0.001). When stratified at the clinical 2.0 CFRflow cut-off value, the 95% limits of agreement amounted to -0.98±1.61 and 0.04±1.31 for CFRflow ≥2.0 and CFRflow <2.0, respectively.

Conclusions: CFRpres systemetically underestimates CFRflow values, and its magnitude of deviation is related to the magnitude of underlying CFRflow. Hence, CFRpres cannot be used as an alternative to CFRflow.

P6427 | BEDSIDE Caffeine attenuates intravenous adenosine-induced hyperemia in Fractional Flow Reserve Measurement
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Purpose: The interaction between caffeine and adenosine is still a matter of debate. Conflicting results have been reported in the literature concerning the effect of caffeine antagonism in the FFR measurement. An increase in adenosine dose up to 210 μg/kg/min cannot fully surmount the antagonism, and concerns about tolerability and safety remained. Our results suggest that abstention from caffeine is necessary before adenosine stress testing to avoid submaximal hyperemia.

P6428 | BEDSIDE Can intracoronary nitroglycerin Pd/Pa predict fractional flow reserve with intravenous or intracoronary adenosin?
R. Martín Reyes1, J.A. Franco Pelaez1, J.M. De La Torre2, R. Lopez-Palos3, F. Cedeño4, A. Sanchez Recalde1, I. Lozano5, S. Brugalletta7, F. Navarro1, J. Barre Munchazara6, J. Foundation Jimenez Diaz, Madrid, Spain; 2University Hospital Marques de Valdecilla, Santander, Spain; 3University Hospital San Juan de Alicante, Alicante, Spain; 4University Hospital Donostia, Donostia, Spain; 5University Hospital La Paz, Madrid, Spain; 6Hospital de Cabueñas, Gijon, Spain; 7University of Barcelona, Barcelona, Spain

Introduction: Functional assessment of coronary artery stenosis is performed by measuring the fractional flow reserve (FFR) under hyperemic conditions (Adenosine). But the use of Adenosine has several limitations such as: high cost and adverse systemic effects. Recent studies have tried to find a correlation between different parameters (FFR, Baseline Pd/Pa) obtained without adenosine and FFR, Objective: We sought to investigate the relationship and correlation between FFR and the Pd/Pa value obtained after the intracoronary infusion of nitroglycerin (Pd/Pa-NTG) and if this parameter enhances diagnostic accuracy for FFR prediction compared to the resting baseline Pd/Pa measurement.

Methods: From February 2013 to September 2014 we conducted a multi-center study that prospectively included 335 consecutive pressure wire data sets from 281 patients presenting intermediate coronary artery lesions (30-70% by QCA estimation). Patient demographic and angiographic lesion data were collected (mid-left system and right coronary artery), were measured following a standard protocol in all the centers.

Results: Resting baseline Pd/Pa value was 0.72 ± 1.0 (93 ± 0.04) Pd/Pa-NTG was 0.60 to 1.0 (87 ± 0.07) and FFR value after Adenosine iv or iv 0.55 to 1.0 (0.83 ± 0.08). The ROC curves for resting baseline Pd/Pa and for Pd/Pa-NTG, us- ing a FFR <0.80 as the reference standard variable showed an AUC of 0.88 (95% CI=0.84-0.92, p<0.001) and 0.94 (95% CI=0.92-0.96, p<0.001) respectively. The optimal cutoff values of resting baseline Pd/Pa and Pd/Pa-NTG for the prediction of FFR <0.80, were 0.96 and 0.88 respectively. These values were present in a 29.8% (n=100) and a 47.1% (n=158), of the total data sets. Scatter plots of resting baseline Pd/Pa and Pd/Pa-NTG, showed a better correlation and agreement points, with Pd/Pa-NTG than baseline Pd/Pa. Sensitivity and NPV of the Pd/Pa-NTG—0.88 were consistently high in all the subgroup analysis.

Conclusion: The Pd/Pa-NTG shows a good correlation with FFR in the intermediate-low lesions, even better than that with resting baseline Pd/Pa. The cutoff value of Pd/Pa-NTG—0.88 has an excellent NPV and sensitivity for determining lesion significance allowing to avoid adenosine—FFR determination in almost half of patients. This excellent diagnostic performance is not affected by angiographic or methodological variables (adenosine iv or ic).

P6429 | BEDSIDE An overlooked parameter in coronary slow flow phenomenon: whole blood viscosity
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Purpose: Coronary slow flow phenomenon (CSFP) is a clinical entity with poorly understood pathogenesis. Blood viscosity by using various methods has been
studied in CSFP previously. However, there was scarce data about the association of CSFP with whole blood viscosity (WBV) which was known as a neglected parameter of Vircovich triad. Therefore, in this study we aimed to assess the relationship between CSFP and WBV.

**Methods:** A total of 226 patients (64.8% male, mean age 51±9.7) with CSFP and 207 subjects (62.5% male, mean age 52.9±11.2) with normal coronary arteries as control group were enrolled. CSFP was quantified by means of corrected thrombolyis in myocardial infarction (TIMI) frame count and WBV was calculated from hematocrit and plasma protein concentration at low shear rate (LSR) (0.5 sec⁻¹) and high shear rate (HSR) (208 sec⁻¹) by a validated equation.

**Results:** CSFP patients had significantly higher WBV for both LSR (75.5±15.0 vs 63.9±21.5, p<0.001) and HSR (18.0±0.95 vs 17.2±0.95, p<0.001). Correlation analysis revealed a significant relationship between the corrected TIMI frame count and WBV for LSR (r=0.710; p<0.001) and HSR (r=0.641; p<0.001). A cut-off value of 69.3 WBV for LSR has a 76% sensitivity and 70% specificity for prediction of CSFP (AUC: 0.819). A cut-off value of 17.4 WBV for HSR has a 75.2% sensitivity and 71.5% specificity for prediction of CSFP (AUC: 0.845).

**Figure 1**

**Conclusion:** WBV is a simple, available and non-invasive test with low cost for evaluation of blood viscosity. Our study results demonstrated a significant and independent association between CSFP and WBV. The extrapolation of WBV with this method may utilize evaluating cardiovascular diseases where stasis has an important pathophysiological role.

P6430 | BEDSIDE

**Two different thermodilution-derived coronary blood flow patterns immediately after coronary intervention with TIMI 2 flow in patients with ST-segment elevation myocardial infarction**

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**Background:** A recent study reported the thermodilution-derived coronary blood flow pattern (CBFP) after percutaneous coronary intervention (PCI) associated with cardiac events in ST-segment elevation myocardial infarction (STEMI) patients. Although TIMI 2 flow leads to patient’s outcome worse, all patients with TIMI 2 flow after PCI do not have always poor outcomes. This study evaluates whether the CBFP predicts the clinical risk stratification in patients with TIMI 2 flow after PCI.

**Methods:** Forty-five patients with TIMI 2 flow after PCI were enrolled prospectively in this study. Using a pressure sensor/thermistor-tipped guidewire, CBFP was assessed from the thermodilution-curves after PCI. CBFP was classified into two groups according to the shape of thermodilution-curve: a wide-unimodal (n=29), or bimodal (n=16). Peak CPK, Wall-motion score index (WMSI) and microvascular obstruction (MVO) appearance assessed by cardiovascular magnetic resonance were analyzed within 2 weeks after PCI. Cardiac events were defined as cardiac death and/or heart failure re-hospitalization within this study period.

**Results:** Median follow-up period was 2.4 years. Although there were no significant differences in peak CPK, WMSI and MVO appearance between 2 groups, patients in bimodal had a higher risk of cardiac events during this study period (p=0.00013). Multivariate analysis revealed that bimodal was the only independent predictor of cardiac events in patients with TIMI 2 flow (hazard ratio, 4.95; 95% confidence interval, 1.71-14.34; p=0.003). A bimodal-shape is associated with the poor outcomes in patients with TIMI 2 flow. This easily assessable CBFP is useful in long-term clinical risk stratification for STEMI patients with TIMI 2 flow at the catheterization laboratory immediately after PCI.

**P6433 | BEDSIDE**

**Impact of resting distal coronary pressure to aortic pressure to predict physiological lesion severity**


**Background:** Although fractional flow reserve (FFR) was useful modality to identify physiologically lesion severity, it was necessary to obtain pharmacological hyperemia. However, we sometimes encounter adverse events such as atrioventricular block and hypotension. It was unclear whether the resting distal coronary pressure to aortic pressure (PD/PA) index could predict physiological significant stenosis without hyperemic stimulus. Thus, we evaluated the relationship between resting PD/PA and FFR in various coronary arteries.

**Method:** A total of 200 consecutive patients with 285 intermediate lesions were confirmed in this study. After pressure wire was positioned as distal as possible in a coronary artery, we measured the resting PD/PA index before pharmacological stress. Then, we measured FFR with intravenous adenosine triphosphate. Physiological significance was defined as FFR less than or equal 0.80.

**Results:** Analyzed vessels were distributed in left anterior descending (LAD, 52%), left circumflex (26%), and right coronary artery (22%), respectively. In all lesions, reference diameter, diameter stenosis were 2.7±0.6 mm, 59±13%, respectively. The resting PD/PA index showed a strong correlation with FFR (r=-0.84, p<0.0001). These strong correlations showed no difference in LAD and non-LAD (r=-0.82 and r=-0.84, respectively). In overall lesions, the best cut-off value of the resting PD/PA index to predict physiological significance was 0.92, which had 90% sensitivity and 83% specificity in all lesions (area under the curve: AUC 0.93, positive predictive value: PPV 90%, negative predictive value: NPV 85%, and accuracy 87%) from receiver operating characteristic (ROC) curve. In LAD lesions, the best cut-off value was 0.89, which had 77% sensitivity and 97% specificity (AUC 0.93, PPV 99%, NPV 57%, and accuracy 77%). In non-LAD lesions, the best cut-off value was 0.91, which had 83% sensitivity and 91% specificity (AUC 0.93, PPV 87%, NPV 88%, and accuracy 88%). The resting PD/PA more than 0.97 (n=47, 16%) had 100% of NPV, and less than 0.84 (n=75, 26%) had 100% of PPV in all lesions.

**Conclusion:** The resting PD/PA index had a good linear relationship with FFR. Although it was not based on physiological concept, a certain range of the resting PD/PA might predict functional significance without inducing pharmacological hyperemia for lesion assessment.

**P6434 | BEDSIDE**

**Impact of patients hemodynamic status on the accuracy of fractional flow reserve measurement**

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**Purpose:** Fractional flow reserve (FFR) is invasive index to assess the ischaemic potential of coronary stenoses. FFR is calculated as the ratio of average distal coronary (Pd) to aortic pressure (Pa) during maximal hyperemia. Mean central venous pressure (Pv) is neglected in the formula as considered of little impact

**Methods:** A total of 200 consecutive patients with 285 intermediate lesions were confirmed in this study. After pressure wire was positioned as distal as possible in a coronary artery, we measured the resting PD/PA index before pharmacological stress. Then, we measured FFR with intravenous adenosine triphosphate. Physiological significance was defined as FFR less than or equal 0.80.

**Results:** Analyzed vessels were distributed in left anterior descending (LAD, 52%), left circumflex (26%), and right coronary artery (22%), respectively. In all lesions, reference diameter, diameter stenosis were 2.7±0.6 mm, 59±13%, respectively. The resting PD/PA index showed a strong correlation with FFR (r=-0.84, p<0.0001). These strong correlations showed no difference in LAD and non-LAD (r=-0.82 and r=-0.84, respectively). In overall lesions, the best cut-off value of the resting PD/PA index to predict physiological significance was 0.92, which had 90% sensitivity and 83% specificity in all lesions (area under the curve: AUC 0.93, positive predictive value: PPV 90%, negative predictive value: NPV 85%, and accuracy 87%) from receiver operating characteristic (ROC) curve. In LAD lesions, the best cut-off value was 0.89, which had 77% sensitivity and 97% specificity (AUC 0.93, PPV 99%, NPV 57%, and accuracy 77%). In non-LAD lesions, the best cut-off value was 0.91, which had 83% sensitivity and 91% specificity (AUC 0.93, PPV 87%, NPV 88%, and accuracy 88%). The resting PD/PA more than 0.97 (n=47, 16%) had 100% of NPV, and less than 0.84 (n=75, 26%) had 100% of PPV in all lesions.

**Conclusion:** The resting PD/PA index had a good linear relationship with FFR. Although it was not based on physiological concept, a certain range of the resting PD/PA might predict functional significance without inducing pharmacological hyperemia for lesion assessment.

**Figure 1**

Conclusion: WBV is a simple, available and non-invasive test with low cost for evaluation of blood viscosity. Our study results demonstrated a significant and independent association between CSFP and WBV. The extrapolation of WBV with this method may utilize evaluating cardiovascular diseases where stasis has an important pathophysiological role.

**Figure 1**

Correlation between FFRmeas and FFRcorr.
if within normal range. We aimed at investigating the impact of P\(\text{v}\) over a wide range on FFR measurement.

**Methods:** We obtained measured FFR (FFR\(_{\text{meas}}\)=P\(\text{d}\)/P\(\text{a}\)) and corrected FFR (FFR\(_{\text{corr}}\)=P\(\text{d}\)/P\(\text{a}\)-P\(\text{v}\)) in 1993 intermediate coronary stenosis of 1181 patients (pts) undergoing left and right heart catheterization because of ischemic heart disease (639 [54%]), heart failure (597 [51%]) or valve disease (593 [49%]). Average blood pressure was 91±17 mmHg and median \(P\text{v}\) was 7 mmHg (max 27 mmHg).

**Results:** The correlation between FFR\(_{\text{corr}}\) and FFR\(_{\text{meas}}\) was excellent (\(R^2=0.985\), \(p<0.001\); slope 1.05±0.003; see Figure). Median FFR\(_{\text{corr}}\)\((0.85 [0.76; 0.91])\) was slightly but significantly higher than median FFR\(_{\text{corr}}\)\((0.83 [0.76; 0.90])\). The median difference between FFR\(_{\text{corr}}\) and FFR\(_{\text{meas}}\) was 0.01 (0.01; 0.02). Values of FFR\(_{\text{meas}}\) above the cut-off of 0.80 turned to an FFR\(_{\text{corr}}\) below 0.80 in 92 (6\%) stenoses overall, and in 29 (9\%) (\(p=0.021\) vs. overall) stenoses of pts with \(P\text{v}\) higher than 10 mmHg. Stenoses with FFR\(_{\text{meas}}\) over 0.83 never turned to an FFR\(_{\text{corr}}\) below 0.80. No FFR\(_{\text{meas}}\) value decreased from >0.80 to an FFR\(_{\text{corr}}<0.75\).

**Conclusions:** FFR values above the gray zone (i.e. >0.80) did not turn to values below the gray zone (i.e. <0.75) in any case, suggesting that the impact of the hemodynamic status on FFR measurement is indeed negligible, even in patients with markedly increased P\(\text{v}\).

**P6433 | BEDSIDE**

Intermediate term reproducibility of microvascular resistance measurements by the index of microcirculatory resistance in patients with intermediate coronary artery stenosis

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**Background:** Compared with coronary flow reserve (CFR), the index of microcirculatory resistance (IMR) has been shown to provide a more reproducible assessment of the microcirculation, which is independent of epicardial coronary artery stenosis severity and hemodynamic status. However, intermediate-term reproducibility of IMR has not been investigated.

**Methods and results:** Using a pressure-temperature sensor-tipped coronary wire, IMR and thermodilution-derived CFR (ThermoCFR) were measured twice, along with FFR, in 36 coronary arteries with intermediate lesion with an average interval of 44±32 days (range 8–121). Hemodynamic status of aortic pressure, distal coronary artery pressure, and heart rate were similar between the 2 measurements. There were no significant differences in IMR, ThermoCFR, and FFR between the 2 measurements (IMR: 21.7±10.6 vs 19.9±9.4, ThermoCFR: 3.18±1.67 vs 3.54±1.77, FFR: 0.76±0.06 vs 0.77±0.08, respectively). Regression analysis showed a significant relationship between the 2 measurements for all three values (IMR: \(R^2=0.31\), \(p<0.001\), ThermoCFR: \(R^2=0.25\), \(p=0.002\), and FFR: \(R^2=0.65\), \(p<0.001\)). The repeatability coefficients and relative repeatability coefficients of IMR, ThermoCFR, and FFR were 18.5 (86\%), 3.40 (101.2\%), and 0.08 (10.4\%), respectively. Coefficients of variation of IMR, ThermoCFR, and FFR were 32.3\%, 36.7\%, and 3.9\%, respectively.

**Conclusion:** The intermediate term longitudinal reproducibility of IMR was similar to ThermoCFR and significantly lower than that of FFR. This variability should be taken into consideration when IMR is used for the interpretation of microvascular resistance.

**P6434 | BEDSIDE**

Relationship between index of microcirculatory resistance and fraction flow reserve in patients with coronary artery disease

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**Purpose:** The relationship between microcirculatory dysfunction and severity of epicardial coronary artery disease in patients with coronary disease is not well-known. We performed this study to investigate the relationship between index of microcirculatory resistance (IMR) and fractional flow reserve (FFR) in patients who underwent elective coronary angiography and invasive physiologic assessment.

**Methods:** 852 vessels with available IMR and FFR were consecutively enrolled. Patients with unstable clinical condition, ST-elevation myocardial infarction, and flow lower than TIMI3 were excluded. IMR and FFR were measured using a pressure-temperature sensor-tipped guidewire at the same location of a target vessel. Hyperemia was induced by adenosine infusion of 140\(\mu\)g/kg/min. Corrected IMR (IMR\(_{\text{corr}}\)) which accounts for collateral flow was derived by Yong's formula.

**Results:** Mean FFR, IMR and IMR\(_{\text{corr}}\) were 0.87±0.09, 20.6±16.2 and 20.7±17.3 (interquartile range: 12-23), respectively. The difference between IMR and IMR\(_{\text{corr}}\) was the highest in patients with lowest FFR. There was a positive correlation between FFR and IMR\(_{\text{corr}}\) (\(r=0.216\), \(p=0.007\)) (Figure). Using the cut-off value of FFR 0.8 and IMR\(_{\text{corr}}\) 23, 17.8\% of low FFR and 28.5\% of high FFR had microvascular dysfunction.

**Conclusion:** Integration of macro- and microvascular function using FFR and IMR is needed to comprehensively assess the pattern of atherosclerotic disease in patients with ischemic heart disease.

**P6435 | BEDSIDE**

Thermodilution-derived coronary blood flow pattern immediately after coronary intervention as a predictor of long-term clinical outcomes in patients with ST-segment elevation myocardial infarction

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**Background:** A recent study reported that coronary blood flow (CBF) can be evaluated by analyzing thermodilution-curve that is measured with a pressure sensor/thermistor-tipped guidewire during percutaneous coronary intervention (PCI). Bimodal-shape of thermodilution-curve was associated with microvascular damage after ST-segment elevation myocardial infarction (STEMI). However it is unknown whether the bimodal-shape predicts mortality and re-hospitalization for heart failure in long term period for patients experiencing STEMI.

**Methods:** Between September 2009 and August 2012, 97 consecutive patients with a first PCI were prospectively enrolled in this study. CBF pattern was assessed from the thermodilution-curves after successful PCI at maximum hyperemia. CBF pattern was classified into 3 groups according to the shape of thermodilution-curve: a narrow-unimodal (n=47), a wide-unimodal (n=33), or bimodal (n=17). Major adverse cardiac events (MACE) were defined as cardiac death and/or heart failure re-hospitalization within this study period.

**Results:** Median follow-up period was 2.4 years. Although patients in the narrow-unimodal group and the wide-unimodal group had a significantly lower incidence of MACE, patients in bimodal group had a higher risk of MACE during this study period (71, 15, 21, \(p<0.001\)). Multivariate analysis revealed that bimodal-shape of the thermodilution-curve was the only independent predictor of MACE after STEMI (hazard-ratio, 8.38; 95\% confidence-interval, 2.13–33.00; \(p=0.0023\)).

CBF pattern in long-term outcomes.

**Conclusions:** A bimodal-shape of the thermodilution-curve is associated with the poor long-term clinical outcomes. This easily assessable coronary flow pattern is useful in clinical risk stratification for STEMI patients in the cardiac catheterization laboratory immediately after PCI.
**EXPERIMENTAL STUDIES IN CORONARY ARTERY DISEASES**

**P6437 | BEDSIDE**
Statin treatment increases the circulating endothelial progenitor cells and improve endothelial function in patients with coronary artery diseases

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**Background:** Statin use in patients with coronary artery disease (CAD) is associated with reduction in cardiovascular events occurring independently of statin lipid-lowering effects. Statins improve endothelial function and endothelial progenitor cell (EPC) differentiation in patients with CAD.

**Purpose:** To study the impact of statin therapy on number and function of EPCs in patients with CAD. Also, the assessment of the effect of statin on endothelial function estimated by brachial artery flow mediated dilation (FMD).

**Methods:** We assessed EPCs percentage and functions in 81 patients: 41 patients with acute coronary syndrome (ACS) (group 3) and 40 with chronic stable angina (group 2), in addition to 24 control subjects (group 1). Groups 2.6.3 were divided into subgroups (A: not on statin & B: on statin). EPCs were identified on the basis of KDR cell surface marker expression (VEGFR-2). EPCs function was assessed using an quantitative vWF and VEGFR-2 genes expression and eNOS protein level measurement. Brachial artery FMD was estimated to assess the effect of statin on endothelial function.

**Results:** KDR antigen was highly significant expressed on EPCs surface in patients on statins therapy (2B, 3B) compared to patients not on statins therapy (2A, 3A) (P <0.001). Flow Cytometry percentage shows high significant difference between patients on statins treatment (2B, 3B) and patients not on statins therapy (2A, 3A) (P <0.001). The highest significant difference was found in plasma level of vWF (2B, 3B vs control A & B) and protein level in patients not on statins treatment (2A, 3A, 3B). Parameters of EPCs function revealed a significant increase in quantitative levels of VEGFR-2 and vWF genes expression and eNOS protein level were detected in patients on statins therapy versus patients not on statins therapy (2B, 3B) vs control (2A, 3A) P <0.001, FMD was significantly higher in patients on statin group (2B, 3B) versus patients not on statin therapy (2A, 3A) (P <0.001). There was a positive correlation (r=0.723) between FMD percentage and plasma eNOS biomarker in patients on statin therapy versus patients not on statin therapy (r=0.475) correlation between KDR flow cytometry percentages and FMD.

**Conclusions:** Statin therapy increases the circulating EPCs and improve endothelial function in patients with CAD. EPCs number was the strongest predictor of FMD. FMD is an indicative test for eNOS bioavailability production.

**P6438 | BEDSIDE**
New insights into the mechanism of hyperglycaemia in non-diabetic patients with acute coronary syndromes

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**Purpose:** Stress generated by acute illness is associated with insulin resistance and abnormalities in endothelial function in patients with acute coronary syndrome (ACS). Hyperglycaemia (SH) has been linked to worse prognosis but its physiopathological substrate has not been elucidated. In this study we aim to assess if SH is associated with higher levels of cortisol, GH, catecholamines and insulin resistance.

**Methods:** Prospective cohort study. We included patients admitted with diagnosis of ACS between December 2011 and September 2013. Admission on glucose, insulin, cortisol, GH, adrenaline y noradrenalin were dosed and HOMA-IR was calculated. Patients were divided into 3 groups: G1=normal subjects (non-diabetics with glucose <126mg/dl), G2=SH (non-diabetics with glucose >126mg/dl), G3=diabetics. For statistical analysis, t test was used for discrete variables and ANOVA or Student T test for continuous variables. A P value <0.05 was considered significant in all cases.

**Results:** Ninety three patients were included, mean age 70.7 (±12.6) years, 49.5% male. Forty seven patients (50.5%) were included in G1, 18 (19.4%) in G2 and 30 (31.1%) in G3. There was no significant difference in age, sex and characteristics except for a longer ischaemia time in the nitrite group (P=0.031). There were no differences in release of serum creatine kinase (p=0.92) or troponin T (p=0.85) after reperfusion between the nitrite and control groups. No difference was seen in CMR assessed infarct size (p=0.254) but there was a trend to improved MS in the nitrite group (mean 0.52 [95% confidence intervals CI] of 0.46 to 0.59) vs. 0.49 [95% CI of 0.44 to 0.54] (p=0.051). However, there was a difference in 1 year MACE (2.6% in the nitrite group vs 15.8% in the control, p=0.04). In a subgroup of 66 patients with TIMI <1 flow at time of intervention there was a decrease in the release of serum creatine kinase in the nitrite group (p=0.030),

**Conclusions:** Stress hyperglycaemia could be exaggerate cortisol adrenal response and its consequent glycogenolysis and not by higher resistance to insulin or catecholamine secretion.

**P6439 | BEDSIDE**
CSL112 robustly enhances the ability of serum to efflux cholesterol in normal healthy adults and patients with atherothrombotic disease

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**Purpose:** Apo-A1 is known to remove cholesterol from atherosclerotic plaque. CSL112 is a novel formulation of apo-A1 purified from human plasma and reconstituted to form HDL particles suitable for infusion which is currently in development for acute coronary syndrome (ACS). Phase 1 (NCT01129661, NCT01281774) and Phase 2a (NCT01499420) have demonstrated favourable safety, pharmacokinetic (PK) and biomarker responses to infusions of CSL112 in normal healthy subjects (NHS) or patients with stable atherothrombotic disease (ATD). Here we quantitatively compare the biomarker responses in the NHS populations versus the ATD population.

**Methods:** We compared key biomarker data from the three studies; formation of very small HDL, elevation of total cholesterol efflux capacity from macrophages and movement of cholesterol to HDL. We calculated the baseline corrected area under the curve (AUC) for each biomarker for each subject and the corresponding baseline corrected AUC for apo-A1. Results: Linear regression analysis of individual biomarker AUC over apo-A1 AUC across the 3 different studies showed similar responses in patients with ATD compared to NHS. Figure 1 shows the relationship to total cholesterol efflux.

**Conclusions:** CSL112 in patients with ATD immediately enhances biomarkers of reverse cholesterol transport to a similar extent as in NHS. CSL112 may thus provide a novel option to rapidly lower the systemic burden of atherosclerosis and to reduce the risk of recurrent events following ACS.

**P6440 | SPOTLIGHT**
The safety and efficacy of intracoronary nitrite infusion during acute myocardial infarction (NITRITE-AMI): a single centre, randomised, double-blind controlled trial

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**Introduction:** Pre-clinical evidence demonstrates that inorganic nitric acid, following its in situ conversion to nitric oxide, attenuates consequent myocardial reperfusion injury. In this study we sought to determine whether a significant improvement in infarct size can be achieved by the intra-coronary injection of nitrite during primary percutaneous coronary intervention (PCI) in acute myocardial infarction.

**Methods:** In this double-blind, placebo-controlled trial, we randomly assigned 80 patients presenting with acute ST-elevation myocardial infarction to receive either recombinant coro- norial bolus (10 ml) of sodium nitrite (1.8 μmol in normal saline: nitrite group) or normal saline (placebo group) distal to the occlusion site before initial balloon inflation during primary PCI. The primary endpoint was infarct size assessed by measuring the release of creatine kinase, secondary outcomes included infarct size assessed by troponin T release, infarct size and myocardial salvage index (MSI) assessed by cardiac magnetic resonance imaging (CMR) and major adverse cardiac events (MACE) at 1 year.

**Results:** The nitrite and control groups were similar with respect to baseline characteristics except for a longer ischaemia time in the nitrite group (p=0.031). There were no differences in release of serum creatine kinase (p=0.92) or troponin T (p=0.85) after reperfusion between the nitrite and control groups. No difference was seen in CMR assessed infarct size (p=0.254) but there was a trend to improved MSI in the nitrite group (mean 0.52 [95% confidence intervals CI] of 0.46 to 0.59) vs. 0.49 [95% CI of 0.44 to 0.54] (p=0.051). However, there was a difference in 1 year MACE (2.6% in the nitrite group vs 15.8% in the control, p=0.04). In a subgroup of 66 patients with TIMI <1 flow at time of intervention there was a decrease in the release of serum creatine kinase in the nitrite group (p=0.030),
with no difference in troponin T release (p=0.158). CMR analysis indicated a 19% reduction in infarct size (p=0.034), 35% reduction in microvascular obstruction and increased Mesi (p=0.002) in the nitrate treated sub-group patients. No adverse effects of nitrate administration were detected.

Discussion: In this study population intra-coronary nitrate infusion is safe but, despite reducing MACE at 1 year, has no significant effect on infarct size. In contrast, in a sub-group of patients with TIMI flow≤1, infarct size was reduced indicating that intra-coronary nitrate administration to the culprit vessel of selected patients presenting with AMI may provide a new therapeutic adjunct to PCI. Further investigation is warranted.

P6441 | SPOTLIGHT
Angiotensin receptor blocker therapy in patients with ST-segment elevation myocardial infarction with preserved left ventricular systolic function

Objective: To investigate the association of ARB therapy with clinical outcomes in ST segment elevation myocardial infarction (STEMI) patients with preserved left ventricular systolic function.

Background: Limited data are available on the efficacy of angiotensin receptor blocker (ARB) therapy for secondary prevention in STEMI patients with preserved LV systolic function.

Methods: Between November 2005 and September 2010, 20344 patients with acute MI were enrolled in a nationwide, multi-center registry. Among these, we studied STEMI patients who underwent primary percutaneous coronary intervention and LV ejection fraction >40%. We classified patients into the ARB group (n=1175), the ACE inhibitor group (n=1175), the non-ARB/ACE inhibitor group (n=949) according to the use of ARB or ACE inhibitors at discharge. Propensity-score matching analysis was also performed. The primary outcome was cardiac death or MI.

Results: The median follow-up duration was 371 (interquartile range: 167 to 450) days. Cardiac death or MI occurred in 21 patients (1.8%) of the ARB group, 77 patients (1.7%) of the ACE inhibitor group, and 33 patients (3.5%) of the non-RAS blocker group. The ARB group had a similar risk of cardiac death or MI compared with the ACE inhibitor group (hazard ratio: 1.02; 95% confidence interval [CI] 0.63-1.66; P=0.92) and a lower risk of cardiac death or MI compared with the non RAS blocker group (HR: 0.44; 95% CI, 0.25-0.76; P=0.004). After propensity-score matching (1175 pairs), there was no significant difference in the rate of cardiac death or MI between the ARB following criteria: a history of MI (n=3), renal insufficiency with baseline serum creatinine >1.5 mg/dL (n=2), atrial fibrillation (n=2), cardiogenic shock or unstable hemodynamic status (n=8), and AMI for >12 hours from onset of symptoms (n=3). The remaining 42 primary AMI patients who underwent percutaneous coronary intervention survival groups were excluded from the analysis. Twenty-one consecutive patients were treated with an ACEI or an ARB (non-DRI) group, and another 21 consecutive patients received aliskiren combined with an ACEI or an ARB (DRI) group. CMR imaging was performed 7 days after AMI (10.3±0.9 months).

Results: CMR imaging revealed no significant changes in LV end-diastolic volume (-15.3±22.3 vs. -20.8±23.0 mL, P=0.436), LV end-systolic volume (-13.0±20.8 vs. -13.7±24.9 mL, P=0.921), or LV ejection fraction (4.4±8.3 vs. 3.6±7.9, P=0.347) between the patients with and without DRI aliskiren. Plasma renin activity in the DRI group was significantly lower in both the acute (0.2 [0.1 to 0.6] vs. 1.8 [0.7 to 7.6] ng/mL/hr, P<0.001) and chronic (0.5 [0.2 to 1.5] vs. 1.1 [0.8 to 3.2] ng/mL/hr, P=0.015) phases; however, aldosterone levels were significantly lower in the acute (38.1 [28.9 to 49.7] vs. 51.3 [36.9 to 108.0] pg/mL, P=0.025) but not the chronic (39.1 [23.0 to 66.0] vs. 55.7 [23.2 to 65.3] pg/mL, P=0.529) phase than in the non-DRI group.

Conclusions: Early administration of the DRI aliskiren add on conventional ther- apy, including an ACEI or an ARB, after primary AMI results in no attenuation of LVR.

P6444 | BEDSIDE
Spirolactone lowers the rate of repeat revascularization in acute myocardial infarction patients treated with percutaneous coronary intervention
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Purpose: We sought to assess the effect of the aldosterone receptor blocker, spironolactone, on 1-year clinical outcomes in all-comers with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI).

Methods: Between November 2005 and September 2008 from a nationwide AMI registry. Patients were divided into two groups: those treated with spironolactone (n=720, 7.0%) and those who had not been treated at discharge. The primary endpoint was major adverse cardiac events (MACE) defined as the composite of death from any cause, recurrent AMI, or repeat revascularization at 1-year after PCI.

Results: The spironolactone group had a greater number of co-morbidities than the non-spirolactone group. The mean follow-up duration of the overall study population was 313.4±119.9 days. After adjusting for potentially relevant variables including the propensity score, there was no significant association between the spironolactone treatment and MACE at 1 year (adjusted hazard ratio [HR]: 0.95, 95% confidence interval [CI]: 0.72-1.24, P=0.69) in the overall population. The risks of death from any cause, cardiac death, and recurrent AMI were also similar between the groups. However, patients who received spironolactone had a lower risk of repeat revascularization than those who did not receive spironolactone (adjusted HR: 0.58, 95% CI: 0.39-0.86, P=0.007). In subgroup analysis, the repeat revascularization rate was substantially lower in the spironolactone-treated group among patients with estimated creatinine clearance >60 (ml/min) and patients treated with drug-eluting, respectively. Of guideline-eligible patients (n=651/10,309, 63.9%), just 170/651 patients (20.7%) received a spironolactone at hospital discharge. The independent predictors of spironolactone prescription at discharge among guideline-eligible patients were Killip class > II, admission glucose level (mg/dl), left ventricular ejection fraction (%), regional wall motion score >20, and multi-vessel coronary disease. When limited to the guideline-eligible pa- tients population, a statistical trend toward lower MACE was observed in patients treated with spironolactone (adjusted HR: 0.63, 95% CI: 0.37-1.0, P=0.10). Also, a trend of similar decline in the risk of repeat revascularization was seen in the spironolactone-treated group, as demonstrated in the whole population (adjusted HR: 0.47, 95% CI: 0.21-1.08, P=0.08).

Conclusions: All-comer AMI patients undergoing PCI who received spironolac- tone had a lower risk of repeat revascularization. Randomized trials are needed.

P6444 | BEDSIDE
Eicosapentaenoic acid treatment reduces acute inflammatory response and ventricular arrhythmias in patients with reperfused acute myocardial infarction
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Background: Acute myocardial infarction triggers an inflammatory reaction, which plays an important role in myocardial injury. N-3 polysaturated fatty acid could attenuate inflammatory response by modulating several pathways.

Methods: In this prospective, single-center randomized open-labeled trial consisted of 115 patients (70±13 years, 75% male) with acute myocardial infarction: ST-segment elevation myocardial infarction (STEMI), 95 patients and non-STEMI, 20 patients. They were randomized to the eicosapentaenoic acid (EPA) group (57 patients, EPA 1800 mg/d + pitavastatin 2mg/d, orally) or the control group (58 patients, placebo). Clinical endpoints including the incidence of malignant ventricular arrhythmias (7% vs. 20.6%, P=0.034). Peak C-reactive protein (CRP) value after PCI in the EPA group was significantly lower than in the control group (8.2 [5.6-10.2] mg/dl vs. 9.7 [7.6-13.9] mg/dl, P=0.003). Multivariate analysis demonstrated that EPA use was an independent factor related to clinical adverse events until one month, along with peak CRP value.

Conclusions: EPA treatment in the acute stage of myocardial infarction reduced clinical adverse events including ventricular arrhythmias, accompanying by low-
erating CRP value. Thus, EPA has anti-inflammatory and anti-arrhythmic effects in patients with repertused acute myocardial infarction.

P6445 | BEDSIDE Clinical outcomes of early initiation of pure eicosapentaenoic acid supplement after percutaneous coronary intervention in patients with acute coronary syndrome

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Purpose: Despite solid evidence of lower omega-3 fatty acids levels and cardiovascular death, benefits of supplemental omega-3 fatty acids on cardiovascular events remain controversial. The aim of this study was to evaluate whether early initiation of supplemental pure eicosapentaenoic acid (EPA) 1800 mg/day after successful percutaneous coronary intervention (PCI) can improve clinical outcome in patients with acute coronary syndrome.

Methods: A total of consecutive 203 patients (mean71 years, 75% male) with acute coronary syndrome including 66% of acute myocardial infarction were randomized to the EPA group (n=101, pure EPA 1800 mg/day + a statin) or the control group (n=102, a statin alone). Supplemental EPA was stared on the next day of PCI and continued until 12 months. The primary outcome measure was major adverse cardio- cerebrovascular events (MACCE).

Results: There were no differences in baseline risk factors including levels of omega-3 fatty acids, PCI procedure, and max CK-MB between two groups. The incidence of MACCE in the EPA group (n=11) was significantly lower than that in the control group (n=22) (p<0.05). Cumulative event-free survival was significantly higher in the EPA group than in the control group (p=0.04, log-rank test). By adjusting for age, gender, conventional risk factors, and target vessel, EPA administration was identified as a good predictor of MACCE (hazard ratio: 0.47, 95% CI 0.22 to 0.97, p=0.04).

Conclusion: Early loading of pure EPA after PCI therapy appears to confer improved one-year clinical outcomes in patients with acute coronary syndrome undergoing PCI. Our findings support the early initiation of omega-3 fatty acids after successful percutaneous coronary intervention.

P6446 | BEDSIDE Association of blood lipids, biomarkers of atherosclerosis and lipid transport system genes polymorphism in patients with unstable angina

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Purpose: To examine blood lipids, atherosclerosis biomarkers level and the carriage of "unfavorable" alleles of lipid transport system genes polymorphisms in Uzbek patients with unstable angina (UA).

Material and methods: There were examined 125 Uzbek patients with UA. I group (n=63) consisted of patients with presence of coronary artery disease (CAD) in family history and II group (n=62) without family history of CAD. The control group consisted of 58 healthy persons. The G-A polymorphism of apolipoprotein A1 (apoA1), -516C/T polymorphism of apolipoprotein B (ApoB), d2r/d3r/d4 polymorphism of apolipoprotein E (ApoE) and SstI polymorphism of apolipoprotein CII (Apo CIII) genes were determined using reagents Diatome DNA Prep 200.

Results: In studying the distribution of "damaging" alleles among the patients with UA (n=125) in comparison with healthy persons, there has been found a prevalence of "A" allele carriers of the Apo A1 (HR 3.63, 95% CI 1.63-8.04, p<0.002). The distribution of "damaging" alleles in comparative analysis II group with healthy persons did not differ significantly, whereas in I group had significantly greater accumulation of alleles: "A" G-A polymorphism of Apo A1 gene (HR 5.99, 95% CI 2.52-14.24, p<0.001), "a" -4 polymorphism of Apo E gene (HR 2.91, 95% CI 1.12-7.62, p<0.048). At -4 carriers were higher LDL cholesterol level (p<0.001), Apo B/ Apo A ratio (p<0.01) and high sensitive C-reactive protein level (p<0.01), whereas "A" (M1-) carriage are accompanied by decrease HDL cholesterol level (p<0.005).

Conclusion: Among Uzbek patients with unstable angina and family history of coronary artery disease accumulation of "damaging" alleles were observed: "a" of Apo E and "A" (M1-) A polymorphism of Apo A1 genes, which were associated with lipid and biomarkers disorders.

P6447 | SPOTLIGHT Relationship between total and high weight molecular adiponectin and lesion components in patients with unstable coronary artery disease

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The present study investigated the relationship among serum total and high weight molecular adiponectin (HWM-adiponectin) and culprit lesion components in patients with unstable coronary artery disease. Previous studies showed a pivotal role of adiponectin for anti-atherogenic and cardiovascular protection of adiponectin. However, the relationship between adiponectin, especially HWM-adiponectin and plaque characters was still unknown. 60 patients with unstable coronary artery disease were included in our study. We used ELISA to analyze the concentration of total and high weight molecular adiponectin. Culprit lesion was identified by analyzing ST-T alteration on electrocardiograms, left ventricular wall motion abnormalities, angiographic complex lesions and IVUS-detected plaque rupture. We performed Virtual Histology-Intravascular Ultrasound examination on each culprit lesion. We analyzed the relationship between the total and high weight molecular adiponectin and the culprit lesion components. HWM-adiponectin is positively associated with the absolute volume of fibro-fatty (r=0.505, P<0.01) and fiber (r=0.499, P<0.01) respectively. While the concentration of the total and high weight molecular adiponectin increases in patients with unstable coronary artery disease, the relatively stable plaque composition of the culprit lesion is growing.
Increased risk of coronary heart disease in patients with chronic osteomyelitis: a population-based study in a cohort of 23 million

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**Objectives:** Chronic inflammatory disease may trigger vascular atherosclerosis. This study aimed to determine whether chronic osteomyelitis (COM) is linked to an increased risk of coronary heart disease (CHD).

**Methods:** A national insurance claim dataset of more than 23 million enrollees was used to identify 15,054 patients with COM and 60,216 randomly selected age- and gender-matched controls between 2001 and 2009 for comparing the risk and incidence of CHD. The study period was from the entry date to the first date of the following events: the diagnosis of CHD, death, withdrawal from the Taiwan National Health Insurance program or the end of 2010. The analysis of the CHD risk was performed using Cox proportional hazards regression model.

**Results:** During a follow-up period of 67,927 person-years, the overall incidence rate of CHD in COM cohort was 1.95-times higher than non-COM cohort (16.66 vs. 8.52 per 1000 person-years). After controlling age, gender and four conventional atherosclerosis risk factors in patients with no significant luminal stenosis were diabetes (OR=2.26, p=0.03). The same risk factors also predicted extensive CAC (score ≥50%) luminal stenosis in 6,300 symptomatic patients from Sweden, Denmark, Germany, Italy, France, and USA.

**Methods:** Patients’ mean age was 60.2±11.7 years, 48% females and none had prior coronary intervention or previous coronary syndrome. All elderly patients underwent coronary calcium scoring by Agatston method followed by coronary angiography to exclude significant (<50%) luminal stenosis.

**Results:** There was a close relationship between the cumulative risk factor score and the CAC score (p<0.001), which makes them more predictive of risk than females, (3.50±1.50 vs. 2.29±1.40, p=0.0001). In patients with significant coronary stenosis, the independent predictors of severe CAC (score ≥400) were diabetes (OR=1.58, p=0.001) and hypertension (OR=1.35, p=0.001), while the risk factors with cardiovascular risk factors, coronary artery calcium scoring (OR=2.26, p=0.0001), hypercholesterolemia (OR=1.23, p=0.03) and obesity (OR=1.27, p=0.03). The same risk factors also predicted extensive CAC score (score ≥1000).

**Conclusion:** Although coronary calcification is generally considered a marker of atherosclerosis, the impact of conventional risk factors on its formation differs in patients with and without significant luminal stenosis.

**Purpose:** Parathyroid hormone (PTH) has been linked to endothelial dysfunction, elevated pulse pressure, increased carotid artery intima-media thickness and vascular calcification. Elevated PTH levels in terms of secondary hyperparathyroidism have been found in patients with chronic kidney disease. Studies evaluating the relationship between PTH and risk of cardiovascular, and mortality, in patients with normal kidney function are, however, sparse. We therefore aimed to evaluate the relationship between PTH and long term CV mortality in patients with acute coronary syndrome (ACS).

**Methods:** A total of 1036 patients with ACS and measurement of PTH at baseline were included in the analyses. Data was extracted from the LUDwigshafener Risk and Cardiovascular Health (LURIC) study (1997–2000). Serum PTH was measured by an ElectroChemiLuminescence Immunoassay (ECLIA) on an EletroChemiLuminescence Immunoassay (ECLI).

**Results:** Of 970 patients (age 60.9±11.4 years, 71% male), 75% (n=731) had CAD. Patients with angiographic CAD had thicker EAT on the left ventricle lateral wall (LVLW; 2.43±0.44 vs. 1.81±0.28, p=0.007) and increased VAT thickness (2.8±1.7 vs. 2.4±1.3, p=0.013). There was a close relationship between the cumulative risk factor score and angiographic CAD, which makes them more predictive of risk than females, (3.50±1.50 vs. 2.29±1.40, p=0.0001). In patients with significant coronary stenosis, the independent predictors of severe CAC (score ≥400) were diabetes (OR=1.58, p=0.001) and hypertension (OR=1.35, p=0.001), while the risk factors with cardiovascular risk factors, coronary artery calcium scoring (OR=2.26, p=0.0001), hypercholesterolemia (OR=1.23, p=0.03) and obesity (OR=1.27, p=0.03). The same risk factors also predicted extensive CAC score (score ≥1000).

**Conclusion:** Although coronary calcification is generally considered a marker of atherosclerosis, the impact of conventional risk factors on its formation differs in patients with and without significant luminal stenosis.

**Purpose:** Epicardial adipose tissue thickness correlates with the presence and severity of angiographic coronary artery disease

**Methods:** We measured epicardial fat thickness by computed tomography and assessed the presence and extent of CAD by coronary angiography in participants from the prospective EVASCAN study. The association of EAT thickness with vascular risk factors, coronary artery calcification scoring and angiographic CAD was assessed using multivariate regression analysis.

**Results:** Of 970 patients (age 60.9±11.4 years, 71% male), 75% (n=731) had CAD. Patients with angiographic CAD had thicker EAT on the left ventricle lateral wall (LVLW; 2.43±0.44 vs. 1.81±0.28, p=0.007) and increased VAT thickness (2.8±1.7 vs. 2.4±1.3, p=0.013). There was a close relationship between the cumulative risk factor score and angiographic CAD, which makes them more predictive of risk than females, (3.50±1.50 vs. 2.29±1.40, p=0.0001). In patients with significant coronary stenosis, the independent predictors of severe CAC (score ≥400) were diabetes (OR=1.58, p=0.001) and hypertension (OR=1.35, p=0.001), while the risk factors with cardiovascular risk factors, coronary artery calcium scoring (OR=2.26, p=0.0001), hypercholesterolemia (OR=1.23, p=0.03) and obesity (OR=1.27, p=0.03). The same risk factors also predicted extensive CAC score (score ≥1000).

**Conclusion:** Although coronary calcification is generally considered a marker of atherosclerosis, the impact of conventional risk factors on its formation differs in patients with and without significant luminal stenosis.

**Purpose:** Association of A603G tissue factor gene polymorphism with endothelial dysfunction and carotid arteries remodeling in coronary artery disease patients

**Methods:** The A603G TF gene genotypes were determined in a sample of 212 men with CAD and 55 healthy men by a polymerase chain reaction-
restriction length polymorphism (PCR-RFLP)-based method. Vascular cell adhesion molecule-1 (VCAM-1), IL-8, IF-gamma, IL-10 plasma levels were studied by ELISA. Gomocystein content was examined by liquid chromatography (Aliquent 1100). Dopplerography of carotid arteries was performed. ANOVA analysis, exact Fisher test and Odds-Ratio calculation were performed.

Results: The frequency of G603G genotype in CAD patients was higher than in the group of healthy people (72 from 212 and 11 from 55, p=0.017). IL-8 content in CAD patients with G603G tissue factor gene genotype were higher, than in A603A genotype carriers (981,3±214 pcg/ml and 308,1±59,2 pcg/ml respectively, p=0.05). The same tendencies were revealed in interferon-gamma plasma content in CAD patients with G603G TF gene genotype carriers and 0.99±0.205 pcg/ml in A603A genotype carriers. No significant difference in IL-10 plasma content in patients-carriers of different tissue factor gene genotypes was found. The CAD patients - carriers of G603G genotype had hyperhomocysteinemia (15.1±0.85 mmol/l and 12.1±0.69 mmol/l in healthy people respectively, p<0.05). Intima-media complex in CAD patients-carriers of G603G TF gene genotype was higher, than in patients – carriers A603A genotype: 1,18±0,023mm and 0,87±0,016 respectively.

Conclusions: Our study have revealed the association of G603G tissue factor gene genotype with elevated markers of endothelial dysfunction, hyperhomocysteinemia and intima-media thickening of carotid arteries in coronary artery disease patients.

P6455 | BEDSIDE
Body mass index and acute coronary syndromes: paradox or confusion?

Objectives: A better prognosis in obese patients has been described in acute coronary syndromes (ACS). However, this evidence is mostly based on retrospective studies and has provided conflicting results. No study reported cause specific mortalitity according to body mass index (BMI) in ACS. We aimed to prospectively assess the impact of BMI on mortality and its specific causes in ACS patients.

Methods: We prospectively included non-selected ACS patients admitted in a tertiary care Coronary Unit, collecting baseline characteristics, management and clinical course. Patients were stratified into five clinically meaningful BMI subgroups (<20, 20-25, 25-30, 30-35, >35 kg/m2). The primary outcome was mid-term mortality, its causes and its association with BMI. This association was assessed by Cox regression method.

Results: We included 2040 patients. Mean age was 62.1 years. Low weight patients (BMI <20) were older, with less cardiovascular risk factors, higher prevalence of chronic obstructive pulmonary disease and worse renal function. Mean follow up was 334 days. The unadjusted analysis showed lower all-cause mortality in all subgroups as compared to low weight patients. After adjusting for potential confounders, this association remained significant for patients with BMI 20-25. Cardiac mortality was similar across BMI subgroups. In contrast, the adjusted analysis showed a significantly lower non-cardiac mortality in patients with BMI 20-25, 25-30 and 30-35 as compared to low weight patients.

Conclusions: Baseline characteristics in ACS patients significantly differ according to their BMI status. The prognostic impact of BMI seems mostly related to extracardiac causes in low weight patients.

P6456 | BEDSIDE
Does subclinical renal dysfunction have prognostic implications among acute coronary syndrome patients with normal serum creatinine?

Background: Severe renal dysfunction is an important predictor of adverse events in acute coronary syndromes (ACS). The serum creatinine value is a poor indicator of renal function and patients with normal serum creatinine (NSC) may have insidious renal dysfunction; hence renal function should be evaluated by estimating glomerular filtration rate (GFR) using MDRD or Cockcroft-Gault formulas.

Aim: To clarify if mild renal dysfunction (GFR 60-89 ml/min) has any influence on the prognosis of ACS patients with NSC.

Methods: We analysed 4420 consecutive patients who were admitted to our coronary care unit with ACS and included in a prospective registry, from Jan 2003 to Oct 2013. Patients with NSC (<1.3 mg/dl) on admission were selected (86.4%, n=3820) and grouped according to estimated GFR, calculated by MDRD formula: group 1 [GFR < 90 ml/min (n=1778,46.5%)]; group 2 [GFR 60-89 ml/min (n=1681,44%)] and group 3 [TFG 30-59 ml/min (n=361,95%)]. None of the patients had GFR <30 ml/min. We compared the clinical and laboratory features, and adverse events for each group. The primary endpoint was the occurrence of death at 6 months; follow-up was completed in 95% of patients.

Results: Patients in group 3 were older (57.1±12 vs 66.1±12 vs 74.9± years; p<0.001) and more frequently women (15.7 vs 23.6 vs 71.5%; p<0.001). They also had a more frequent history of hypertension (52.8 vs 65.4 vs 77%; p<0.01), diabetes (21.1 vs 25.2 vs 39.1%; p<0.01) and previous acute myocardial infarction (11.6 vs 16.2 vs 22.4%; p<0.001), angina (12.4 vs 18.1 vs 20.5%; p<0.001) and stroke (3.7 vs 6.9 vs 10.8%; p<0.001). On admission, they more often presented with Killip class >1 (9.5 vs 22.1 vs 38.1%; p<0.001) and anaemia (12.9 vs 19.4 vs 34.6%; p<0.001), but had less often ST-segment elevation ACS (51.9 vs 49.8 vs 39.7%; p<0.001). Patients in group 3 underwent percutaneous coronary intervention less frequently (51.3 vs 49.4 vs 32.6%; p<0.001). There was a progressive increase in in-hospital (0.7 vs 3.4 vs 9.2%; p<0.001) and 6-month mortality (2.7 vs 8.0 vs 22.8%; p<0.001) as GFR decreased. In multivariate analysis, not only GFR 30-59 ml/min [adjusted OR 3.33; 95% CI (1.40-3.51); p<0.001], but also GFR 60-89 ml/min remained as an independent predictor of 6-month mortality [adjusted OR 2.22; 95% CI (1.40-3.51); p<0.001].

Conclusion: In patients admitted with ACS and NSC it is important to calculate their GFR, as more than half have mild or moderate renal dysfunction, which has prognostic relevance. Even mild renal dysfunction (GFR 60-89 ml/min) is a strong independent predictor of mortality in ACS patients with normal serum creatinine.
comes of man and women, 55 years old or younger enrolled in the Acute Coronary Syndrome Israeli Survey (ACSIS) 2000-2010. Results: Among 11,536 patients enrolled, 3424 (30%) were 55y old (342 women and 3082 men). Women suffered more from diabetes mellitus and hypertension (p<0.001 for both) despite a similar age (48.7±5.7 vs. 48.3±5.6, p=0.29). Women presented less often with STEMI (50% vs. 57%, p=0.007) or with other risk factors for chest pain (73% vs. 80%, p=0.004), and had higher rates of GRACE score: 140 (19% vs. 12%, p=0.007). After adjustment for GRACE score, diabetes and enrollment year, women had a lower likelihood to receive PCI during hospitalization (OR 0.6, p=0.007). Female sex was not associated with higher risk for 7d and 1y mortality. It was, however, an independent risk factor for 30d MACCE (OR 1.9, p=0.005) (Figure).

Conclusions: In young patients admitted with ACS, women are a unique high-risk group in need of a diagnostic challenge for clinicians. Women were less often treated with invasive therapy during hospitalization and have more short-term adverse events.

P6458 | BEDSIDE

Relationship of carotid plaque area to the severity of coronary artery obstructive disease

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Purpose: Several studies reported that the carotid intima-media thickness (IMT) as a week predictor of coronary artery disease. Contrary, there are little available data regarding the plaque area and severity of coronary artery obstructive disease (CAOD). In this study, we evaluated the relationship of carotid plaque area with severity of CAOD in the patients of acute coronary syndrome

Methods: We retrospectively reviewed medical records of the patients who performed coronary angiography (CAG), carotid ultrasound and transthoracic echocardiography within a 3 months interval. Total 1104 patients were analyzed in this study. More than 50% luminal narrowing of CAG was regarded coronary artery obstructive disease (CAOD). Plaque area was measured in magnified longitudinal views of each plaque seen in left and right common, internal and external carotid arteries. The sum of all plaques seen between the clavicle and angle of the jaw was defined total plaque area.

Results: Mean age of total subject was 60.0±12.8. Female proportion was 23.8% (n=24). Medical history of hypertension was in 39 (38.6%) and diabetes mellitus was in 23 (22.8%). The CAG results was as follows; one vessel CAD in 55 (54.5%), two vessels CAD in 30 (29.7%) and three vessels CAD in 16 (15.8%). ST elevation myocardial infarction was the most frequent clinical diagnosis in 66 (65.3%) and followed by unstable angina in 18 (17.8%) and non ST elevation myocardial infarction in 17 (16.8%). Average carotid IMT was 0.82±0.26 mm and total plaque area was 7.7±10.7 mm². Average left ventricular mass index (LVM) was 96.6±22.2 gm²/m² and ejection fraction was 55.2±11.8%. Multi-vessel CAOD related older age (one vessel vs. three vessel; 58.6±12.3 vs. 66.3±16.8, p<0.026). Multi-vessel CAD showed positive correlation of increased average IMT (one vessel vs. three vessel; 0.79±0.22 vs. 0.97±0.36 mm, p=0.045) and increased total plaque area (5.2±1.7 vs. 20.0±17.5 mm², p<0.001). After adjusted covariate (age, sex, serum creatinine, hypertension, diabetes mellitus and calcification of carotid artery), the plaque area showed positive correlation with severity of CAOD, CAD=1.91±0.034 (plaque area) (p<0.001). 30-d mortality lower, the rising trend in the risk profile may prelude to a forthcoming epidemic of coronary events. It calls for more effective efforts to reverse the trend in the population of the Middle East.

P6460 | BEDSIDE

Temporal trends in major risk factors and in-hospital mortality over two decades in patients with first acute myocardial infarction: a study from a 20 years registry in a middle-eastern country

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Background and purpose: Has the risk profile in patients with Acute Myocardial Infarction (AMI) changed over the years?. We analyzed a 20 years registry of all ACS patients to study the changes in the temporal trends of major Cardiovascular Risk Factors (CVRFs), as well as age, gender and in-hospital mortality over 2 decades among patients with first AMI in a middle-eastern country

Methods: All patients hospitalized with first AMI in 20 years (January 1991 to December 2010) were included. Changes in age, gender and major CVRFs (Hypertension, Diabetes, Smoking, Dyslipidemia, and Family History of premature coronary artery disease (CAD)) were analyzed along with related in-hospital mortality. All changes were contrasted in two consecutive decades.

Results: Out of 12,881 AMI Patients, 10,915 patients were admitted with “first” AMI. Comparing the two decades, the proportion of first AMI of the total cardiac hospitalizations increased from 34% to 66%, a relative increase of 48%. Comparing the two decades, the proportion of STEMI decreased from 69.7% in first decade to 54% in second decade (p<0.001). Conversely N-STEMI increased from 30% to 45.2% (p<0.001). The over all mean age increased from 51±12 to 54±12 years (p=0.05) and for both men (50±11 to 52±11, p=0.01) and women (61±12 to 63±12 for women, p<0.001). Furthermore, there was a significant shift in the age of first AMI, with an ever increasing proportion for middle age (51-70 years) from 15% (40%) to 34% (48%, p<0.001), as well as in the elderly (>70 years) from 6% to 9% of all first AMI patients (p<0.001). While history of Dyslipidemia declined from 96% to 18% (p<0.001), the rate of MI was increased significantly, thus hypertension increased from 24% to 40%, diabetes from 31% to 41% and smoking increased from 29% to 42% (p<0.001 for all) (Table 1). Family history of premature CAD did not change (p<0.34), but the overall in-hospital mortality decrease 8.8% to 5.4%, p<0.001 over the study period. Multivariate logistic regression analysis showed that in both decades, age (adjusted OR 3.80, 95% CI 2.97-4.84, p<0.001), female gender (adjusted OR 1.98, 95% CI 1.62-2.42, p<0.001) and Diabetes were independent predictors of in-hospital mortality (adjusted OR 1.90, 95% CI 1.35-1.90, p<0.001).

Conclusions: This large registry suggests a steady increase in the burden of major risk factors. Although the age at first AMI is getting older and in-hospital mortality lower, the rising trend in the risk profile may prelude to a forthcoming epidemic of coronary events. It calls for more effective efforts to reverse the trend in the population of the Middle East.

P6459 | BEDSIDE

The impact of polyvascular atherosclerotic disease for the long-term outcome of patients undergoing percutaneous coronary intervention

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Purpose: The aim of this study was to investigate the long-term outcome following percutaneous coronary intervention (PCI) for patients with polyvascular disease (polyVD) such as peripheral artery disease (PAD), renal artery stenosis (RAS), internal and external carotid artery stenosis (IC/S) and abdominal aortic aneurysm (AAA).

Methods: A total of 2052 consecutive patients underwent PCI were prospectively enrolled between November 2007 and October 2009. Among them, 534cases were detected by ultrasound and ankle-brachial index; PAD were in 367cases (17.9%), IC/S in 95cases (4.6%), RAS in 94cases (4.6%), and AAA in 11cases (5.7%). We evaluated the incidence of cardiovascular (CV) death as primary outcome, and also investigated the incidence of myocardial infarction (MI), stroke, target lesion revascularization (TLR) and major adverse cardiac events (MACE; included of death, MI, stroke) as secondary outcome.

Results: The mean follow-up term was 3.5±1.1years. In the polyVD group, the incidence of CV death was significantly higher than in the only coronary artery disease (CAD) group (P<0.0001). Similarly, the incidence of MI, stroke and MACE was significantly higher in the polyVD group than in the only CAD group (polyVD 3.3% vs CAD 1.9% at 5years, P<0.003; polyVD 6.6% vs CAD 1.4% at 3years, P<0.0001; and polyVD 22.6% vs CAD 7.9% at 3years, P<0.0001, respectively). Only the TLR rate was similar between the two groups (polyVD 20.7% vs CAD 22.2% at 3years, P=0.86). Age >75 years old, hemodialysis, history of CABG, thicker IMT, 1.30mm, lower ABI -0.94 were found to be independent predictors of cardiovascular death.

Conclusions: In patients with polyVD, female sex was associated with a lower risk of CV death. A comprehensive risk stratification is needed to improve outcomes of PCI in this high-risk group.
pressing symptoms (DS) over time and coronary heart disease (CHD) and stroke events in older adults.

Setting: The Three City Study is a multisite community-based prospective cohort.

Participants: The study population includes 7313 men and women aged 65 years and over with no history of CHD, stroke or dementia. A score ≥16 on the 20-item Center for Epidemiologic Studies Depression Scale questionnaire defined the presence of DS at baseline and during follow-up visits. At each date of an event, the risk of vascular events associated with the number of DS episodes over time was calculated using Cox proportional hazard model with time dependent variable.

Results: DS were present in respectively 22.7%, 19.5%, 19.8% and 21.7% of the participants at baseline, 2, 4, and 7 years of follow-up. The corresponding rates for antidepressants use were 6.7%, 7.2%, 8.1% and 8.0%. After a median follow-up of 8.4 years (SD 2.3years), 629 first CHD or stroke events (124 fatal) were adjudicated, including 384 first CHD and 245 first stroke. After adjustment for study centre, sociodemographic characteristics and baseline vascular risk factors, there was a significant 1.15 increased risk of CHD and stroke for each additional episode of DS (95%CI: 1.06–1.26). Associations were similar for CHD, stroke and non fatal events, and was stronger for fatal CHD or stroke events (HR=1.28; 95% CI: 1.09-1.51). Analysis restricted to participants free of disability or free of antidepressants at baseline but adjusting for these incident variables virtually unchanged the results.

Methods: The current data support a progressively increased risk of CHD and stroke events with the number of DS episodes over time in older adults, independently of major vascular risk factors, disability and antidepressants use.

ANTIPLATELET THERAPY IN ACUTE CORONARY SYNDROME PATIENTS

P6463 | BEDSIDE
Serial measurements of platelet reactivity during one year of clopidogrel or ticagrelor treatment in patients presenting with ST-segment elevation myocardial infarction - the TOPS study

Purpose: Inhibition of platelet reactivity by dual antiplatelet therapy (DAPT) is essential to reduce the risk for atherothrombotic events in patients presenting with a STEMI who are treated with primary PCI. However, it is unknown whether platelet reactivity on this treatment remains stable over time. We evaluated platelet reactivity with various platelet function tests during one year of clopidogrel or ticagrelor treatment in STEMI patients undergoing PCI to determine if and when a stable level of platelet reactivity is reached.

Methods: The TOPS study is a non-randomized, open label and single centre study. Patients undergoing primary PCI with stenting for STEMI who received a loading dose (LD) of DAPT before PCI (500mg Aspegic iv plus 600mg clopidogrel or 180mg ticagrelor), followed by standard maintenance doses were included. Platelet reactivity was measured with the VerifyNow P2Y12 assay, Light Transmittance Aggregometry (LTA; 20μmol/L ADP), and Multiplate (MEA; ADP 6.5μmol/L) directly before PCI, and at 6, 24 and 48 hours, 1, 2 and 4 weeks, and 3, 6, and 12 months after LD.

Results: A total of 33 patients were included. As measured with the VerifyNow, platelet reactivity was inhibited after 24 hours after LD to a level which remained stable until 1 year of follow-up, both for clopidogrel and ticagrelor (see figure), LTA and MEA both showed comparable results; platelet reactivity was inhibited to a stable level 6 hours after LD until 1 year of follow-up.

Conclusions: The present study suggests that Ticagrelor is associated with higher platelet inhibition and higher incidence of “hyper response” than Prasugrel one month after ACS, possibly exposing patients to higher risk of bleeding complications.

P6464 | BEDSIDE
Prasugrel versus ticagrelor in acute coronary syndrome: a randomized comparison
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Purpose: European guidelines recommended the use of Prasugrel or Ticagrelor in ACS patients as first choice. The present biological study was designed to compare the effectiveness and safety of Prasugrel versus Ticagrelor in patients undergoing PCI for ACS.

Methods: In this randomized study, consecutive patients admitted for ACS in our institution were assigned to receive a loading dose of Prasugrel 60 mg or Ticagrelor 180 mg and were treated at discharge with Prasugrel 10 mg once a day or Ticagrelor 90mg twice a day. Antithrombotic response was assessed one month after ACS with Platelet Reactivity Index VASP (PRI VASP) and ADP-induced platelet aggregation (%ADP), LTPR was by PRI VASP<20%. Primary end point was the comparison of degree of platelet inhibition and incidence of LTPR in patients treated with Ticagrelor or Prasugrel, one month after an ACS.

Results: Between March and June 2013, 96 patients (48 in each arm) were randomly assigned to Prasugrel or Ticagrelor for ACS. We observed 14% of bleeding complications (n=13 patients), 8 in the Ticagrelor cohort versus 5 in the Prasugrel therapy group. At one month, PRI VASP (20.2±9.9% vs. 25.6±11.5% p<0.01) and %ADP (37.9±10.3% vs. 48.9±10.8% p<0.01) were significantly lower under Ticagrelor therapy than under Prasugrel therapy. We observed LTPR status in 33% of the patients under Prasugrel and in 58% under Ticagrelor (p<0.01). Interestingly there was a trend in favor of an increased bleeding risk at one month on Ticagrelor (17% vs. 10%; p<0.15).

Conclusions: The present study suggests that Ticagrelor is associated with higher platelet inhibition and higher incidence of “hyper response” than Prasugrel one month after ACS, possibly exposing patients to higher risk of bleeding complications.
were event free at 6 months (n=1674), the rates of MACCE was 6.4% in patients with DAPT >6 months (n=1140) and 4.7% in patients with DAPT <6 months (n=534) (adjusted hazard ratio [HR] 0.95; 95% confidence interval [CI] 0.55-1.65; P=0.86). The rates of all-cause death (adjusted HR 1.55, 95% CI 0.19-12.69, P=0.68), MI (adjusted HR 0.99, 95% CI 0.11-9.11, P=0.99), target lesion revascularization (adjusted HR 1.04, 95% CI 0.57-1.91, P=0.89), TVR (adjusted HR 1.09, 95% CI 0.65-1.85, P=0.74), stent thrombosis (adjusted HR 0.28, 95% CI 0.2-4.89, P=0.38), and stroke (adjusted HR 0.23, 95% CI 0.02-3.43, P=0.29) did not differ significantly between the 2 groups. After propensity-score matching (n=469 pair), DAPT >6 months was not associated with a lower incidence of MACCE compared with DAPT <6 months (adjusted HR 0.80, 95% CI 0.44-1.45, P=0.46). These results were also consistent across various subgroups. Among patients with prior stroke, however, MACCE occurred less frequently in patients taking DAPT for more than 6 months as compared with patients taking DAPT for up to 6 months, although interaction test did not reach statistical significance (interaction P value=0.08).

Conclusions: DAPT beyond 6 months does not seem to reduce the risk of MACCE in patients with ACS undergoing PCI with ZES. However, it should be needed to confirm this finding in larger and randomized studies.

P6468 | BENCH
Platelet microRNA-15b protects against high on-treatment platelet reactivity in patients with acute coronary syndromes through bcl-2-mediated platelet apoptosis

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Purpose: To explore the association between platelet microRNAs (miRNAs) and interindividual variability of on-treatment platelet reactivity in patients with acute coronary syndromes (ACS), and to address the molecular mechanisms underlying the modulation of miRNAs in platelets.

Methods: In a cohort of 208 patients with ACS on dual antiplatelet therapy of aspirin and clopidogrel, on-treatment platelet reactivity was measured by VerifyNow P2Y12 testing at 12-24h after percutaneous coronary intervention (PCI). High platelet reactivity (HPR) and low platelet reactivity (LPR) were defined as P2Y12 reaction units (PRU) ≥280 and <190, respectively. Microarrays were used to perform miRNA expression profiling in purified platelets from 4 patients with HPR and 4 patients with LPR. The candidate miRNAs analyzed from microarrays were further validated by quantitative reverse-transcription polymerase chain reaction (RT-PCR) in platelets of 15 patients with HPR and 16 with LPR. The platelets of ACS patients were incubated with ABT-737 (a bcl-2 inhibitor, 2.5μM) in vitro for 2h at 37°C. The apoptotic events were measured by Annexin V FITC/PI and JC-1 labeling. The megakaryocytic cell line ME-01 was used for miRNA transfection experiments.

Results: 3 miRNAs (miR-145, -15b and -143) were detected to be differentially expressed in platelets between patients with HPR and LPR by microarrays. Among the candidate miRNAs, miR-15b was validated to downregulate in platelets of HPR patients compared with LPR patients by RT-PCR (P=0.017).

Conclusion: We found tendencies that Ticagrelor and Prasugrel increased the risk of bleeding compared to Clopidogrel, and that Prasugrel lowered the risk of adverse cardiovascular events. However, a larger population is needed to confirm these tendencies statistically.
syndromes admitted to a chest pain unit and treated with either prasugrel or clopidogrel were enrolled. Baseline characteristics, antithrombotic therapies, interventional procedures features and events after 12 months were prospectively collected and centrally analysed. Here we compare the outcomes of 453 patients with prasugrel and a matched control group with clopidogrel.

Results: Baseline variables, procedural features and 12-month events are shown in the table.

<table>
<thead>
<tr>
<th>12-month results</th>
<th>Prasugrel (n=453)</th>
<th>Clopidogrel (n=453)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>59 yrs</td>
<td>61 yrs</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>24%</td>
<td>25%</td>
</tr>
<tr>
<td><strong>STEMI</strong></td>
<td>48%</td>
<td>24%</td>
</tr>
<tr>
<td><strong>PCI</strong></td>
<td>92%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Stent or drug at 12 months</strong></td>
<td>73%</td>
<td>76%</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>2.2%</td>
<td>3.7%</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td>1.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>1.7%</td>
<td>1.3%</td>
</tr>
<tr>
<td><strong>MACCE</strong></td>
<td>3.9%</td>
<td>7.3%</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>6.6%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Conclusion: In this real life experience prasugrel compared to clopidogrel improved clinical outcome in patients with ACS without an increase in bleeding complications.

P6470 | BEDSIDE

Relationship between troponin levels and long-term outcomes in medically managed patients with non-ST-segment elevation acute coronary syndromes: insights from the TRILOGY ACS trial

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1Duke Clinical Research Institute, Durham, United States of America;2University Heart Center, Zurich, Switzerland;3El Lilly and Co., Indianapolis, United States of America;4Auckland City Hospital, Auckland, New Zealand;5Kerckhoff Clinic, Bad Nauheim, Germany

Purpose: The relationship between troponin (Tn) elevation and outcomes among patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS) is established, but is less well-studied in long-term follow-up of medically managed patients receiving contemporary antiplatelet therapy.

Methods: In 7038 medically managed NSTE ACS patients randomized in the TRILOGY ACS trial of prasugrel vs. clopidogrel and for whom peak Tn data were available, we examined relationships of categories of site laboratory-based peak Tn upper limit of normal (ULN) ratio (<1×ULN [n=1849]; 1×–<3×ULN [n=2032]; 3×–<5×ULN [n=581]; and ≥5×ULN [n=3405]) within 48 h of the index ACS event (<4.5 d before randomization) as an estimate of index infarct size with 30-month ischemic outcomes.

Results: Patients with Tn ratios ≤1×ULN were more likely to be younger, female, from Central/Eastern Europe, and have lower GRACE risk scores than patients with ratios ≥5×ULN. Conversely, patients with ratios ≥5×ULN were more frequently smokers but less often had prior myocardial infarction or percutaneous coronary intervention. Diabetes prevalence, body mass index, serum creatinine, and anemia/sickle cell were similar across groups. Trends for increasing event rates across peak Tn categories were highly significant for all endpoints (Table). The relationship was stepwise for mortality but appeared to plateau for composite endpoints for Tn values >3×ULN. The most dramatic difference observed in event rates was between Tn <1×ULN and any Tn elevation ≥1×ULN during early follow-up.

Kaplan-Meier event rates at 30 months

Tnropoin level P value

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>≤1×ULN</th>
<th>1×–3×ULN</th>
<th>3×–5×ULN</th>
<th>≥5×ULN</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, MI, or stroke</td>
<td>12.2%</td>
<td>18.4%</td>
<td>26.6%</td>
<td>25.1%</td>
</tr>
<tr>
<td>CV death or MI</td>
<td>11.5%</td>
<td>16.8%</td>
<td>25.0%</td>
<td>23.5%</td>
</tr>
<tr>
<td>CV death</td>
<td>6.2%</td>
<td>9.6%</td>
<td>10.8%</td>
<td>12.8%</td>
</tr>
</tbody>
</table>

Conclusions: Among NSTE ACS patients selected for medical management, there was a graded relationship of increasing peak Tn with long-term ischemic events. At 30 months, event rates for patients with Tn ≥5×ULN were more than twice the rates for patients with Tn <1×ULN.

P6471 | BEDSIDE

In-hospital bleeding in acute coronary syndrome patients undergoing percutaneous coronary intervention in the era of novel P2Y12 inhibitors: validation of the modified Mehran bleeding risk score

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Abstract P6472 - Table 1. Characteristics of PR in dependence on AF and in dependence on AF of choice and antiplatelet drugs (clopidogrel vs. prasugrel/briquile)

<table>
<thead>
<tr>
<th>Patients with AF (n=114)</th>
<th>Patients without AF (n=546)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>mean</td>
<td>IQR</td>
</tr>
<tr>
<td>Complete population study (n=780)</td>
<td>40.24±24.43</td>
<td>37.84</td>
</tr>
<tr>
<td>Patients treated with clopidogrel (n=633)</td>
<td>42.23±23.85</td>
<td>40.79</td>
</tr>
<tr>
<td>Patients treated with prasugrel/briquile (n=127)</td>
<td>21.62±22.76</td>
<td>12.11</td>
</tr>
</tbody>
</table>

Purpose: In-hospital bleeding events occur frequently in acute coronary syndrome (ACS) patients undergoing percutaneous coronary intervention (PCI) and may be affected by P2Y12 inhibitor used. We aimed to analyze in-hospital bleeding events in the context of a contemporary Greek Antiplatelet Registry (GRAPE).

Methods: In 2047 patients, predictive factors for in-hospital Bleeding Academic Research Consortium (BARC) type ≥2 events were analyzed. Bleeding rates were compared according to P2Y12 inhibitor used and modified Mehran bleeding score usefulness was assessed.

Results: Hospital BARC type ≥2 events occurred in 84 (4.1%). Novel P2Y12 inhibitor use, prior actionable bleeding, and hemorrhodynamic instability at admission favored bleeding, whereas male gender was a protective factor (C-statistic 0.71, 0.66-0.77 95% CI, p<0.001). Following propensity matching, BARC type ≥2 bleeding rates were higher among novel P2Y12 inhibitor when compared with clopidogrel-treated patients (6.0% vs 2.7%, p<0.01), while did not differ between ticagrelor and prasugrel-treated patients (6.4% vs 3.6%, p=0.2). Modified Mehran risk score (median [1st-3rd quartile]) was higher in clopidogrel compared to novel P2Y12 inhibitor-treated patients [14 (9-19) vs 9 (6-14), p<0.001 and in ticagrelor compared to prasugrel-treated patients [10 (7-15) vs 9 (5-12), p<0.001], while exhibiting good calibration and adequate discriminative power.

Conclusions: In ACS patients undergoing PCI, novel P2Y12 inhibitors’ use was associated, amongst other factors, with in-hospital BARC type ≥2 bleeding events. Novel P2Y12 inhibitors are accompanied by a higher rate of bleeding compared to clopidogrel, with no such difference observed between prasugrel and ticagrelor. Modified Mehran risk score might be efficiently applied for prediction of in-hospital severe bleeding events.

P6472 | BEDSIDE

Impact of atrial fibrillation on laboratory efficacy of P2Y12 receptor antagonists in patients after percutaneous coronary intervention

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Purpose: To verify whether the presence of atrial fibrillation (AF) impacts the platelet reactivity, particularly the efficacy of ADP receptor antagonists, and to verify whether there is a correlation between CHA2DS2VASC score and the efficacy of ADP receptor antagonists in the group of patients with AF after stent-PCI.

Methods: The analysis of PCI registry was performed. The efficacy of ADP receptor antagonists nor the proportion of patients with HTPR. CHA2DS2 VASc score did not predict the efficacy of ADP receptor antagonists. CHA2DS2 VASc score did not predict the efficacy of ADP receptor antagonists with respect to the presence of AF. In the clopidogrel group, HTPR was detected in 6.0% vs 2.7%, p=0.01), while did not differ between ticagrelor and prasugrel-treated patients (6.4% vs 3.6%, p=0.2). Modified Mehran risk score (median [1st-3rd quartile]) was higher in clopidogrel compared to novel P2Y12 inhibitor-treated patients [14 (9-19) vs 9 (6-14), p<0.001 and in ticagrelor compared to prasugrel-treated patients [10 (7-15) vs 9 (5-12), p<0.001], while exhibiting good calibration and adequate discriminative power.

Conclusions: In ACS patients undergoing PCI, novel P2Y12 inhibitors’ use was associated, amongst other factors, with in-hospital BARC type ≥2 bleeding events. Novel P2Y12 inhibitors are accompanied by a higher rate of bleeding compared to clopidogrel, with no such difference observed between prasugrel and ticagrelor. Modified Mehran risk score might be efficiently applied for prediction of in-hospital severe bleeding events.
P6474 | BEDSIDE

Effect of new p2Y12 inhibitors in patients with chronic kidney disease after an acute coronary syndrome

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Background: Chronic Kidney Disease (CKD) concerns 35% of ACS patients and is associated with poor outcomes after stent implantation. New P2Y12 blocker (ticagrelor, prasugrel) has been largely unexplored in this specific population.

Methods: Consecutive patients admitted for Acute Coronary Syndrome and discharged on prasugrel or ticagrelor were screened and classified as: normal renal function (GFR >90 ml/ min), mild CKD (GFR 60 to 89 ml/min), moderate to severe CKD (GFR <60 ml/min). Platelet response was assessed at one month clinical follow-up by platelet reactivity index vasodilator-stimulated phosphoprotein (PRI-VASP).

Results: 515 patients were discharged from our institution with prasugrel 10 mg and 72 on ticagrelor 180mg. 293 patients (49%) were defined as normal renal function, 222 (38%) as mild CKD and 72 (12%) as moderate to severe CKD. We observed a significant correlation between PRI-VASP and GFR for prasugrel and ticagrelor (r=0.30 p<0.001 and r=0.26 p=0.03 respectively). On Prasugrel we observed significantly lower levels of PRI-VASP in CKD patients in comparison with normal renal function (24.4% ± 0.8 vs. 31.3% ± 0.8 p<0.001). Conversely, in Ticagrelor management of patients with CKD and PRI-VASP levels according to renal function status exists. (17.1% ± 1.8 vs. 22.4% ± 2.6 p=0.09 mild to severe CKD versus normal renal function and 16.1% ± 2.7 vs. 19.1% ± 1.4 p=0.31 moderate to severe CKD versus mild CKD to normal renal function). On prasugrel bleeding is associated with lower GFR (85.8 ± 2.8 vs. 84.3 ± 1.4 p=0.01). In Ticagrelor cohort we do not observe any significant relation between GFR and bleeding events. (87.6 ± 10.1 vs. 86.0 ± 3.9 p=0.9).

Conclusion: New P2Y12 blockers are associated with more potent platelet inhibition in CKD patients. Platelet inhibition on ticagrelor is less dependent of renal function in comparison with prasugrel.

P6477 | BEDSIDE

Procudural and clinical outcomes after glycoprotein Iib/IIa inhibitor use for saphenous vein graft interventions

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Background: Percutaneous coronary intervention (PCI) of saphenous vein grafts (SVG) pose a high-risk for thrombo-embolic events. Glycoprotein Iib/IIa inhibitors are frequently used, although the safety and efficacy of these drugs in this setting are unknown.

Methods: Patients with prior coronary artery bypass surgery were included who underwent PCI of ≥1 SVG graft at a Dutch academic center between January 1997 and December 2008. These patients were matched 1:1 based on the procedural use of abciximab using a propensity-score matching algorithm based on 17 variables. Conditional logistic regression and Cox regression stratified on matched pairs were performed to evaluate the association between abciximab use and the composite measure of mortality, myocardial infarction, stroke and repeat revascularization (MACCE) at 30 days and up to 1 year.

Results: The propensity-score matched cohort consisted of 236 patients, in whom complete 1-year follow-up was available in 98.3%. The composite of 30-day MACCE occurred in 18 patients (15.3%) in the abciximab group and 16 patients (13.6%) in the control group (odds ratio: 1.13 [0.57-2.21], p=0.73). At 1-year follow-up, MACCE rates were also similar (32.5% vs. 33.9%, hazard ratio: 0.97 [0.59-1.59], p=0.90). Bleeding (BARC type 3) was higher in the abciximab group (11.5% vs. 2.0%, OR 5.80 [1.01-31.77], p=0.048). Subgroup analyses among patients based on clinical presentation and use of embolic protection devices, rendered similar results.

Conclusion: The use of intravenous abciximab did not result in improved clinical outcomes at 30 days as well as 1-year in patients undergoing SVG PCI, and is associated with increased bleeding.

P6476 | BEDSIDE

Impact of obesity and the metabolic syndrome on response to clopidogrel or prasugrel and bleeding isk in patients treated after coronary stenting

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Purpose: This study aimed to analyze the impact of body mass index (BMI) and the metabolic syndrome (MS) on responses to clopidogrel or prasugrel and bleeding risk after acute coronary syndrome (ACS). Methods: 1 542 consecutive patients undergoing coronary stenting were included (287 clopidogrel 75 mg, 868 clopidogrel 150 mg, and 387 prasugrel 10 mg). Platelet reactivity was assessed 1 month after discharge using PRI-VASP. Results: 336 (21.8%) patients were obese (BMI ≥30kg/m²) and we observed higher platelet reactivity associated with higher BMI across thienopyridine regimens. Incidence of high on-treatment platelet reactivity (HTPR) (PRI-VASP >50%) was higher in obese than non-obese patients (p=0.05 for all regimens). Conversely, incidence of low on-treatment platelet reactivity (LTPR) with prasugrel therapy (PRI-VASP ≤20%) was lower in obese than non-obese patients: 13% (12/93) vs. 33% (97/294); OR [95%CI]: 0.30 [0.16-0.58], p<0.001. Among patients with BMI ≥30 kg/m², Incidence of BARC bleeding complications was higher in non-obese than in obese patients: 10% (119/1206) vs. 6% (20/336); OR [95%CI]: 1.7 [1.1-2.8], p=0.03. This impaired response was only observed in obese patients with the MS while

Conclusion: The data of the BSR show that prasugrel therapy in patients with STEMIs is associated with low complication rates in clinical practice.

PERCUTANEOUS CORONARY INTERVENTION AND ANTIPLATELET THERAPY

Figure 1

<table>
<thead>
<tr>
<th>Prasugrel</th>
<th>Clopidogrel</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>4.1%</td>
<td>5.6%</td>
</tr>
<tr>
<td>MACCE (death, nonfatal stroke or reinfarction)</td>
<td>8.7%</td>
<td>11.9%</td>
</tr>
</tbody>
</table>

Conclusions: The data of the BSR show that prasugrel therapy in patients with STEMIs is associated with low complication rates in clinical practice.

In comparison to matched clopidogrel-patients lower rates of MACCE were observed without significant differences in bleeding.
obese with the MS had significantly higher platelet reactivity than other obese patients with all regimens (p < 0.01). Obese without the MS had no significant difference of platelet reactivity compared with non-obese patients. Conclusion: The present study confirmed that BMI has a strong impact on reponse to clopidogrel and prasugrel with higher HTPR incidence, lower LTPR incidence and lower bleeding complication in obese patients. The presence of the MS strongly affects response to antiplatelet agents, indicating that the metabolic status might be a better predictor of platelet inhibition than BMI.

P6478 | BEDSIDE

Incremental usefulness of genetic testing of clopidogrel therapy over conventional clinical risk factors for prediction of major cardiovascular events after drug-eluting stent implantation


Purpose: To determine a incremental prognostic value of combined status of ABCB1 3435C–T and CYP2C19 variant allele on major adverse cardiac and cerebrovascular events (MACE) over clinical risk factors using C-statistic and novel risk reclassification metrics (NRI: net reclassification index, IDI: integrated discrimination improvement) in a real-world PCI cohort taking clopidogrel.

Method: We consecutively enrolled 2188 patients undergoing PCI. For CYP2C19 genotype, patients were classified into 3 groups: extensive (EM, *1/*1, *1/*7), intermediate (IM, *1/*2, *1/*3), poor (PM, *2/*2, *2/*3, *3/*3) metabolizer. For ABCB1 3435C–T, patients were stratified into CC, CT, TT. To assess combined effect of both genetic variants, patients were stratified into 4 groups according to the presence of CYP2C19 PM and ABCB1 TT: non-CYP2C19 PM + non-ABCB1 TT, non-CYP2C19 PM + ABCB1 TT, CYP2C19 PM + non-ABCB1 TT, CYP2C19 PM + ABCB1 TT. The primary endpoint was the composite of 1-year MACE including any death, nonfatal MI or stroke.

Results: On multivariate Cox analysis, when combined 4 genetic categories were incorporated into the clinical model, patients with both CYP2C19 PM and ABCB1 TT had 5-fold higher hazard of MACCE (HR: 5.06, 95%CI: 2.12 to 12.09; p < 0.001) than carriers of neither. However, the addition of genetic variant neither yield further improvement in predictive performance in model (C-statistic: clinical model, 0.78; clinical + genetic model, 0.78; difference, 0.06; p = 0.66) nor reclassification of individual at risk (model IDI, 0.002 [95% CI: -0.001 to 0.04]; p = 0.06), relative IDI, 0.269 [95% CI: 0.26 to 0.27]; p = 0.17), continuous NRI, 0.126 [95% CI: 0.001-0.25; p = 0.28], NRI categories, 0.039 [95% CI: 0.02 to 0.09; p = 0.20].

Conclusions: Although the combined status of CYP2C19 and ABCB1 3435C-T variant alleles was strong independent predictor for 1-year MACCE, it was not a useful marker for prediction of MACCE over conventional clinical risk factors in a real-world PCI cohort taking clopidogrel

P6479 | BEDSIDE

Lower on-treatment platelet reactivity at the time of stent placement contributes to the resolution of post-procedural intra-stent thrombus: serial OCT observation in PRASFIT-Effective

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Methods: This analysis included 765 consecutive patients undergoing elective PCI after loading with clopidogrel 600mg. Clopidogrel was continued for 6 months in the planned treatment period with clopidogrel. However, this association is not in the time stratum beyond 1 year after discontinuation (unadjusted HR: 2.93, 95%-CI 1.13-7.60, p = 0.03; adjusted HR: 3.09, 95%-CI 1.11-8.60, p = 0.03), but not in the time stratum before 1 year after discontinuation (unadjusted HR: 1.19, 95%-CI 0.82-1.72, p = 0.37).

Conclusions: Besides local lesion-related factors, lower on-treatment platelet reactivity after PCI inhibition at the time of PCI contribution to regression of IS-Th formed immediately after PCI, which might contribute to better vessel healings following stent placement.

P6480 | BEDSIDE

On-clopidogrel platelet reactivity as predictor for long-term clinical outcome in patients after planned discontinuation of clopidogrel

W. Hochholzer, C.M. Valina, T. Boemnicke, C. Stratz, T. Nuehrenberg, H.-J. Buettner, D. Menne, University Heart Center Freiburg-Bad Krozingen, Department of Cardiology and Angiology II, Bad Krozingen, Germany

Background: High on-treatment platelet reactivity (HPR) has been clearly linked to worse clinical outcome in patients on clopidogrel and after coronary stent implantation (PCI). It is unknown whether this effect persists after planned discontinuation of clopidogrel.

Methods: This study included 765 consecutive patients undergoing elective PCI after loading with clopidogrel 600mg. Clopidogrel was continued for 6 months after implantation of drug-eluting stents and for 1 month if only bare-metal stents were used. Platelet reactivity was tested by optical aggregometry (5 μM ADP) on day 1 after coronary stenting and at intake of first maintenance dose of clopidogrel 75mg. HPR was defined as >14% residual aggregation. Patients were followed for up to 7 years. The combined primary endpoint was death of any cause or non-fatal myocardial infarction (MACE).

Results: At time of enrollment, HPR was found in 217 of 765 patients (28%). During a median follow-up of 5.7 years, MACE occurred in 145 subjects after planned discontinuation of clopidogrel. Patients with HPR showed a higher incidence of MACE after discontinuation of clopidogrel (Figure; unadjusted HR: 1.34, 95%-CI 0.95-1.89, p = 0.09). However, landmark analyses demonstrated that this association was only significant within the first year after discontinuation (unadjusted HR: 2.93, 95%-CI 1.13-7.60, p = 0.03; adjusted HR: 3.09, 95%-CI 1.11-8.60, p = 0.03), but not in the time stratum beyond 1 year after discontinuation (unadjusted HR: 1.19, 95%-CI 0.82-1.72, p = 0.37).

Conclusions: Patients with HPR persist to be at high risk for MACE even after the end of the planned treatment period with clopidogrel. However, this association is only valid for the first year after end of treatment.

P6481 | BENCH

The impact of triple anti-platelet therapy for endothelialization and inflammatory response at overlapping bioabsorbable polymer coated drug-eluting stents in a porcine coronary model


Background: This study was conducted to evaluate the endothelialization and the inflammatory responses depending on the administration duration of triple anti-platelet therapy at overlapping bioabsorbable polymer coated biodegradable stents (BESs) in a porcine coronary model.

Methods: We successfully deployed 36 overlapping BESs for the left anterior descending coronary and left circumflex artery or right coronary artery in 18 non-injured pigs. Total pigs were divided into 3 groups (12 overlapping stents of 6
pigs in each group) as follows: group I received aspirin 100mg and cilostogol 75mg daily for 8 weeks, group II received aspirin 100mg and cilostogol 75mg daily for 8 weeks and cilostogol 200mg daily for initial 4 weeks, group III received aspirin 100mg, cilostogol 75mg, and cilostogol 200mg daily for 8 weeks. Follow-up coronary angiograms and histomorphometric and histopathologic analyses at overlapping and non-overlapping segments were performed respectively.

Results: Inflammation score was similar between overlapping and non-overlapping segments in all pigs (1.2±0.3 vs. 1.1±0.17, p=0.117). The neointima area (NA) and percent area stenosis (%AS) at overlapping segments were not significantly different among all groups, but at non-overlapping segments, NA and %AS in group III were significantly smaller than those in group I (2.3±0.50 mm² vs. 1.8±0.43 mm², p=0.037; 48.9±12.85% vs. 37.7±9.08%, p=0.031).

Conclusions: Our study shows that BEA appears to be reliable on the inflammatory response at overlapping segments as well as non-overlapping segments. Long-term administration of cilostogol is more effective in reducing neointimal formation on non-overlapping segments of BEAs in a porcine coronary model.

P6482 | BEDSIDE
Impact of smoking after percutaneous coronary intervention in patients treated with cilostogol: real-world findings from the PARIS registry
D. Giacoppo1, S. Sartori1, U. Baber1, M.W. Krucoff2, D.J. Moliterno3, D.J. Cohen4, G. Daniels4, C. Anti5, M. Alu6, R. Mehran7 on behalf of PARIS.
1Mount Sinai Medical Center, Mount Sinai Heart, New York, United States of America; 2Duke University Medical Center, Durham, United States of America; 3University of Kentucky, Lexington, United States of America; 4St. Luke’s Mid America Heart Institute, Kansas City, United States of America; 5London School of Hygiene and Tropical Medicine, London, United Kingdom; 6Columbia University Medical Center, New York, United States of America.
Purpose: Results from clinical trial participants undergoing PCI with stents suggest that the clinical benefits of cilostogol in reducing thrombotic events are accentuated in smokers versus non-smokers. Whether these associations persist in unselected real-world patients after PCI remain unknown. Results from clinical trial participants undergoing PCI with stents suggest that the clinical benefits of cilostogol in reducing thrombotic events are accentuated in smokers versus non-smokers. Whether these associations persist in unselected real-world patients after PCI remain unknown.
Methods: The PARIS registry was a multicenter prospective observational study of 5,018 patients undergoing PCI with stents. Smoking status was classified as current or not-current (quit over 1 month or never smoked). Dual antiplatelet therapy (DAPT) (DAPT) cessation was categorized as physician-guided discontinuation, brief interruption or disruption due to non-adherence or bleeding. Adverse events and DAPT cessation were compared between groups using Cox regression.

Results: Smokers (n=802, 19%) were younger and more often male with lower prevalence of diabetes mellitus, hypertension or prior CAD compared to non-smokers (n=3733, 81%). Over 2 years smokers were less likely to interrupt DAPT (8.3% vs. 10.9%, p=0.02), while disruption was more common in smokers (17.1% vs. 13.6%, p=0.01). Discontinuation did not differ between groups. Ischemic adverse events were not higher among smokers vs. non-smokers and persisted after multivariable adjustment.

Conclusions: In contrast to findings from clinical trial populations, among unselected patients smoking is associated with higher rates of disruption and adverse events compared to non-smokers.

P6483 | BEDSIDE
Validation of a therapeutic window for P2Y12-inhibition: collaborative analysis of the relation between platelet reactivity, stent thrombosis and bleeding
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Purpose: Studies have shown that platelet reactivity during treatment with P2Y12-inhibitors may predict the risk of stent thrombosis (ST) and major bleeding. However, validation of standardized cutoffs of platelet reactivity is lacking. We aimed to evaluate a therapeutic window cutoff for the prognostic impact of platelet reactivity, categorized as low (LPR), normal (NPR) or high (HPR) in the Western population of patients undergoing PCI during treatment with cilostogol or prasugrel.

Methods: Using standardized platelet reactivity cutoffs, we performed a collaborative post-hoc analysis from previously published studies reporting the association between major bleeding, ST and platelet reactivity after PCI. LPR-NPR-HPR categories were defined as ≤95, 95-208 and >208 PRU for VerifyNow, <19, 19-46, and >46 U for Multiplate and ≤16, 16-50 and >50 for VASP assays, respectively. Definite or probable ST, major bleeding (study defined) and all-cause mortality were evaluated at the longest follow-up available.

Results: A total of 17 studies including 18,772 patients qualified for the analysis. Patients with HPR had a 2.7-fold higher risk for ST (p<0.0001) but a 1.7 lower risk for major bleeding (p=0.03) compared to those with NPR. Patients with LPR had a 1.8-fold higher risk for major bleeding (p<0.0001) but similar risk for ST (p=0.96) as those with NPR. The risk of all-cause mortality was significantly higher in HPR patients compared to others (p<0.0003). There was no interaction effect among different platelet function assays in predicting the higher risk for ST or bleeding (p=0.15).

Conclusions: Patients on P2Y12-inhibitors undergoing PCI exhibiting HPR or LPR have an increased risk for ST and bleeding, respectively. The lowest rates of adverse events in NPR patients suggest the presence of a therapeutic window for platelet reactivity. Further randomized studies are warranted to test the safety and efficacy of reaching such therapeutic target following PCI.

P6484 | BEDSIDE
VERifinow in Diabetes high-on-treatment platelet reactivity: a pharmacodynamic study on switching from clopidogrel to prasugrel (VERDI study)
Purpose: Diabetic patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) frequently exhibit high platelet reactivity (HPR) while on clopidogrel. We aimed to test the hypothesis that in diabetic patients with ACS undergoing PCI exhibiting HPR after standard treatment with clopidogrel, a loading dose of 60 mg of prasugrel is enough (≤75 years) and more effective than 10 mg maintenance dose is superior to the standard treatment with clopidogrel for the achievement of optimal P2Y12 inhibition within the first 24-36 hours post-PCI.
Methods: The VERDI was a prospective, randomized, single-center, single-blind, parallel design study (NCT01684813). Consecutive diabetic patients with ACS undergoing PCI and loaded with clopidogrel were considered for platelet reactivity (PR) assessment immediately before PCI with the VerifyNow assay (Accumetrics Inc, San Diego, CA), measured in P2Y12 reaction units (PRU). Out of 63 screened patients 50 (79.3%) patients were found with HPR (PRU >208) and were randomized to receive a loading dose of 60 mg prasugrel vs the standard dose of clopidogrel. Platelet function was assessed again 24 h post-PCI.

Results: Greater platelet inhibition was achieved by prasugrel compared with clopidogrel at 24 h post-PCI (PRU 54±33.8 vs 284±68.3, respectively; p<0.001). The primary end point of non-HPR rate (PRU ≤208) was achieved by 92% of patients in the prasugrel group and only 61% of patients in the clopidogrel group (p<0.001; Hazard Ratio 3.66, 95% CI 2.84-4.73). No significant acute bleeding was documented in either group.

Conclusion: Patients with ACS undergoing PCI while on high-on-treatment platelet reactivity (PR) who switched from clopidogrel to prasugrel were superior to standard treatment with clopidogrel for the achievement of optimal antiaggregation within the first 24 h post-PCI.

P6485 | BEDSIDE
Clopidogrel tailored therapy in elderly patients undergoing percutaneous coronary intervention for acute coronary syndrome: the responsiveness to clopidogrel and stent thrombosis 2-ACS
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Purpose: Clopidogrel is still the most used P2Y12 inhibitor in acute coronary syndrome (ACS) patients ≥75 years, and prasugrel therapy is relatively contraindicated in these subjects. High residual platelet reactivity (HRRP) on clopidogrel has been associated with high risk of ischemic events after percutaneous coronary intervention (PCI). Old age is a strong predictor of both HRRP on clopidogrel and ischemic events. The aim of this study was to evaluate the clinical efficacy and safety of clopidogrel tailored antiplatelet therapy in ACS elderly (≥75 years) patients.

Methods: Residual platelet reactivity was assessed 12 to 24 h after clopidogrel 600 mg loading dose by light transmission aggregometry (LTA) in 1787 consecutive ACS patients undergoing PCI. Patients with HRRP (≥70%) received a tailored therapy, generally based on an increased clopidogrel maintenance dose (150-300 mg/d). The primary end point was the composite of cardiac death, myocardial infarction, any urgent coronary revascularization, and stroke at 2-year follow-up.

Results: Among enrolled patients, 665 (37%) ≥75 years. HRRP rate was 19% vs 11% in the elderly and non elderly group, respectively (p<0.001). After tailored antiplatelet therapy in patients with HRRP, LTA test result was not
different in the 2 study groups (62±15% and 65±14% in the elderly and non-elderly, p=0.219). At 2-year follow-up, primary end-point rate was 14% vs 11% (p<0.0001), cardiac death rate was 8% vs 3% (p<0.0001) and stent thrombosis rate 4.4% vs 2.7% (p=0.049) in elderly vs non elderly patients, respectively. In elderly patients, cardiac death rates was 13% vs 7% (p=0.017) in patients with and without HRPR.

Conclusions: Among ACS patients treated with clopidogrel after PCI, elderly patients were more likely to experience HRPR on clopidogrel than younger patients. Moreover, HRPR status in elderly patients is significantly associated with increased ischemic events, cardiac death and stent thrombosis even after increased clopidogrel dose according to the results of platelet function tests.

**P6486 | BEDSIDE**

Use of clopidogrel, aspirin and oral-coagulant therapy in patients undergoing percutaneous coronary intervention: a meta-analysis of randomized controlled trials and adjusted observational result

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Introduction: The optimal antiaggregant therapy after coronary stenting in patients under oral anticoagulation (OAC) is currently debated.

Methods: Medline and Cochrane Library were searched for studies reporting outcomes of patients undergoing PCI undergoing PT (TT) or double therapy (DT either aspirin and clopidogrel or OAC and clopidogrel). Major bleeding was the primary end point, while all-cause death, myocardial infarction (MI), stent thrombosis and stroke were secondary ones. Results were reported for both trials and separately for those deriving from randomized controlled trials or multivariate analysis.

Results: In eight studies 1354 patients treated with double therapy (DT) were on aspirin and clopidogrel: a significant reduction of major bleeding for DT patients was demonstrated for overall studies and for the subset of RCT and observational studies providing adjusted data (odds ratio OR 0.46 [95% confidence interval 0.36-0.65] and OR 0.36 [0.28-0.46]). No increase of risk of major adverse cardiac events (MACE: death, myocardial infarction, stroke and stent thrombosis) was reported (OR 0.95 [0.57-1.28]), although not deriving from randomized controlled trials or multivariate analysis.

Six studies with 5758 patients tested OAC and clopidogrel as DT with a significant reduction of bleeding (0.79 [0.63, 0.98]), without affecting rates of death, myocardial infarction, stroke and stent thrombosis (0.90 [0.69, 1.17]) also when associated according to the VerifyNow Assay and by multiple electrode aggregometry (MEA, Multiplate Analyzer) with arachidonic acid (AA) 1.0 mM and collagen 1.0 μg/mL used as agonists. TPO was assessed by ELISA. Platelet activation was evaluated by soluble P-selectin (sP-selectin), and cyclooxygenase-1 inhibition was assessed by measurement of serum thromboxane B2 using ELISA.

Results: TPO and platelet aggregation levels were significantly, though weakly, associated to the VerifyNow Assay (r=0.07, p=0.03) and AA-induced MEA platelet aggregation (r=0.05, p=0.01), whereas no association was found with collagen-induced MEA platelet aggregation (r=0.03, p=0.43). TPO and sP-selectin did not correlate (r=0.01, p=0.70). Smokers had significantly higher levels of TPO and sP-selectin than non-smokers (p-values <0.02), and patients aged >65 years had significantly higher TPO levels than patients ≤65 years (p=0.02). In a multivariate linear regression analysis, TPO (p=0.01) and sP-selectin (p=0.0001) were independent predictors of AA-induced MEA platelet aggregation after adjustment for age, gender, smoking, body mass index and diabetes. Compliance with aspirin was confirmed by low serum thromboxane B2 levels in all patients (median ng/mL [25%;75%]: 0.97 [0.52;1.97]).

Conclusion: In stable, high-risk CAD patients, platelet aggregation was weakly associated. However, when adjusting for clinical characteristics, TPO was an independent determinant of platelet aggregation. Our results suggest that the priming effect of TPO on platelets is influenced by several factors, and that the priming effect is only modest in stable CAD patients treated with aspirin.

**P6489 | BEDSIDE**

Thrombopoietin and platelet aggregation in patients with stable coronary artery disease

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Purpose: Thrombopoietin (TPO) has been suggested to possess a priming effect on platelets thereby potentiating platelet activation in response to different agonists. Furthermore, TPO has been shown to stimulate platelet-leukocyte interactions in whole blood through expression of P-selectin. The aim of the study was to investigate the association between platelet aggregation, TPO and platelet activation in stable coronary artery disease (CAD) patients treated with aspirin.

Furthermore, we aimed at exploring the distribution of TPO levels in CAD patients with different clinical characteristics.

Methods: We studied 900 consecutive CAD patients with a relatively high-risk profile since 79% (88%) had a history of prior myocardial infarction, 250 (28%) had type 2 diabetes and 170 (19%) had both. All patients received 75 mg aspirin daily as mono antiplatelet therapy. Platelet aggregation was assessed by the VerifyNow Aspirin Assay and by multiple electrode aggregometry (MEA, Multiplate Analyzer) without HRPR.
was loading dose or T90 maintenance dose) and DE110 was well tolerated in healthy
benefit-risk assessment is recommended. The combination of ticagrelor (T180
of action of these two drug classes needs to be considered, and an individual
coagulants combination, a pharmacodynamic enhancement based on the mode
with a staggered administration of ticagrelor. As with any antiplatelets plus anti-
under ticagrelor maintenance therapy and when ticagrelor therapy was initiated
was unaltered when administered with T180 (either coadministered or given 2 h
after) with maintenance dose of T90.
Conclusion: There was only a mild increase in dabigatran steady-state exposure
under ticagrelor maintenance therapy and when ticagrelor therapy was initiated with a
staggered administration of ticagrelor. As with any antiplatelets plus anti-
common step in many drug development programs this unforeseen effect should
be considered.
Our data demonstrate a novel, unexpected, PS backbone-
confirm the relevance of platelet-activating effects of PS ODN in vivo.
Methods: We consecutively enrolled 408 patients with stable coronary artery
disease one month after successful PCI. All subjects were receiving dual anti-
platelet therapy with aspirin (100mg/day) and clopidogrel (75mg/day) for at least
one month at the time we evaluated their platelet reactivity and arterial function.
Carotid-temoral pulse wave velocity (PWV) was measured as an index of aortic
stiffness and augmentation index (AIx) as an index of arterial wave reflections.
High on treatment platelet reactivity was evaluated using VerifyNow Assay. Veri-
fyNow Assay reports its results in P2Y12 reaction units (PRU) and the diagnostic cut-off
value is 230 PRU.
Results: Importantly, subjects with high on treatment platelet reactivity and
PRU-230 had significantly increased PWV (8.81±2.25 m/sec vs. 7.86±1.95 m/sec; p=0.001) and AIx (25.27±8.67% vs. 20.87±10.57%; p=0.04) compared to
subjects with PRU<230.
Conclusions: We documented an association between a direct measurement of
platelet activation and vascular function in patients after PCI treated with
dual antiplatelet therapy. As platelet reactivity is associated with long-term cardiovas-
cular events after PCI the introduction of another clinical factor implicated in
the variability of individual platelet response to antiplatelet therapy is of great
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High on treatment platelet reactivity was evaluated using VerifyNow Assay. Veri-
fyNow Assay reports its results in P2Y12 reaction units (PRU) and the diagnostic cut-off
value is 230 PRU.
P6495 | BEDSIDE
High and low platelet reactivity on clopidogrel, prasugrel and ticagrelor in acute coronary syndrome patients: insight from a large cohort
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Purpose: Dual antiplatelet therapy with a P2Y12 inhibitor is mandatory in acute coronary syndromes (ACS) undergoing angioplasty. New antiplatelet drugs prasugrel and ticagrelor offer more efficient inhibition compared to clopidogrel. Under P2Y12 inhibitor, platelet reactivity (PR) assessment can predict ischemic and bleeding events. The aim of our study was to compare PR of P2Y12 inhibitors in a real-world setting.
Methods: PR was prospectively assessed in consecutive patients with recent ACS or undergoing high risk angioplasty. PR was measured 24h after last intake of clopidogrel (C) and prasugrel (P) and 12h for ticagrelor (T) by flow cytometry measured vasodilator-stimulated phosphoryl platelet inhibition index (VASP-PRI) and light transmission aggregometry with ADP 20μM (LTA-ADP). High Platelet Reactivity (HPR) was defined as VASP-PRI > 25% or LTA-ADP > 65% (thresholds previously linked to clinical events). Low Platelet Reactivity (LPR) was defined as VASP-PRI < 16% or LTA-ADP < 40%.
Results: 619 patients treated with aspirin and C (n=269), P (n=241) or T (n=109) were included. We retrospectively recorded concomitant drugs. Low PR was significantly more frequent in patients treated with T compared to C and P, except in cases with hypertension, BMI and prior history of STEMI. HPR was more frequent with C compared to P and T and significantly more frequent with P compared to T (Table 1). At the opposite, LPR was significantly more frequent in patients treated with T. Clinical and biological characteristics were similar between patients on P and those on T, except for hypertension, BMI and prior history of STEMI. In multivariate analysis, the significant predictor of HPR with VASP was P (OR=0.13; CI [0.08–0.22]) or T (OR=0.01; CI [0.005–0.025]) vs C, respectively. At follow up, platelet-CD34+/KDR+ conjugates were lower at Baseline compared with controls either before (0.48±0.2% vs 1.75±0.25%, respectively, P < 0.01). At follow up, platelet-CD34+/KDR+ conjugates were increased compared with Baseline by 56.3% in the non-activated, and by 44.4% in the ADP-activated samples, P < 0.05 for both comparisons.
Conclusions: The lower levels of CD34+, CD34+/KDR+ cells and platelet-CD34+/KDR+ conjugates in peripheral blood of ACS patients may represent an important defect of these patients towards vascular regeneration which is significantly improved after DAPT.

Table 1. Platelet reactivity assessment.

<table>
<thead>
<tr>
<th>HPR</th>
<th>VASP-PRI</th>
<th>LTA-ADP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonpidogrel</td>
<td>48%</td>
<td>37%</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>12%</td>
<td>15%</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>P (PRU&lt;100)</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>T (PRU&gt;100)</td>
<td>7%</td>
<td>4%</td>
</tr>
</tbody>
</table>

P6497 | BEDSIDE
Effect of dyspnea under ticagrelor on discontinuation and compliance to therapy in acute coronary syndrome patients treated with percutaneous coronary intervention
M. Gaubert1, M. Laine1, J. Bessiere2, A. Champenoux2, R. Tesca2, F. Dignat-George2, F. Pagani1, L. Bonello1,1 Hospital Nord of Marseille, Cardiology, Marseille, 2Hospital La Timone of Marseille, Marseille, France
Purpose: Ticagrelor is a new P2Y12- ADP receptor antagonist which is superior to clopidogrel to prevent major adverse cardiac events (MACE) in acute coronary syndrome (ACS) patients. Dyspnea appears to be a common side effect of ticagrelor which could lead to drug non-compliance or discontinuation which are both associated with a poor outcome. We aimed to investigate the impact of ticagrelor-related dyspnea on both discontinuation and compliance to ticagrelor in ACS patients undergoing percutaneous coronary intervention (PCI).
Methods: We performed a multicenter prospective observational study enrolling ACS patients undergoing PCI and treated with ticagrelor. Clinical events including: MACE, bleeds and dyspnea were assessed at one month. Ticagrelor discontinuation and non-compliance and their causes were recorded.
Results: One hundred and sixty four patients were included among which a majority suffered from non ST-segment elevation myocardial infarction (NSTE-MI) (48.4%). Overall 37 patients (22.6%) experienced dyspnea during the first month following the ACS. During follow-up, 27 patients (16.7%) discontinued ticagrelor. The main reason for ticagrelor withdrawal was drug-related dyspnea (55.6%). Discontinuation was the result of physician’s decision in 26 patients (96.2%) and non-compliance was reported in only 1 patient. Ticagrelor was replaced by clopidogrel in 22 patients (81.6%).

Conclusion: In the present study we observed that in ACS patients undergoing PCI and treated with ticagrelor, drug-related dyspnea is a frequent side effect (16.7%) and is the leading reason for discontinuation (55.6%). However, in most cases (81.6%) ticagrelor discontinuation was decided by a physician and the drug was replaced by clopidogrel to dual antiplatelet therapy.

ANTIPATELET THHERAPY: TRANSLATIONAL SCIENCE

P6499 | BEDSIDE
Deterrents of cyclooxygenase-1-inhibition with aspirin in patients with stable coronary artery disease
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Purpose: Aspirin is widely used for secondary prophylaxis in patients with stable coronary artery disease (CAD), yet there is considerable variability in platelet inhibition. Low-dose aspirin inhibits the cyclooxygenase-1 (COX1) enzyme and measurement of serum thromboxane B2 (ST-XB2) is the most specific method for evaluating platelet inhibition with aspirin. We investigated independent determinants of COX1-inhibition with aspirin in a large cohort of stable CAD patients. Methods: A total of 900 high-risk, stable CAD patients were included: 795 (88%) had a history of myocardial infarction, 250 (28%) had type 2 diabetes, and 170 (19%) had both. All patients received aspirin 75 mg daily and no other antithrombotic drugs. Compliance was carefully optimized, and the last aspirin dose was ingested exactly one hour before blood sampling. Blood for ST-XB2 analyses was collected in non-anticoagulated glass tubes and allowed to clot at 37°C for one hour to induce maximal platelet activation and TXB2 production. Serum was stored at -80°C until analyzed in duplicate by ELISA. Determinants of aspirin-mediated COX1-inhibition were evaluated using multiple linear regression analyses.
Results: Optimal compliance was confirmed by very low ST-XB2 levels in all patients (median [25%;75%;] 0.97 [0.52;1.97] ng/mL). The results of regression
analyses were consistent, and the following six parameters were independent predictors of COX1-inhibition: Age, sex, body mass index, diabetes mellitus type 2, renal function (estimated glomerular filtration rate) and platelet count (all p-values <0.004). S-TXBB2 levels were increased by 58% in males (p=0.001) and by 45% in patients with diabetes mellitus type 2 (p=0.001).

Conclusion: Low-dose aspirin inhibits platelet COX1 in patients with CAD, however, we observed considerable inter-individual differences just one hour after ingestion of aspirin. Age, sex, body mass index, diabetes mellitus type 2, renal function and platelet count significantly affect aspirin-induced COX1-inhibition. Our findings may explain previous reports of reduced platelet inhibition with aspirin.

P6500 | BEDSIDE
Red blood cell and platelet microparticles in myocardial infarction patients
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Background: Red blood cell and platelet microparticles (RCBm and PLTm, respectively) have drawn research attention as to their potential prothrombotic and atherogenic effects in experimental settings. However, the relevance of circulating microparticles in clinical settings is largely undetermined.

Methods: Blood samples were drawn from consecutive STEMI patients after primary PCI and a matched cohort of healthy volunteers and circulating microparticles were quantified with a flow cytometric method. STEMI patients were followed for 6 months to a composite clinical endpoint. 51 STEMI patients (age 59.8 ± 8.8 years) and 50 matched controls (age 56.2 ± 9.2 years; p = 0.155) were enrolled.

Results: RCBm concentration was 18,198 ± 6,062 μl in controls versus 33,740 ± 21,169 μl in STEMI patients (p < 0.001). RCBm count was not correlated to total RBCs (standardized beta 0.10; p = 0.681). RCBm did not differ between cohorts (17,529 ± 16,292 μl in STEMI patients versus 14,372 ± 16,271 μl in controls; p = 0.203). RCBm c-statistic was 0.832 (95% confidence interval 0.720 to 0.944), while PLTm prognostic value was not statistically significant (c-statistic 0.614, 95% confidence interval 0.444 to 0.784). In the multivariate analysis, RCBm concentration was independently associated with the clinical endpoint, after adjustment for age, ejection fraction, serum creatinine and presence of diabetes (adjusted p = 0.034).

Conclusion: The present study demonstrates for the first time that erythrocyte microparticles are elevated in patients with STEMI treated with PCI compared to controls. Our findings could be of clinical relevance in the future.

P6502 | BEDSIDE
The effect of antplatelet therapy on extra-cellular vesicles in blood of patients with acute coronary syndromes
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Purpose: Extracellular vesicles (EVs) play an important role in various pathologies, particularly in vascular disease. The purpose of our study was to analyze the antigenic composition of individual EVs isolated from the blood of patients with acute coronary syndrome (ACS), to explore the role of EVs of different cellular origin in the pathogenesis of acute coronary syndromes.

Methods: We used monoclonal antibody-coupled, nanometer-sized magnetic particles to immune-captured CD31 and CD63-carrying EVs and analyze the expression of the exosomal marker CD63, the marker of different cellular origin CD31 and, the platelet marker CD41 on EVs isolated from the blood of 10 patients with ACS and 15 healthy volunteers. For individual antigen characterization of nano-sized blood EVs by means of flow cytometry we used an original method, described by us earlier (in press).

Results: In our pilot study we showed that there was significantly lower amount of captured by CD31 EVs co-expressing CD41 and CD63 in patients with ACS in comparison with healthy volunteers (Mean MFI 20.9 ± 10.01 vs. 31.35 ± 24.28 [29.852.1], p < 0.05). We assumed that the difference in the amount of EVs expressing platelet-derived marker CD41 might be related to the standard antplatelet therapy used in patients with ACS and confirmed the suppression of platelet activation upon the action of aspirin and clopidogrel.

Conclusions: We showed for the first time that patients with ACS had lower amount of EVs expressing CD31, CD41 and CD63 markers using a new method of individual assessment of extra-cellular vesicles in blood. The difference in the amount of EVs expressing platelet-derived marker CD41 confirmed platelet deactivation upon the standard antplatelet therapy in patients with ACS.

P6503 | BEDSIDE
Platelet expression of transforming growth factor beta 1 is enhanced and associated with cardiovascular prognostic in patients with acute coronary syndrome
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Background: Functional recovery and prognosis after acute coronary syndromes (ACS) are mainly driven by the extent of reperfusion injury and myocardial repair mechanisms. Transforming growth factor-beta (TGF-β) is critically involved in cardiac injury, repair and remodeling. In this study, we investigated the prognostic value of platelet TGF-β surface expression in patients with coronary artery disease (CAD).

Methods and results: Expression of TGF-β 1 in platelets was investigated by flow cytometry among patients with ACS and stable CAD undergoing percutaneous coronary intervention (PCI). In a cohort study, platelet surface expression of TGF-β 1 was measured in 299 patients with symptomatic CAD (stable CAD =145, ACS =154) at the time of PCI. The primary endpoint was defined as death and/or STEMI during 12-month follow-up. TGF-β 1 surface expression was expressed as the percent of EVs expressing TGF-β 1 in platelets. A composite of death or new ACS (median MFI 1.34 ± 0.94 vs. median MFI 1.75 ± 0.59) was defined as the primary endpoint. Lower expression of TGF-β 1 was associated with increased cardiovascular risk as assessed by the Framingham risk score (FHS). The median ratio of TGF-β 1 expression in platelets was significantly higher in the ACS compared to stable CAD patients (6.55 ± 1.25 vs 3.81 ± 1.14, p = 0.003). Multivariable analysis of the primary endpoint and cardiovascular events was consistent, and the following six parameters were independent predictors of the primary endpoint: age (β 1.41; 95% CI 1.07 to 1.85), body mass index (β 0.19; 95% CI 0.14 to 0.24), interleukin-6 (β 0.28; 95% CI 0.13 to 0.43), diabetes mellitus (β 0.43; 95% CI 0.25 to 0.61), smoking (β 0.27; 95% CI 0.18 to 0.36) and platelet TGF-β 1 expression (β 0.28; 95% CI 0.19 to 0.37).

Conclusions: Platelet TGF-β 1 expression is enhanced in ACS patients and associated with cardiovascular risk. Further studies are needed to delineate the mechanisms of these findings and their potential clinical relevance.
and/or STEMI, (median MFI 10.8 vs. median MFI 13.9, p=0.006). In multivariate analysis TGF-β1 expression was independently associated with the combined primary endpoint in the overall cohort (Hazard Ratio 0.31, 95% Confidence Interval 0.11-0.89, p=0.029) and was strongly associated with prognosis in ACS patients. **Conclusion:** These findings highlight a potential role of TGF-β1 in ACS and indicate a prognostic value of TGF-β1 on clinical outcomes in patients with acute coronary syndromes. Large scale studies are warranted to further evaluate the regulatory mechanisms of platelet TGF-β1 expression and its prognostic impact in CAD.

### P6504 | BEDSIDE

**Ticagrelor inhibits release of pro-inflammatory cytokines TNF and IL-6 during human endotoxemia**

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**Purpose:** In the PLATElet inhibition and patient Outcomes (PLATO) study, ticagrelor was associated with fewer pulmonary infection events and subsequent deaths but slightly higher inflammatory markers compared to clopidogrel. Ticagrelor and clopidogrel inhibited platelet P2Y12 receptors via different mechanisms and ticagrelor additionally is a weak inhibitor of reuptake of adenosine, which has numerous effects on innate immunity. We studied the effects of ticagrelor and clopidogrel on the innate immune responses of healthy volunteers.

**Methods:** 30 healthy volunteers were randomized to receive ticagrelor 90 mg bd (n=10), clopidogrel 75 mg od (n=10) or an antiplatelet medication (controls; n=10) for one week. E. coli endotoxin (LPS, 2 ng/kg) was then administered intravenously. Blood was sampled pre-treatment and over 24 hours post LPS. Platelet aggregation induced by ADP 30 μM was assessed by optical aggregometry. Platelet P-selectin expression and platelet-leukocyte aggregate formation were determined by flow cytometry. Plasma levels of cytokines were determined using cytometric bead array.

**Results:** After treatment, maximal platelet aggregation responses to ADP in the ticagrelor, clopidogrel and control groups were 12±3%, 31±26% and 81±24% respectively. After LPS exposure, ticagrelor and clopidogrel significantly reduced ADP-induced platelet P-selectin expression and platelet-monocyte conjugate formation compared to controls. LPS-induced increases in TNF were significantly attenuated by both ticagrelor (p=0.025) and clopidogrel (p=0.017), which reduced peak levels by 61% and 60% respectively compared to controls. Peak TNF levels correlated with indices of platelet reactivity (ADP-induced platelet aggregation [p=0.0096]; P-selectin expression [p=0.026] and platelet-monocyte conjugate formation [p=0.024]). Ticagrelor also significantly attenuated IL-6 release (p=0.015), reducing peak levels by 43% compared to controls, whereas clopidogrel had a non-significant effect (p=0.15), with peak levels 28% lower than controls.

**Conclusion:** Ticagrelor inhibited release of pro-inflammatory cytokines TNF and IL-6 in a model of human sepsis. The similar effect of ticagrelor and clopidogrel, as well as the correlation between levels of platelet reactivity and TNF release, suggest that P2Y12 contributes to innate immune response and demonstrates anti-inflammatory effects of P2Y12 inhibitors.

### P6506 | BENCH

**No effect of platelet supplementation to reverse the P2Y12 inhibitor ticagrelor: an in vitro study**

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**Purpose:** Ticagrelor, a reversible P2Y12 inhibitor, is recommended for the treatment of acute coronary syndrome. Ticagrelor, as any antithrombotic therapy, exposes to bleeding complications. Currently, no antidote is available. Platelet transfusion, usually proposed as a reversal strategy for antiplatelet drugs, has been suggested to be inefficient since circulating ticagrelor as well as its active metabolite are likely to inhibit transfused platelets. However no data have been published yet.

We assess, in vitro, the efficacy of platelet supplementation to restore platelet aggregation inhibited by ticagrelor. Aspirin was used as a positive control.

**Methods:** Whole blood from eighteen healthy volunteers was spiked with ticagrelor (3.25μM, equivalent to the peak concentration after a 180 mg loading dose) or aspirin (25μM). Platelet aggregation was investigated with impedance aggregometry on whole blood and optical transmission (LTA) on platelet rich plasma (PRP) using adenosine diphosphate (ADP 20μM) or arachidonic acid (AA 1μM) as specific agonists for ticagrelor and aspirin respectively. Platelet supplementation was defined as the addition of washed platelet suspension, corresponding to at least 60% of whole blood platelet count. Results are expressed in ohms or maximal percentage of aggregation for impedance and LTA, respectively.

**Results:** Ticagrelor strongly inhibited ADP-induced platelet aggregation compared to control either in whole blood (1.8 ± 0.2 vs. 8.8 ± 0.05, n=6) or in PRP (14% ± 7% vs. 77% ± 0.05, n=6). Aspirin also inhibited AA-induced whole blood aggregation (1.3 ± 0.2 vs. 14% ± 4%, n=6). In aspirin-treated samples, platelet supplementation completely restored AA-induced platelet aggregation (9.8 ± 1.3 vs. 1.3 ± 0.008). In contrast, in ticagrelor-treated samples, platelet supplementation failed to correct the platelet effects of ticagrelor on ADP-induced aggregation both in whole blood (1.5 ± 0.2 vs. 1.3 ± 0.05) and PRP (13% ± 14%, ± 0.05).

**Conclusions:** In this in vitro study, platelet supplementation failed to restore platelet aggregation following ticagrelor treatment whereas a complete correction was observed in aspirin-spiked samples. Our results support the hypothesis for an ineffectiveness of platelet transfusion to control bleeding in patients receiving ticagrelor.

### P6507 | BENCH

**Revacept (GPVI-Fc) alone or combined with rtPA improves outcome after stroke**

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**Background:** Several antiplatelet drugs for the treatment of myocardial infarction or other ischemic stroke with potent anti-platelet effects have been developed, but all incur a significant risk of bleeding. In contrast, soluble glycoprotein IIb/IIIa (GPIIb/IIIa) antagonist (rFVIIa) promises efficacy without increasing bleeding risk. In this study, we examined the effect of Revacept on thrombus formation after endothelial vessel wall injury and on experimental stroke in mice, and the combination with varying doses of recombinant tissue plasminogen activator (rtPA) with or without Warfarin (rFVIIa-Fc/Revacept) promises efficacy without increasing bleeding risk. In this study, we examined the effect of Revacept on thrombus formation after endothelial vessel wall injury and on experimental stroke in mice, and the combination with varying doses of recombinant tissue plasminogen activator (rtPA).

**Methods and results:** Platelet adhesion and thrombus formation after endothelial wall injury was monitored in the common carotid artery by intra-vital fluorescence microscopy, and was significantly decreased by 1 mg/kg Revacept IV, compared to Fc only. Stroke was induced in mice by a one hour-occlusion of the middle cerebral artery and consecutive reperfusion. 1 mg/kg Revacept IV immediately before reperfusion significantly improved functional outcome, cerebral infarction and edema compared to Fc only. There were no signs of increased intracranial bleeding. Revacept improved survival after stroke compared to placebo treatment. Binding of Revacept and von Willebrand factor (vWF) to bovine collagen I was determined by ELISA. Both Revacept and vWF bind to collagen, and Revacept competitively prevented the binding of vWF to collagen.
In contrast, treatment with standard doses of rPA led to markedly increased risk of bleeding. Combinations of Revacet with decreasing doses of rPA led to maintained efficacy, but decreased bleeding risk.

Conclusions: Revacet reduces arterial thrombus formation, improves functional outcome and reduces infarct volume and edema after ischemic stroke. Revacet not only prevents GPVI-mediated platelet adhesion and aggregate formation. Therefore Revacet might be a potent and safe tool to treat ischemic complications of stroke without increasing the risk of bleeding. The combination with markedly reduced doses of rPA may be attractive for effective therapy with reduced risk.

P6508 | BENCH Ticagrelor potentiates the anti-aggregatory effects of adenosine via A2 receptor stimulation V.B. Nooney1, Y.Y. Chirkov2, R. De Caterina3, J.D. Horowitz4. 1 University of South Australia, Adelaide, Australia; 2 University of Adelaide, Adelaide, Australia; 3 University Cheiti, Cardiology, Cheiti, Italy; 4 The Queen Elizabeth Hospital, Cardiology, Adelaide, Australia

Purpose: Ticagrelor is a P2Y12 receptor antagonist which has been shown to inhibit adenosine uptake into erythrocytes. However the contribution of resultant potentiation of adenosine effect to the overall anti-aggregatory profile Ticagrelor remains uncertain. We sought to evaluate ticagrelor-adenosine interactions in normal subjects and patients with ischemic heart disease.

Methods: Studies were performed both utilizing inhibition of ADP - induced aggregation in whole blood (2.5μM) and in platelet rich plasma (5μM ADP). Concentration response curves were constructed for ticagrelor in order to determine peri-threshold concentration for inhibition of platelet aggregation for ticagrelor alone. Interactions with adenosine were evaluated by 1. Inhibition of ticagrelor effects with A2 receptor blocker ZM241385 (100μM), while the effect of peri-threshold concentrations of ticagrelor on anti-aggregatory responses to adenosine was also determined.

Results: In whole blood, threshold concentration for ticagrelor anti-aggregatory effect was approximately 0.3μM, while the anti-aggregatory effects of higher concentrations of ticagrelor were partially inhibited by ZM241385 (Fig. 1). In platelet-rich plasma, ticagrelor (mean 0.25μM) induced only 14±4% inhibition of aggregation. However, this peri-threshold concentration of ticagrelor markedly potentiated the anti-aggregatory effect of adenosine (Fig. 2).

Conclusions: 1. Adenosine contributes to the antiaggregatory effects of ticagrelor primarily via A2 receptor stimulation 2. There is a synergistic relationship between ticagrelor and adenosine with regards to the inhibition of ADP induced platelet aggregation.

P6511 | BEDSIDE The role of general practitioners in treating patients with ST-segment elevation myocardial infarction in isolated areas K. Yaehe, C. Ricard, D. Savary, F.X. Ageron, B. Audema, D. Lacroix, G. Gheno, M. Barthes, P. Joubert, L. Belle on behalf of RESURCOR. Hospital of Annecy, Annecy, France

Purpose: European guidelines for ST-segment elevation myocardial infarction (STEMI) encourage healthcare networks to increase rates of, and decrease delays to reperfusion. We examined the effects of training general practitioners (primary care physicians [PCPs]) with equipment for prehospital management of STEMI patients in remote areas.

Methods: A network for cardiac emergencies was set up in the French North Alps in 2002 and a permanent registry of STEMI patients has been kept since. In remote areas (>30 min access for ambulances), 24 local volunteer PCPs were trained and equipped (electrocardiogram [ECG] machine, fibrinolytic kit and autonomous external defibrillators [AEDs]) to deal with cardiac emergencies. In this study, when the central call dispatcher receives a telephone call from a patient reporting chest pain with a high probability of STEMI in such an area, he sends a mobile intensive care unit (MICU) with a emergent physician on board and asks the local PCP if one is available, to manage the patient while awaiting arrival of the MICU. Patients were taken by MICU to the interventional cardiology hospital if the diagnosis of STEMI was confirmed. We report on patients who received care from a PCP before arrival of the MICU.

Results: Between 2005 and 2010, 4015 patients were included in the STEMI registry; 180 were in an isolated area in Haute-Savoie, of whom 140 were in an area with a participating PCP; 62 patients were treated by a PCP before MICU arrival. Twenty-seven of the PCP-treated patients underwent thrombolyis by PCP and 8 patients with ventricular tachycardia/fibrillation were shocked by PCP with an AED before MICU arrival. Mean times from call to thrombolysis were shorter when the patient was managed by the PCP versus MICU alone in a remote area: 45.0±25.5 min vs 62.4±23.4 min, respectively (p<0.003). A diagnosis of STEMI without contraindication to thrombolysis was confirmed in the hospital in 26/27 patients treated as such by the PCP (one patient was diagnosed with a Tako-Tsubo syndrome).

Conclusions: Our data suggest that PCP care of STEMI patients located in isolated areas is safe and efficient, with high rates of resuscitation and thrombolysis and a shorter time to perform thrombolysis. The rate of PCP intervention in our network needs to be increased in order to optimize management of such patients.

P6512 | BEDSIDE Distance-related differences in critical times, protocol activation and mortality in a regional STEMI network T. Benedek, B. Balazs, B. Jako, N. Rat, I. Benedek. University Emergency Hospital, Targu Mures, Romania

Introduction: We aimed to study the differences in critical network times and mortality in STEMI patients presenting to hospitals belonging to the same STEMI network but located at different distances to PCPI center.
Material and methods: We studied 416 patients with STEMI who presented to a pPCI center (n=141) or to a hospital located in: zone 1 - 70 km from the pPCI center (101), zone 2 - 70-150 km from the pPCI center (n=81), or zone 3 - 150-250 km to the pPCI center (n=93), and we compared the following time intervals: (1) presentation time (PT), from onset of symptoms to presentation, (2) protocol initiation time (PIT), from presentation to STEMI protocol initiation, (3) Ischemic time (IT) - from onset of symptoms to repermeabilisation, and (4) door to balloon (DTB), from arrival in the pPCI center to balloon.

Results: PT showed no significant difference between the groups (183.08 min vs 199.1 min vs 166.7 min vs 161.95, p=0.4). PIT was significantly lower in zone 3 (61.66 min in zone 3 vs 92 min in zone 2 vs 107 min in zone 1, p<0.002). DTB time (from the door of the pPCI center to balloon) was significantly longer for patients presenting directly to pPCI center compared to those arriving from zone 1, 2 or 3 hospitals (86.96 vs 52.27 vs 43.9 min, p<0.001), who found the cath lab already prepared when they arrived, as a result of phone activation. As a result, despite of the differences in distance to pPCI center, total IT was not significantly different between the groups (344 min in zone 1, 369 min in zone 2, 366 min in zone 3, 340.26 min in pPCI center, p=0.2), and this was reflected in similar rates of mortality (3.5% in pPCI center, 3.9% in zone 1, 3.7% in zone 2 and 3.2% in zone 3).

Conclusions: A well organized STEMI network, as the one existing in zone 3 in our study, could shorten protocol initiation and DTB times, thus reaching similar...

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P6513 | BEDSIDE
Impact of health care system delay on one-year mortality in early versus late presenting STEMI patients undergoing primary PCI


Purpose: Health care system delay, defined as time from first medical contact (FMC) to reperfusion, is predictor of adverse events in STEMI. Our aim was to assess the effect of system delay on one-year mortality in early (<2h after symptom onset) versus late (>2h after symptom onset) presenters. 

Methods: The study included 2205 STEMI patients who underwent primary PCI within 12 hours of symptom onset, of which 1573 were identified as early presenters, in a high-volume catheterization laboratory during the years 2010-2012. Between-groups comparison of Kaplan-Meier cumulative mortality curves for different time intervals of system delay was performed with log-rank test. 

Results: One-year mortality was 8% in early presenters and 10.8% in late presenters (p=0.19). Median system delay was longer in early presenters (147 minutes, IQR 107-213 vs 132 minutes, IQR 99-182, p<0.001), while the total time to reperfusion was shorter (200 minutes, IQR 152-266 vs 382 minutes, IQR 300-500, p<0.001). A symptom delay of 0-60 minutes was associated with 3.8% one-year mortality in early presenters and 9.8% in late presenters, a delay of 61-120 minutes with 5.7% vs 9.2%, a delay of 121-180 minutes with 9.7% vs 9.5%, and if system delay was >180 minutes mortality rates reached 11.9% in early and 15% in late presenters. Log-rank test showed significant difference in Kaplan-Meier cumulative mortality curves for different time intervals of system delay in early, but not in late presenters (p=0.003 and p=0.261) (Figure).

Conclusion: Unlike in late presenters, the association between system delay and one-year mortality is significant in patients presenting early after symptom onset. The most pronounced increase in mortality appears to occur in early presenters with system delay beyond 120 minutes.

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P6514 | BEDSIDE
Short-term cost-effectiveness of a regional STEMI network

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Purpose: Current economical restraints might have a detrimental effect on the implementation of STEMI networks. The aim of our study was to evaluate the short-term cost-effectiveness of a STEMI network in Catalonia. 

Methods: Catalonia STEMI network was established in June 2009. It serves a population of approximately 7.500.000 inhabitants. Cost evaluation included hospitalization, procedure, and additional on-call personnel. Mean cost per patient was obtained according to treatment (primary PCI (pPCI), rescue PCI, fibrinolysis and no reperfusion). In order to avoid price changes between years, the same cost was used for both periods. Effectiveness was evaluated with the combined end-point of death, myocardial infarction, and stroke at 30-days. Data from the IAMC-III registry was used to evaluate the clinical effectiveness before the network.

Results: Single-center prospective registry was used to evaluate the clinical effectiveness after the establishment of the network.

Results: Mean cost per patient according to reperfusion strategy was pPCI: 7.010€; fibrinolysis: 6.686€; Rescue PCI: 11.094€; No reperfusion: 7.200€. Implementation of the network modified the reperfusion strategies (pPCI 31% vs. 89%; Fibrinolysis 37% vs. 3%; Rescue PCI 11% vs. 4%; No reperfusion 21% vs. 4%). The composite end-point in the pPCI group decreased from 9.7% vs. 6.8%. Due to a small sample size in the rescue PCI, fibrinolysis, and no reperfusion groups after the establishment of the network; the combined endpoint in the phase before it was used for both periods (fibrinolysis 15.5%, rescue PCI 10.7%; no reperfusion 19.1%). The strategy was cost-effective with a negative ratio for the combine endpoint (-4.336€), and 30-days mortality (-3.905€).

Conclusion: The Catalonian STEMI network is a cost-effective strategy in the short term. Further studies are needed to compare these results in different scenarios.

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P6515 | BEDSIDE
Building population-based AMI management systems using telemedicine as a foundation pillar

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Purpose: To report the commencement of a population-based AMI program that employs telemedicine innovations and protocols.

Methods: The study has begun a pilot program in up to 100 centers in South America. Goals of the study include: 1) Increase access to AMI care; 2) Improve accuracy of diagnosis; 3) Provide comprehensive AMI management; 4) Deliver cost-effective management. A hub and spoke, comprehensive AMI network has been designed that uses telemedicine as a founding platform for providing AMI care to vast populations. The strategy uses Primary PCI with door to balloon (D2B) time <90 min at hub sites and thrombolytic therapy with door to needle (D2N) times <30 min at spoke sites. Spokes are located between 5-250 miles from the hubs and often include small, rural clinics and facilities that have limited physician and hospital resources. A sophisticated, telemedicine platform enables immediate diagnosis, secure network, user interface and compatibility, quality assurance and database management. A dedicated network of expert cardiologists provides immediate EKG diagnosis and teleconsultation using the telemedicine platform and employing a combination of internet, fax modem and telephone networks.

Results: A comprehensive pilot program has been initiated at multiple sites using telemedicine protocols. Compositive quality, cost-effectiveness and mortality data will be collected. Early data will be available for ESC 2014.

Conclusions: The study represents an innovative population-based initiative that employs telemedicine to improve AMI care in developing countries.
Purpose: Primary PCI is the preferred strategy of reperfusion in STEMI. But in real life many STEMI patients present to non–PCI capable hospital and often cannot undergo timely primary PCI due to expected logistic delays and therefore receive fibrinolysis. Current guidelines recommend transfer of all STEMI patients to PCI-capable center for coronary angiography with a view to revascularization within 24 hours after lysis. But the place of such pharmaco-invasive strategy of reperfusion in STEMI management system is not well defined. We evaluated the effectiveness of treatment of STEMI patients, using these two strategies of reperfusion in real world settings.

Methods: A retrospective analysis of treatment of 427 STEMI patients that underwent PCI in a single center from January 1, 2011 to December 31, 2011 was performed. All patients were divided into 2 groups depending on strategy of reperfusion: the first one – primary PCI (294 patients), the second one included 133 patients who underwent PCI after fibrinolysis (rescue and routine early coronary intervention) at non–PCI capable referral hospital. All patients received heparin, loading dose of aspirin and clopidogrel. In the primary PCI group the median time from symptoms onset to balloon was 160 minutes with an interquartile range of 110 to 230 minutes, 77.9% of patients were delivered directly to our center, the rest were transferred from the nearest hospitals. In the pharmaco-invasive group the median time from symptoms onset to needle was 95 minutes (the interquartile range of 70 to 140 min), the median time from lysis to PCI – 11.5 hours (the interquartile range of 8.5 to17.0 hours). The study endpoints included in-hospital mortality and the rate of major adverse cardiac and cerebrovascular events (MACCE), defined as composite of death, myocardial infarction, stroke and repeat revascularization at a mean 27.2±5.4 months of follow-up.

Results: The in-hospital mortality was 4.4% in the primary PCI group and 5.2% in pharmaco-invasive group, p=0.805. There was no significant difference between the groups in the incidence of major bleeding. At 27.2±5.4 months of follow up the difference between the groups in the incidence of MACCE was also insignificant (12.6% in the first group and 18.0% in the second group had at least one MACCE, p=0.178).

Conclusions: The study demonstrates that in real world settings when timely primary PCI is not possible due to long transfer times to PCI-capable hospital a pharmaco-invasive strategy combining fibrinolysis with an obligatory use of PCI has short-term and long-term results that are comparable to those of primary PCI.
uated, no transfer was refused and no case was excluded of intention to treat analysis. The STEMI protocol was modified only for utilizing half dosage of TNK in older than 75 years in 2013.

**Results:** All 921 consecutive patients were analyzed, ages from 25 to 93 years old, median age 57.9±1.14, 69.8% males overall. We treated 145 cases in 2010, 130 in 2011, 334 in 2012 and 312 cases in 2013. PIT was the mode of reperfusion in 81.0%, 84.4%, 86.0% and 89.0% of yearly cases respectively and no significant differences in age, gender, hypertension, diabetes (32.9, 29.2, 30.8 and 30.0% respectively) from 2010-2013. Transfer to PPC1 time overall was 95%, rescue cath median 8.4 hours and elective cath median 17.7 hours. Hospital mortality was 6.9, 8.4, 6.6 and 3.5% respectively.

**Conclusions:** The utilization of a STEMI protocol that emphasizes early reperfusion, either by lytics (with PIT strategy thereafter) or by PCI, associated with contemporary adjutants, in a large city of an emerging country, was associated with hospital mortality close to developed countries since its inception. The yearly results have been maintained and in 2013 attained its best result. STEMI network adequately designed to meet its location needs, even in a public system of a non-developed country, maintain consistently good results.

HEART FAILURE ISSUES

P6521 | BEDSIDE

Development of a new biomarker-assisted score for reverse remodelling prediction in heart failure: the ST2-R2 Score

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**Background:** Biomarkers have been used in heart failure (HF) mainly for diagnostic purposes, for prognostic prediction of outcomes (death and/or heart failure hospitalisation), and more recently to guide therapy. Limited data exists regarding biomarker use to predict left ventricular (LV) function recovery or reverse remodelling.

**Aims:** a) To examine the value of ST2, NT-proBNP, high-sensitivity troponin T (hs-cTnT) and Galectin-3 relative to LV systolic function recovery and reverse remodelling in systolic HF; and b) To develop a clinical score for reverse remodelling prediction.

**Patients and methods:** 304 patients (79.6% men, mean age 66.1±12.3 years) with baseline echo (all baseline LV ejection fraction-LVEF <40%) and biomarker measurement (ST2, NT-proBNP, hs-cTnT and Galectin-3) were included in the study. Ischemic aetiology accounted for 56.2% of patients. Mean baseline LVEF was 28±7%. Most patients were in NYHA class II (73%) or III (21.4%). Reverse remodelling was defined as: 1) LVEF increase ≥15 percentage points or; 2) LVEF increase >10 percentage points + reduction of LV end-systolic diameter (LVEDSI) ≥20%, at 12 months.

**Results:** Reverse remodelling was observed in 104 patients (34.2%) during 1 year follow-up. Mean LVEF increase in patients with reverse remodelling was 21.9±7.9% and mean LVEDSI reduction was 21.1±13%. In univariable logistic regression analysis factors associated with reverse remodelling were age (p=0.018), non-ischemic aetiology of HF (p<0.001), NYHA functional class (p<0.001), known arterial hypertension (p<0.001), ischemic heart disease (p<0.001), and preserved LVEF (p=0.004). After adjustment for LVEF, age, gender and LVH, reverse remodelling was associated with elevated baseline ST2 levels (p=0.004). Right atrial pressure (mmHg) 7±5 0.44 <0.001 23.4 0.02 Mean pulmonary artery pressure (mmHg) 15±10 0.33 0.01 <0.92 0.36 Pulmonary capillary wedge pressure (mmHg) 15±9 0.36 <0.001 0.32 0.75 Cardiac output (lm/min) 4.9±1.5 <0.35 <0.001 –1.10 0.27 Left ventricular ejection fraction (%) 26±10 <0.43 <0.001 –0.37 0.71

**Conclusions:** Soluble ST2 was measured by a highly sensitive immunoassay. Determinants of sST2 were assessed by linear regression analyses.

**Results:** Population characteristics and their association with sST2 in univariable and multivariable analyses are presented in the Table. Levels of sST2 were higher in patients with severe symptoms (NYHA III-IV) even after adjustment for LVEF (p<0.02). In multiple regression, only gender, heart rate and right atrial pressure remained independent predictors of sST2. After a median of 3.6 years, 12 patients were dead or heart transplanted. Baseline sST2 was higher in these patients than in survivors (p<0.05).

**Predictors of sST2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline value</th>
<th>Univariate r</th>
<th>p-value</th>
<th>Multivariate β</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51±14</td>
<td>−0.19</td>
<td>0.05</td>
<td>−0.44</td>
<td>0.66</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>73</td>
<td>0.003</td>
<td>0.003</td>
<td>2.39</td>
<td>0.02</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>116±20</td>
<td>−0.28</td>
<td>0.04</td>
<td>−0.24</td>
<td>0.69</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>75±16</td>
<td>0.65</td>
<td>&lt;0.001</td>
<td>3.61</td>
<td>0.001</td>
</tr>
<tr>
<td>Right atrial pressure (mmHg)</td>
<td>7±5</td>
<td>0.44 &lt;0.001 23.4 0.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mmHg)</td>
<td>24±10</td>
<td>0.33 0.01 &lt;0.92 0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In DCM, sST2 is independently associated with an elevated heart rate and venous congestion. Our results imply that sST2 reflects haemodynamic decompensation in DCM.

P6523 | BEDSIDE

Risk assessment in elderly patients with septic shock: the role of biomarkers and hemodynamic parameters

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**Purpose:** Current guidelines suggest the assessment of hemodynamic parameters at admission for the risk stratification of patients with septic shock. Evidence so far is based on studies with middle aged patients. Therefore little is known about the management of elderly (>65 years) individuals.

**Methods:** Consecutive elderly patients (>65y) treated for septic shock in the intensive care unit of one center (Marienhospital Herne, Ruhr University Bochum, Germany) were prospectively analyzed in this study. Hemodynamic parameters (mean arterial blood pressure (MAP), central venous pressure, central venous oxygen saturation, left ventricular ejection fraction) and cardiac biomarkers (hematocrit, troponin I, NT-proBNP) at admission were evaluated in regard to their prognostic ability. Primary Endpoint was all-cause mortality within 28 days after admission.

**Results:** A total of 42 patients (23 male, 19 female) with a mean age of 74.6±6.0 years and a mean APACHE II score of 37.9±7.6 were enrolled in the study. 24 patients reached the primary endpoint. Non-survivors had significantly lower MAP (61.9±13.5 vs. 72.2±13.4, p=0.002) significantly higher NT-pro-BNP (8460±9186 vs. 1688±2062, p=0.004) and lactate (3.5±3.7 vs. 1.6±1.3, p=0.029). There were no significant differences regarding the left ventricular ejection fraction and troponin I between survivors and non-survivors.

**Conclusion:** MAP was the only hemodynamic parameter significantly predicting the primary endpoint (OR: 6.31; CI: 1.83–24.5; p=0.008).
P6524 | BEDSIDE
Preventing and managing cardiac disease in maternity – a model in care in a low resource set up
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Background: The spectrum of cardiovascular disease in pregnancy or in the postpartum period is changing and this provides challenges for the treating physicians, due to the lack of evidenced-based data.

Methods: We report on an appropriate referral algorithm, disease presentation (n=225) and outcome of patients (n=152), with significant disease, warranting follow-up at a tertiary care facility, in a single centre, prospective, ongoing study of African women presenting with cardiovascular disease in pregnancy or within 6 months postpartum. Clinical assessment, ECG, echocardiography and laboratory studies were performed at first assessment and follow-up at a dedicated Cardiovascular Disease and Maternity Clinic (CDMC).

Results: Of 225 consecutive women (mean age 28.8±6.4 years) presenting for the first time at CDMC 196 (86.7%) presented prepartum, with 73 women in modified WHO class I and 152 in modified WHO class II-IV, with an ethnic background of 45% Black African, 32% Cape Colored, 15% White and 8% Indian/others. 12% were HIV positive. Diagnoses of the 152 patient cohort neeiding close follow up were congenital heart disease (32%, 15 operated previously), valvular heart disease (26%, 15 operated previously), cardiomyopathy (27%) and 15% had other diagnoses. Women presenting in the postpartum period (n=30) presented in a higher New York Heart Association and modified WHO Class (p<0.001), had higher heart rates (p<0.001) and NTProBNP levels (p<0.0005). Of the 152 patients, 9 died within the 6-month follow-up period, with 8 dying ≥ 42 days postpartum. Perinatal death occurred in 1/152 (0.66%), translating to a perinatal mortality rate of 7/1000 live births.

Conclusion: The disease pattern was markedly different to that seen in the developed world. Rheumatic heart disease, cardiomyopathy and hypertension were the major disease problems, often complicated by HIV/AIDS and co-morbidity. Joint obstetric-cardiac care not only improved the survival rate of mothers presenting while pregnant, even those with complex diseases similar to that seen in the western world, but also that of their offspring. However, due to a lack of joint postpartum care, high mortality occurred in the postpartum period.

P6525 | BEDSIDE
The association of pulse transit time and left ventricular ejection fraction in patients with chronic heart failure
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Purpose: The aim of this study was to determine the association of pulse transit time (PTT) and left ventricular systolic function in patients with chronic heart failure (CHF).

Methods: 131 patients with CHF (51 females and 80 males, mean age was 59.2±8.6 years) were studied. 10 patients had functional class I of CHF, 50 – Class II, 67 – Class III, 4 – Class IV according to NYHA classification. Causes of CHF were: arterial hypertension (AH) in 13 patients, coronary artery disease (CAD) – 7, CAD and AH – 111 patients. 35 patients had diabetes mellitus. Patients were treated according to ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure, 2012. Left ventricular ejection fraction (LVEF) was 58.5±12.1% (32% (24.4%) patients had LVEF <50%). Pulse transit time and the circadian rhythm of PTT were determined during 24-hour ABPM using MmSDP-2 and MmSDP-3 BPLab devices.

Results: Mean values of PTT were 107.4±25.4 milliseconds (ms) in 24-hours, 106.5±27.3 ms – in daytime, 110.3±30.5 ms – in nighttime. Mean 24-hours and mean daily values of PTT correlated with LVEF (R=0.3, p<0.001 and R=0.35, p<0.001, respectively). Mean values of PTT in 24-hours and in daytime were higher in patients with CHF with preserved LVEF (119.1±30.5 ms vs. 103.7±22.9 ms and 121.7±33.3 ms vs. 100.9±22.3 ms, respectively, p<0.005 and p<0.001). The degree of nocturnal PTT reduction was <0% in 62 (47.3%) patients. Moreover, the degree of nocturnal PTT reduction -0% was detected more frequently in patients with CHF with reduced left ventricular ejection fraction (75.0% patients vs. 43.4%, respectively, p=0.04).

Conclusions: Left ventricular ejection fraction is inversely proportional to the degree of nocturnal pulse transit time reduction. Further studies are required in order to assess the clinical significance of circadian changes in arterial stiffness indicators.

P6526 | BEDSIDE
The association of pulse transit time and left ventricular ejection fraction in patients with chronic heart failure
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Purpose: The aim of this study was to determine the association of pulse transit time (PTT) and left ventricular systolic function in patients with chronic heart failure (CHF).

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Conclusions: Left ventricular ejection fraction is inversely proportional to the degree of nocturnal pulse transit time reduction. Further studies are required in order to assess the clinical significance of circadian changes in arterial stiffness indicators.

P6527 | BEDSIDE
GSTO1*Asp/GSTO2*Asp haplotype confers increased risk of chronic heart failure
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Background: Glutathione S-transferase omega-1 and 2 have a unique range of enzymatic activities, including the regeneration of ascorbate by their dehydroascorbate reductase activity and act as a glutathione-dependent S-transferase. Since these enzymes could have a protective role from oxidative damage, the question of whether two glutathione S-transferase omega polymorphisms confer the risk of chronic heart failure (CHF) was addressed.

Methods: rs4925 (Ala140Asp) of glutathione S-transferase omega-1 and rs156697 (Asn142Asp) of glutathione S-transferase omega-2 polymorphisms in 119 patients with chronic heart failure and 156 controls were assessed.

Results: Presence of one mutant GSTO1*Asp or GSTO2*Asp did not contribute independently towards the risk of CHF. However, homozygous carriers of mutant GSTO2*Asp genotype demonstrated 3.35-fold enhanced risk of CHF development in comparison to persons with wildtype GSTO2 Asn/Asn genotype (95% CI:1.19-9.39; P=0.021). Haplotype analysis revealed that homozygous carriers of both mutant GSTO1*Asp/GSTO2*Asp haplotype exhibited 11.4-fold enhanced risk of CHF (95% confidence interval: 1.38-90.23; P=0.034). Regarding the distribution of particular glutathione S-transferase omega genotype among various NYHA classes, the highest frequency of mutant GSTO1*Asp and GSTO2*Asp alleles were found in NYHA IV patients.

Conclusion: Based on results obtained it may be concluded that GSTO2*Asn142Asp polymorphism could play an important role as a risk factor for the development of CHF.

P6528 | BEDSIDE
Features of electrocardiogram and echocardiography in patients with cardiac involvement of myasthenia gravis
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Purposes: Myasthenia gravis (MG) primarily affects not only skeletal muscle but...
also heart muscle through the production of autoantibodies. Cardiac involvement is rare, but accompanies with poor prognosis. In the present study, we aimed to clarify the features of electrocardiogram, echocardiography, and clinical course in patients with MG.

Methods: Of 174 patients who diagnosed as MG between 2001 and 2012 in our hospital, retrospectively analyzed 84 patients who were examined both by electrocardiogram and echocardiography. Of the 84 patients, 32 patients were excluded for having other underlying disease such as hypertension, ischemic heart disease, or chronic kidney disease. We also investigated the clinical course of these patients from diagnosis to 2013.

Results: Thirty one (56.5%) had ECG abnormalities; 19% had atrial fibrillation; 15% had atrio-ventricular block; 53% had non-specific ST depression; and 50% had negative T waves. There was no difference in age and sex between normal ECG and an abnormal ECG group, but the rate of administration with steroids and anticholinergic agents was higher in the abnormal ECG group. No cardiac death was observed in normal ECG group. Four (4.7%) patients had decreased ejection fraction (below 55%) and they all had ECG abnormalities, in which the mean (standard deviation: SD) duration from the onset of MG was 10.5 (9.8) years, and the mean (SD) ejection fraction was 34.7 (7.2) %. Two patients had thymoma and underwent thymectomy. Of the 4, 1 patient died of colon cancer. The other 2 patients were started to be treated with immunosuppressive agents because of cardiac dysfunction with good clinical course. However, one had died due to acute decompression heart failure approximately one month after self-discontinuation of immunosuppressive agents.

Conclusions: ECG abnormalities, especially atrial fibrillation, were commonly observed in patients with MG. Of those with ECG abnormalities, an additional echocardiographic examination may be useful for the detection of cardiac involvement of myasthenia gravis as this may help an early detection and thus timely treatment, since this cardiomyopathy associated with MG has poor prognosis but can be treatable.

Invasive exercise hemodynamic evaluation in LVAD patients: A new insight for progressive aortic regurgitation

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Purpose: LVAD implantation in patients with advanced HF is closely associated with functional improvement together with improved survival. However, the magnitude of benefit varies considerably, likely reflective of multiple underlying contributors. The central hemodynamic response to exercise in LVAD is not well characterised, and we hypothesised that this may represent one source of functional variability. Furthermore the impact of developing LVAD related hemodynamic complications such as aortic regurgitation (AR) and right heart failure (RHF) could also impact on functional changes. We therefore aimed to test the hemodynamic response in LVAD patients and to correlate these with functional capacity and the presence of progressive AR or RHF.

Methods: 39 patients (mean age 44±15yrs) with a 3rd generation LVAD underwent symptom limited invasive hemodynamic testing during right heart catheterisation. These patients were also followed up with serial echocardiography and 6 minute walk testing.

Results: Exercise in LVAD patients was associated with a modest rise in total cardiac output, with a non-significant rise in LVAD output (Table). PA and PCWP pressures both increased significantly. Echocardiographic evidence of progression in AR grade (≥1) was evident in 5 patients over the post RHC follow-up period. In these patients there was a higher peak mean PA pressure (27±6 mmHg) compared to those without progressive AR (20±5 mmHg vs P<0.05). Exercise hemodynamics were not related to LVAD output.

Conclusion: Invasive exercise hemodynamic testing provides novel insights into integrated circulatory performance after LVAD. In particular exercise hemodynamic testing may provide a means of early detection of developing aortic regurgitation after LVAD.

Predictive value of delayed-enhancement magnetic resonance imaging in recent-onset dilated cardiomyopathy

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Introduction: Finding of delayed enhancement (DE) in the left ventricle on magnetic resonance imaging (MRI) predicts poor clinical outcome in patients with chronic dilated cardiomyopathy (DCM). Similar predictive value of DE has not yet been established in the patients with recent-onset DCM.

Methods: MRI was performed in 101 consecutive patients with recent-onset idiopathic DCM (age, 44±13 years; men, 71%); LVEF, 24±6%; LVEDD 67±6 mm; NYHA 2.9±0.8; duration of symptoms, 7±6 weeks). The patients were followed for a median of 2.5 years (IQR, 1.1 to 3.6). Observed cardiovascular events were related to baseline clinical characteristics, levels of cardiac biomarkers, and the presence of any DE in the left ventricle.

Results: DE was present in 65 patients. During the follow-up, 10 patients died in a median time of 1.1 years (IQR, 1.1 to 3.6). Observed cardiovascular events were related to baseline clinical characteristics, levels of cardiac biomarkers, and the presence of any DE in the left ventricle.

Conclusion: Presence of DE in the left ventricle seems to be a reliable marker of poor clinical outcome in patients with recent-onset idiopathic DCM.
Conclusion: The interval-force relationship is a powerful non-invasive means to assess the mortality risk of cardiac patients.

Conclusions: In this large group of HF patients no significant increase in fluid retention as a trigger of AF-onset was observed. In contrast, AF onset was associated with an immediate increase of fluid retention and an increased risk for subsequent HF hospitalization. Our data indicate a larger impact of AF-onset on worsening HF than vice versa.

Conclusions: In symptomatic patients with HF, PWV is primarily associated with increase in diffuse interstitial but not replacement myocardial fibrosis, irrespective of the underlying etiology. This relationship is stronger in NICMs, and also gender specific.

Conclusions: Galectin-3 is associated with myocardial replacement fibrosis as well as non-ischaemic dilated cardiomyopathy.
the hypothesis that galectin-3 is involved in cardiac fibrosis and remodelling, and that its assay may help to select high risk DCM patients.

**P6537 | BEDSIDE**

Pattern of ubiquitin expressions depends on advancement of heart failure in patients with idiopathic dilated cardiomyopathy

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**Background:** The ubiquitin–proteasome system is responsible for degradation of most cellular proteins and plays an essential role in nearly all aspects of cellular function and homeostasis, critical for cell survival and death. Ubiquitination of protein leads to their proteasomal degradation or less frequently to autophagy or plays non-proteasomal cellular role.

**Aim:** Evaluation of UBI expression (UBIX) as a feature of heart failure (HF).

**Methods:** Endomyocardial tissue samples of left ventricle wall were obtained from 60 pts (85% of males, mean age 46±14 years) with clinical symptoms of HF (LVEF<45%). UBXI and localization were investigated in histological sections by immunohistochemical method with use of anti-UBI (DAKO) antibody and Western-blotting method (WB). Deparafinized sections stained with hematoxylin-eosin and Trichom Masson were assessed in terms of histopathology including cardiomyocyte hypertrophy (CH) and tissue fibrosis. CH and fibrosis were assessed using morphometric software.

**Results:** AUBX expression in immunohistochemical and WB revealed four groups of myocardial tissue samples: type A, normal, gentle staining of UBI in cardiomyocyte cytoplasm (89±15%); type B, increased, intensive staining in cardiomyocyte cytoplasm (249±40%); type C, increased, intensive staining in cardiomyocyte cytoplasm and nucleus (198±32%); and type D, decreased or lack of UBI staining (8±13%). Analysis showed different patterns of UBXI with statistiscal significance or tendency between all groups according to LVEF, LVEDD and NT-proBNP fibrosis and CH (see table).

<table>
<thead>
<tr>
<th>UBXI</th>
<th>LVEF</th>
<th>LVEDD</th>
<th>NT-proBNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td>44.8±10</td>
<td>58.3±6</td>
<td>772±234</td>
</tr>
<tr>
<td>Type B</td>
<td>37.6±15</td>
<td>61.8±8</td>
<td>1321±456</td>
</tr>
<tr>
<td>Type C</td>
<td>27.2±7</td>
<td>66.2±5</td>
<td>1562±822</td>
</tr>
<tr>
<td>Type D</td>
<td>27.5±7</td>
<td>67.3±5</td>
<td>2155±608</td>
</tr>
</tbody>
</table>

Conclusions: Different types of UBXI correspond with changes in cardiomyocyte structure. UBXI especially type C and D is associated with CH, higher rate of fibrosis and NT-proBNP level, increased LVEDD and lower LVEF.

**P6538 | BEDSIDE**

Low birth weight and etiology of heart failure at adult age – can NTproBNP provide additional data?

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**Purpose:** It is well known that antenatal conditions and genetic structure determine postnatal growth, with proven influence on susceptibility to adult cardiovascular diseases, especially ischemic heart disease. Conversely, the influence of fetal growth restriction (evident by low birth weight-LBW) on non-ischemic cardiomyopathies (CMP) in adults has not been studied. We studied our center's heart failure population, and compared birth weights (BW) and NT-proBNP (brain natriuretic peptide) levels among different patient groups.

**Methods:** During 2012 and 2013 628 adult patients with different types of CMP were hospitalized in our center. Birth weight data were available for 130 patients; these patients were included in our observational study. The patients were categorized in groups according to the respective etiology of CMP: 49 patients had idiopathic CMP; 37 patients had ischemic CMP; 20 patients had secondary CMP (valvular, toxic or hypertensive); 14 patients had postmyocardial CMP; 5 patients had hypertrophic CMP (HCM), and 5 patients had ARVD. The cut-off value for LBW was set at 2500gm. In contrast all group 2 patients with a CCR5del32 polymorphism (w/del32 (n=57) and del32/del32 (n=4)) were alive at the end of the study (Fig-1A).

**Results:** Among all birth weights were as follows: postmyocardial CMP 3131±743 g, ARVD 4821±250 g, idiopathic CMP 3547±852 g, idiopathic CMP 3547±852 g, secondary CMP 3763±568 g, and HCM 3990±980 g. The lowest BW was found in postmyocardial CMP and was shown to be significantly lower compared to the ischemic CMP group (p<0.05). Average NT-proBNP values (pg/ml) among subgroups were as follows: idiopathic CMP 5780±1127, secondary CMP 8175±1887, and ARVD 1487±822, and ARVD 1487±822. NT-proBNP was significantly higher in patients with idiopathic CMP compared to ischemic CMP (p<0.03 and p<0.02 respectively). Furthermore, in the group of patients with idiopathic CMP, the patients with LBW had significantly higher NT-proBNP values (102763±9227 pg/ml) than patients with normal birth weight (5245±5137 pg/ml; p<0.03). Considering all data, BW showed a weak but significant negative correlation to NT-proBNP values (Pearson correlation coefficient -0.17 (p<0.02)).

**Conclusion:** This observational study supports our previous findings of lower average BW among postmyocardial CMP patients. An association was also established between LBW and NT-proBNP values in patients with idiopathic CMP. Additionally, birth weights were negatively correlated to NT-proBNP values. These data could potentially contribute to the fetal programming thesis, indicating that “in-utero” stress makes a lifelong influence on the CV system.

**P6539 | BEDSIDE**

Awake Cheyne-Stokes respiration: clinical and prognostic significance in a vast contemporary cohort of systolic heart failure patients

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**Purpose:** Cheyne-Stokes respiration characterized by periodic apnea/hypopnea of central origin (CSR) has been described both during sleep and awake state in heart failure (HF) patients, and is associated with worse prognosis. However, no prospective evaluation and prognostic value of awake CSR is still incomplete compared to contemporary medical and device therapy.

**Methods:** The study enrolled 439 consecutive HF patients (aged 65±13, 76% males; NYHA class I-II 67%, III-IV 33%, LVEF, 32±6%, mean±SD) on optimal medical therapy. All patients underwent thorough clinical and echocardiographic evaluation, cardiorespiratory monitoring, cardiopulmonary exercise testing (CPET) and 24-hour continuous polygraphic recording of ECG and respiratory activity (nasal flow plus chest and abdomen respirometers) and were then categorized into five groups (median 33 months, interquartile range 15-53), using cardiac mortality as endpoint.

**Results:** Three groups were identified according to severity of awake CSR (Apnea/Hypopnea Index, AHI ≥ 5, 15; AHI ≥ 15, 30; AHI > 30, 40), Higher degree of awake CSR was associated (p<0.01) with age, male gender, smoking, higher LV end systolic diameter (but no differences in LVEF), higher plasma N-terminal fragment of probrain natriuretic peptide and norepinephrine, lower peak VO2, higher VE/VO2, higher ventricular dimension and pulmonary artery systolic pressure, higher frequency of non-sustained ventricular tachycardia. Sleep CSR was more frequent in patients with diurnal AHI ≥ 15, (median AHI: 35; interquartile range 26-46 vs. 6, i.e. 3-12 in patients with diurnal AHI <5; p<0.01). 53 events occurred at follow-up. At Kaplan-Meyer (KM) analysis, patients with AHI >15 had worse prognosis (Log Rank=6.5, vs diurnal AHI <5, p<0.01).

**Conclusions:** Awake CSR is associated with neurohumoral activation, worse right ventricular function increased arrhythmic burden, lower functional capacity and worse prognosis. Specific therapeutic strategies should be searched for diurnal CSR, which is a frequent finding in HF patients and harbors significant clinical informations and worse prognosis.

**P6540 | BEDSIDE**

CCRSdel32 polymorphism is a protective factor in non-ischemic cardiomyopathy

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**Objective:** To gain insight into the long-term effect of the CCR5 genotype in patients with clinically suspected myocarditis or dilated cardiomyopathy (DCM). A 32-basepair deletion (del32) in the CC chemokine receptor 5 (CCR5, RANTES) gene leads to deficiency of this receptor for various chemokines. Homozygosity results in reduced susceptibility to HIV infections and is furthermore associated with an improved outcome in diabetes and coronary heart disease.

**Methods:** We determined its frequency by PCR in 300 consecutive patients (mean ±SD age, 49.6±13.9 years; 194 men) with reliable information on the all cause six year mortality. Occurrence of the endpoint death was determined through direct contact with the patient, contact with family members or inquiries at the registration office. All patients gave written informed consent for genetic analysis. The protocol was approved by local medical ethics committee of the University Hospital.

**Results:** Fourteen out of 239 CCR5 wildtype individuals (group 1) had died within average 6 years. In contrast all group 2 patients with a CCR5del32 polymorphism (w/del32 (n=57) and del32/del32 (n=4)) were alive at the end of the study (Fig-1A). The reduced mortality of patients with a 32-basepair deletion (del32) (p=0.032) of the CCR5 receptor possibly indicates the CCR5del32 polymorphism as a protective factor in patients with acquired cardiomyopathies. The CCR5 genotype did not correlate with a persisting myocardial inflammation. Diabetes was only present in wildtype patients but not in patients with impaired CCR5 receptor (p<0.001) but the increased mortality rate was not associated with increased BMI. p<0.015. NT-proBNP was significantly higher in patients with idiopathic CMP compared to ischemic CMP (p<0.03 and p<0.02 respectively). Furthermore, in the group of patients with idiopathic CMP, the patients with LBW had significantly higher
B19V was not significantly different between group 1 and 2 (EV: 12.2%, vs 9.4%; p<0.568). B19V: 33.3%, vs 18.7% (p<0.076) or HHV6: 20.1% vs 15.1% (p<0.408), respectively. Furthermore, there was no correlation between myocar-
dial infection by enterovirus, HHV6 or erythrovirus with the 6-year-mortality (EV: p<0.514; HHV6: p=0.818; B19V: p=0.510, respectively).

Conclusion: For the first time, our CRIdel32 polymorphism is an independent genetic factor that influences outcome in patients with clinically suspected myocarditis and DCM, not associated with myocardial inflammation, diabetes or viral infections.

P6541 | BEDSIDE

Daytime vs night-time central apnea in mild vs moderate-to-severe systolic heart failure

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Purpose: Central sleep apnea (CSA), characterized by periodic apnea/hypopnea of central origin has been described both during night-time and day-time in systolic heart failure (HF) patients, and is associated with worse prog-
nosis. However, its clinical significance in mild left ventricular dysfunction (left ventricular ejection fraction -LVEF-<40% -50%) has never been specifically ad-
dressed.

Methods: The study enrolled 439 consecutive HF patients (aged 65±13 years, 76% males; NYHA class I-II 67%, III-IV 33%, 32%±9, mean±SD) on guideline recommended therapy. Of these, 105 patients had mild left ventricular (LV) dysfunction (EF>35%, Delta140%, aged 68±10 years, 71% males; NYHA class I-II 67%, III-IV 33%, 32±9, mean±SD), 334 patients had moderate severe LV dysfunction (LVEF<40%, aged 64±14 years, 77% males; NYHA class I-II 65%, III-IV 35%, 32±9, mean±SD). Patients were enrolled in the cardiology department between 2010 and 2013 for cardiac amyloidosis underwent clinical, biological, echocardio-
graphy and polygraphy assessment to diagnose sleep apnoea syndrome (SAS).

Results: Our data show, for the first time, that CSA is 34% more frequent in mild LV systolic dysfunction vs moderate LV dysfunction (p=0.03). CSA is strongly associated with worse prognosis (AHI5-15 34%, AHI>15 50%, log-rank 0.04, p=0.007). Night-time CSA, on the other hand, failed to show a prognostic value in both mild and moderate-severe LV dysfunction.

Conclusions: Central apnea is a frequent phenomenon even in patients with mild LV systolic dysfunction, where it could represent a compensatory and not yet detrimental factor; in fact, day-time CSA is similarly prevalent in the two subsets of the population (mild vs moderate-severe LV dysfunction) but it holds prognostic value only in more advanced disease states. Night-time CSA is more frequent in moderate-severe left ventricular dysfunction, but it lacks prognostic value in this population of guidelines-recommended therapy.

P6542 | BENCH

Increased circulating HMGB1 and decreased soluble TLR4 in myocarditis and dilated cardiomyopathy

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Purpose: Myocarditis is an inflammatory heart disease which can lead to the de-
velopment of dilated cardiomyopathy and heart failure. Viral infection is a major cause of acute cardiac failures. TLRs (Toll like receptors) are multi-ligand receptors playing an important role in inflammatory processes. Some TLRs have been re-
ported to be responsible for the exacerbation of the inflammatory response to viral infec-tion, playing an important role in inflammatory processes. Some TLRs have been re-
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Methods: The study enrolled 439 consecutive HF patients (aged 65±13 years, 76% males; NYHA class I-II 67%, III-IV 33%, 32±9, mean±SD) on guideline recommended therapy. Of these, 105 patients had mild left ventricular (LV) dysfunction (EF>35%, Delta140%, aged 68±10 years, 71% males; NYHA class I-II 67%, III-IV 33%, 32±9, mean±SD), 334 patients had moderate severe LV dysfunction (LVEF<40%, aged 64±14 years, 77% males; NYHA class I-II 65%, III-IV 35%, 32±9, mean±SD). Patients were enrolled in the cardiology department between 2010 and 2013 for cardiac amyloidosis underwent clinical, biological, echocardio-
graphy and polygraphy assessment to diagnose sleep apnoea syndrome (SAS).

Results: Our data show, for the first time, that CSA is 34% more frequent in mild LV systolic dysfunction vs moderate LV dysfunction (p=0.03). CSA is strongly associated with worse prognosis (AHI5-15 34%, AHI>15 50%, log-rank 0.04, p=0.007). Night-time CSA, on the other hand, failed to show a prognostic value in both mild and moderate-severe LV dysfunction.

Conclusions: Central apnea is a frequent phenomenon even in patients with mild LV systolic dysfunction, where it could represent a compensatory and not yet detrimental factor; in fact, day-time CSA is similarly prevalent in the two subsets of the population (mild vs moderate-severe LV dysfunction) but it holds prognostic value only in more advanced disease states. Night-time CSA is more frequent in moderate-severe left ventricular dysfunction, but it lacks prognostic value in this population of guidelines-recommended therapy.
Previous analyses suggest that heart failure (HF) therapy guided by B-type natriuretic peptide (BNP) or NT-proBNP might not be equally effective in all HF patient groups, particularly those aged ≥75 years, but reasons remain unclear.

Methods: To determine interactions between (NT-pro)BNP-guided therapy and reduced (HFrEF; n=1731) versus preserved ejection fraction (HFpEF; n=301) as well as comorbidities (hypertension, renal failure, COPD, diabetes, cerebrovascular insult [CVI], peripheral vascular disease [PVD]) on outcome, independent of HF rEF. Randomized trials enrolling patients with systolic HF, assessing BNP and/or NT-proBNP plasma levels and risk of cardio-vascular events in patients with chronic heart failure (HF) has been previously demonstrated. However, it is unclear whether changes of BNP and NT-proBNP predict morbidity in chronic HF patients. The aim of our study was to explore the association between changes in BNP and NT-proBNP plasma levels and risk of hospital admission for HF worsening in chronic HF patients. The relationship between B-Type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) plasma levels and risk of cardio-vascular events in patients with chronic heart failure (HF) has been previously demonstrated. However, it is unclear whether changes of BNP and NT-proBNP predict morbidity in chronic HF patients. The aim of our study was to explore the association between changes in BNP and NT-proBNP plasma levels and risk of hospital admission for HF worsening in chronic HF patients. The relationship between B-Type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) plasma levels and risk of cardio-vascular events in patients with chronic heart failure (HF) has been previously demonstrated. However, it is unclear whether changes of BNP and NT-proBNP predict morbidity in chronic HF patients. The aim of our study was to explore the association between changes in BNP and NT-proBNP plasma levels and risk of hospital admission for HF worsening in chronic HF patients.
Conclusions: In HF patients, reduction of BNP or NT-proBNP levels is associated with reduced risk of hospitalization for HF worsening.

P6550 | BENCH
Diprydamole-induced C-type natriuretic peptide mRNA overexpression in minipig with pacing-induced left ventricular dysfunction
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Purpose: Molecular, neurohormonal, and haemodynamic changes occur in the setting of ventricular dysfunction (LVfD) of ischemic or non-ischemic origins. Recently it was demonstrated that diprydamole (DP), a phosphodiesterase inhibitor able to increase the intracellular levels of cAMP and cGMP, restores ischaemic tissue blood flow stimulating angiogenesis through a protein kinase A-dependent effect. Hence, C-type natriuretic peptide (CNP) overexpression in the setting of LVfD vascular tone, is expected to mimic the stimulation-motility-stimulus effect of NO via a cGMP-dependent mechanism. Aim of this study was to assess the role of concomitant treatment with DP on CNP levels in blood and myocardial tissue of minipigs with pacing-induced LVfD.

Methods: LVfD was induced by pacing at 200 bpm in the right ventricular (RV) apex of minipigs undergoing concomitant DP therapy (5 mg/kg p.o.) (DP+, n=4) or placebo (DP−, n=4). Four sham operated minipigs (C-SHAM) were used as controls. All animals underwent a 2D EchoDoppler examination immediately after single coronary stent-implantation and after 4-weeks of RV tachycardia pacing. Animals were sacrificed after 4 weeks pacing and cardiac tissue collected in each minipig from 6 regions of the LV wall. In LVD animals blood samples were also drawn at baseline and after 4 weeks pacing and CNP plasma levels were determined by radioimmunoassay. CNP, natriuretic peptide receptor (NPR-B, NPR-C and BNP cardiac mRNA expression were examined by Real Time-PCR in all animals.

Results: After 4 weeks of pacing, LV fractional shortening (LVFS) was markedly reduced in DP− and to a lower extent in DP+ (21.5±2.2%, 31.4±4.4%) as compared to baseline (DP−:38.0±3.3%, DP+:40.3±1.4%; p<0.0001, p=0.03 respectively) LVD was unchanged in C-SHAM (43.3±3% vs 44.2±3%). CNP gene expression resulted lower in DP− (0.13±0.03) with respect to C-SHAM (0.51±0.01) and DP+ (0.43±0.2) as well as NPR-B (C-SHAM: 0.42±0.06, DP−:0.32±0.06, DP+:0.63±0.1) (0.011 DP− vs DP+). NPR-C mRNA expression was significantly (p=0.001) lower both in DP− (0.33±0.06) and DP+ (0.45±0.07) with respect to C-SHAM (1.2±0.2). As expected, the mRNA expression BNP levels were higher in LVD as compared to C-SHAM. CNP plasma levels resulted higher in DP+ compared to DP− (22.0±7.1, 15.8±3.8 pg/ml respectively, p=0.37).

Conclusion: These data suggest that DP may serve as a preconditioning agent in the setting of LVfD. Next to DP, other pharmacological agents able to modulate vascular tone, are expected to mimic the stimulation-motility-stimulus effect of NO via a cGMP dependent mechanism.

P6551 | BENCH
Dual-acting angiotensin-receptor neprilysin inhibition attenuates post-myocardial infarction cardiac remodelling and angiotensin-II-induced cardiorenal injury in vitro
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Background: Novel angiotensin-receptor neprilysin (NEP) inhibitors (ARNi) demonstrated benefits above single RAAS-blockade in early clinical trials, but effects of ARNi in in vitro and in angiotensin-II (AngII) induced hypertrophy and fibrosis in cardiorenal cell lines are unknown. We evaluated novel ARNi in AngII treated cardiac fibroblasts, renal proximal tubular epithelial cells and renal tubular epithelial cells.

Methods: Ten-week-old male C57BL6J-background wild type (WT) mice and IL-11 null (IL-11−/−) were subjected to transaortic constriction (TAC). Sequential serum IL-11 levels myocardial IL-11 mRNA expressions were determined by real time RT-PCR in WT mice. From 1 week before TAC surgery, IL-11 null mice were administered either (IP) saline intraperitoneally or recombinant IL-11 intraperitoneally (10ng every other day) for 3 weeks. Cardiac function was assessed by transesophageal echocardiography. Two weeks after TAC operation, myocardial samples were obtained. Haematoxylin and eosin stained sections and Masson’s trichrome staining sections were prepared.

Results: IL-11 concentration in serum and IL-11 expression in myocardial tissue increased gradually after TAC in WT mice. Forty-seven percent of TAC-operated IL-11−/− mice and 12% of TAC-operated WT mice died of heart failure by 14days. TAC-operated IL-11−/− mice exhibited more severe left ventricular (LV) remodeling, characterized by reduced LV fractional shortening (34±2%; vs 46±1%, p<0.05), cardiomyocyte hypertrophy, extensive interstitial fibrosis and elevation of fetal gene expressions (α-skeletal actin: 20.9±1.2 fold vs 6.5±1.3 folds, p<0.05) compared with TAC-WT mice. Recombinant IL-11 given intraperitoneally improved the survival rate to 100% following TAC operation in IL-11−/− mice. Furthermore, exogenous IL-11 administration suppressed ventricular fetal gene expressions to non-TAC-operated level, whereas LV enlargement and contractile dysfunction were only partially suppressed in IL-11−/− mice following TAC (LV fractional shortening: 39±2%).

Conclusions: Circulatory IL-11 exerts opposing effects on cardiomyocyte hypertrophy and cardiac fibrosis under pressure-overload. IL-11 induced in the heart may have an effect such as preserving contractile function.

P6553 | BEDSIDE
Real-time sympathetic nerve activity in heart failure is accelerated and correlated with cardiac sympathetic nerve activity evaluated by 123I-MIBG Imaging
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Background: Cardiac sympathetic nerve activity evaluated by cardiac 123I-MIBG scintigraphy has been shown to have diagnostic and prognostic significance in heart failure (HF). Renal sympathetic nerve activity (SNA) is also accelerated in some HF patients, whether they have heart failure (HF) or not. However, it remains unknown whether there is correlation between heart and kidney sympathetic nerve activity (SNA) in heart failure. In this study, we evaluated SNA of heart and kidney in HF by 123I-MIBG Imaging.

Methods: The subjects were 101 consecutive patients hospitalized for HF (NYHA class II and IV) and 30 consecutive patients served as a control group without HF (group C). Between March 2012 and December 2013. HF Patients were classified into 2 groups: group R (LVEF<50%: mean 35.2±8.3%, n=53, 69.9±12.6 years) and group P (LVEF≥50%: mean 65.3±6.1%, n=48, 78.3±12.1 years). Symptomatic normal LV function (mean LVEF 67±1.6%, n=30, 49.2±13.0 years), 123I-MIBG scintigraphy was evaluated as the heart-to-kidney ratio and the kidney-to-mediastinum ratio in the delayed image (H/M and K/M) and the washout rate (heat; HWR and kidney; kWWR) respectively. Plasma BNP concentration, BUN,Cr and eGFR were also measured in all subjects.

Results: In group R P/H:M was significantly lower and HWRo was significantly higher than in group C (H/M (R2.0±0.54*, P2.21±0.58*, C2.95±0.44), hWHR (R5.5±6.9*, P4.82±1.36*, C27.7±10.7%; *p<0.01 vs C). Although BNP
was higher in group R than P (R780±589**, P417±586 pg/ml, p<0.01 vs. P), there is no significant differences in H/M and eGFR between groups R and P [eGFR (R: 58.7±20.3, P: 52.4±17.5±min/1.73m²)]. Correlation between heart and kidney in HF was significant [Y=0.976+0.357X: r=0.43, p<0.00 1 (K/M and H/M) and Y=63.99+0.253X: r=0.29, p<0.01 (K/Wor and H/Wor)]. Correlation between heart and kidney in group R and P was also significant respectively [R: r=0.39, p<0.01, P: r=0.45, p<0.01 (K/M and H/M)].

Conclusions: These results suggest that there is a positive correlation between heart and kidney about SNA in HF. Furthermore, SNA is correlated with cardiac SNA regardless of type of heart failure.

P6554 | BEDSIDE
Prognostic value of soluble ST2 in patients with dyspnea
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Objectives: Soluble ST2 (ST2) has emerged as a novel biomarker with exceptionaldiscriminatory predictive value in heart failure. The aim of this study was to investigate prognostic utility of ST2.

Methods: We recruited 138 patients presenting to the emergency department and the outpatient department with dyspnea. We performed to measure ST2 level and BNP. Outcome measure were all-cause mortality and readmission at 6 month. The prognostic value of ST2 was evaluated in comparison to BNP.

Results: Median concentrations of ST2 were higher among decedents and patients with readmission at 6 month (110.08± vs. 66.756 ng/ml; p<0.0035). Median concentrations of BNP were also higher among decedents and patients with readmission at 6 month (500.00 vs. 274.47 pg/ml; p=0.0497). Analyzing receiver operating characteristic (ROC) analysis, the area under the curve (AUC) for ST2 and BNP to predict 6-month mortality and readmission were 0.750 and 0.652, respectively. ST2 was more strong predictor compared with BNP.

Conclusion: ST2 is a strong and independent predictor of 6-month mortality and readmission. ST2 may provide clinicians with an additional tool for guiding treatment in patients with dyspnea.

P6555 | BEDSIDE
Sustained hyponatremia in acute phase associates with high in-hospital mortality in acute heart failure syndrome patients
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Background: Hyponatremia is one of the most common electrolyte disorders in acute heart failure (AHFS) patients. Many studies have shown that presence of hyponatremia at admission associate with high morbidity and mortality in AHFS patients. However, in some patients high sodium serum level will be corrected by general treatment for AHFS. In this study, we investigated whether correction of hyponatremia in acute treatment for AHFS associates to prognosis.

Methods: We retrospectively included 554 AHFS patients who were admitted to the first treatment in heart failure in 2011 to December 2012. Patients were divided into three groups; hyponatremia at admission and also at 2 days after admission (hypo-hypo group), hyponatremia at admission and not at 2 days after admission (hypo-normo group), and normonatremia at admission (normo group). Hyponatremia was defined as serum sodium concentration <135 mmol/L. Endpoint was in-hospital mortality.

Results: Of all cohorts, 42 patients (7.6%) were in hypo-hypo group, 40 patients (7.2%) were in hypo-normo group, and 472 patients (85.2%) were in normo group. In-hospital mortality for these three-groups were 21.4%, 12.5%, and 5.9%, respectively (P=0.005). In multivariate analysis, hypo-hypo group was an independent predictor for in-hospital mortality (HR 2.74, 95% CI: 1.11-6.78, P=0.029) but hyponatremia group were not (HR 1.78, 95% CI: 0.85-3.09, P=0.30).

Conclusion: In AHFS patients, sustained hyponatremia of more than 2 days after admission contributes to worse prognosis.

P6556 | BEDSIDE
Impact of left ventricular hypertrophy and plasma norepinephrine level for cardiovascular events in elderly hypertensive patients - JMS ABPM wave 1 study
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Background: The predictive value of electrocardiographic left ventricular hypertrophy (LVH) for cardiovascular disease (CVD) onset has been well established. However, the underlying mechanism remained unclear.

Methods and results: 514 hypertensive patients (mean 72.3 years old; 37% men) were recruited. LVH was defined as Sokolow-Lyon voltage over 35mV. The incidence of CVD was prospectively ascertainment. During an average of 41 month (171 had partial collapsibility (25% & <50%, group II), while 61 patients had poor collapsibility (<25%, group III). After adjustment for age, sex, body mass index, LVEF, LV mass index, diabetes mellitus and heart failure, group II had significantly higher concentration of serum creatinine (SCr) as compared with group I (1.34±0.06 vs 0.95±0.08 mg/dl; p=0.00001), TnT was increased in CRS group respect to HF group (156 ng/mL IC 7-13 vs 5.93 pg/ml IC 3.9-8.8 pg/ml; p<0.05). NGAL measurements revealed more increased levels in CRS respect to HF group (156 ng/mL IC 129-186 vs 89.1 mg/L IC 72-109 p<0.0001), TNFalpha was increased in both groups. Patients with CRS showed increased levels of Urea (BUN) and urea/creatinine ratio (108.9 mg/dl IC 98-120 vs 51 mg/dl IC 46-55 p<0.001), BUN >78 mg/dl, BUN creatinine ratio <46.3 and TnT >0.27 mg/dl can discriminate patients with cardiovascular mortality from patients with neurohumoral and biomarker pattern has been poorly evaluated. The aim of this study is to measure inflammatory activation, neurohumoral status and kidney and myocardial damage in patients with CRS compared to patients with Heart Failure (HF) and preserved renal function.

Methods: We analyzed 246 patients on the basis of renal function (Group I preserved renal function defined as eGFR >50 ml/min/1.73 m³, and Group II 126 patients with eGFR 50 ml/min/1.73 m³). In each group we calculated the Neurohumoral status (TFN-Fb B type natriuretic peptide, BNP, Neutrophil Gelatinase-Associated Lipocalin (NGAL), Tropomin T (TnT), osteoprotegerin (OPG) and blood urea nitrogen (BUN)) were measured. The power of all laboratory parameters in detecting CRS was evaluated by Receiver Operating Characteristics (ROC) curve analysis and logistic regression analysis.

Results: A significant increase in BNP in CRS patients compared to HF patients with preserved renal function, (626.4 pg/ml IC 518-749 vs 487.8 pg/ml IC 411-578 p=0.05) was revealed. IL-6 was significantly higher in CRS group (436 pg/ml IC 7-13 vs 5.93 pg/ml IC 3.9-8.8 p<0.05). TGF-β, IL-6, IL-8, TNFα, BNP, TFN-Fb and NGAL levels were measured in each group and the ROC analysis showed that only NGAL levels >1.34 mg/dl, BNP >78 mg/dl, TFNα >0.27 mg/dl can discriminate patients with cardiovascular mortality from patients with neurohumoral and biomarker pattern well with good sensitivity and specificity (p<0.001).

Conclusions: In patients with CRS renal tubal damage is increased respect to patients with HF and preserved renal function. These patients also displayed higher neurohumoral and cardiac injury activation. The current biomarkers pattern could be used for an early diagnosis of renal impairment in acute and chronic HF.

DIASTOLIC DYSFUNCTION I

P6559 | BEDSIDE
Collapsibility of inferior vena cava as a predictor of renal dysfunction and clinical outcomes
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Background: Renal dysfunction is frequently observed in patients with heart failure with preserved left ventricular ejection fraction (LVEF) and renal vein congestion may be a cause of renal dysfunction. However, there are few studies that investigate this hypothesis. Collapsibility of inferior vena cava (IVC) during inspiration may be a surrogate of estimated right atrial pressure and we investigated whether IVC collapsibility can predict worse clinical outcomes.

Methods: We reviewed echocardiograms and measured maximum/minimum diameter of IVC and IVC collapsibility from the past medical database in our inpatient online clinical information system and blood chemistry was obtained as well. Clinical status was assessed during follow-up.

Results: There were 1,166 patients enrolled in the study (Mean age = 63.8±13.4 years, 676 male). 929 patients had good collapsibility of IVC (>50%, group I), 171 had partial collapsibility (<25% & <50%, group II), while 61 patients had poor collapsibility (<25%, group III). Adjustment for age, sex, body mass index, LVEF, LV mass index, diabetes mellitus and heart failure, group III had significantly higher concentration of serum creatinine (SCr) as compared with group I (1.34±0.06 vs 0.95±0.08 mg/dl; p=0.00001), TnT was increased in CRS group respect to HF group (156 ng/mL IC 7-13 vs 5.93 pg/ml IC 3.9-8.8 pg/ml; p<0.05). There was an additive effect of LVEF and high norepinephrine level on CVD risk.

Conclusions: In older hypertensive patients, LVAH is associated with high 24-hour BP and high norepinephrine level. However the predictive value of LVAH is independent of 24-hour BP and circulating norepinephrine level.
LAVI (ml/m²) 26.2 ± 6
E/e' 6.4 ± 2.2
E/A 1.9 ± 0.7
E deceleration time (ms) 158 ± 32
e' (cm/s) 12.2 ± 2.2

Purpose: Long QT syndrome (LQTS) is an arrhythmogenic cardiac ion channelopathy which has been considered a purely electrical disease. However, recent reports have indicated mechanical abnormalities in LQTS patients. We aimed to explore systolic and diastolic function in LQTS patients.

Methods: We included 192 genotyped LQTS patients with no concomitant cardiac disease. Age and sex matched healthy individuals served as controls (n=59). By echocardiography, we assessed left ventricular (LV) ejection fraction (EF) and speckle tracking global longitudinal strain (GLS) (16 LV segments), E-wave, A-wave, E deceleration time and e' (mean of septal and lateral e') were recorded by Doppler. Left atrial volume index (LAVI) was calculated. Heart rate corrected QT interval (QTc) was assessed by 12-lead ECG.

Results: In the 192 LQTS subjects, systolic function by GLS and diastolic function by e' and E deceleration time were reduced compared to healthy (all p<0.05) (Table). LAVI was enlarged in LQTS (p<0.01). QTc and LAVI correlated in LQTS (R=0.17, p<0.05), but not in healthy (R=0.33, p=0.13).

Conclusions: LQTS patients had a subtle reduction in both systolic and diastolic function compared to healthy LAVI was enlarged in LQTS, indicating a mechanical-endothelial association. These alterations may represent mechanical consequences of ion channel disease.

P6560 | BEDSIDE
Electro-mechanical alterations in patients with long QT syndrome
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Purpose: To evaluate systolic and diastolic function in patients with long QT syndrome (LQTS).

Methods: We included 192 LQTS patients with no concomitant cardiac disease and 59 healthy controls matched for age and sex. All patients underwent 12-lead ECG, echocardiography, and cardiac magnetic resonance imaging (CMRI). LV systolic function was assessed by CMRI-derived LV mass (LVMM), LV ejection fraction (LVEF), and LV mass index (LVMI). LV diastolic function was assessed by LV filling pressures and transmitral flow velocity ratios (E/A, E/e').

Results: LV systolic function was preserved in most patients, with LVEF ranging from 50% to 70%. LV diastolic function was impaired in a significant proportion of patients, with increased LV filling pressures and decreased E/A ratio. LVMM was elevated in all patients, with a mean value of 150 g/m² (95% CI: 140-160 g/m²).

Conclusions: LQTS patients have preserved LV systolic function but impaired LV diastolic function, with increased LV filling pressures and decreased LV filling velocities. This suggests that LQTS patients may be at risk for diastolic heart failure.

P6561 | BENCH
Cardiopulmonary exercise testing in diastolic heart failure: the link that has been missing
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Background: Diastolic dysfunction (DD) is a common consequence of hypertension even in pts with preserved left ventricular systolic (LVSF) and diastolic function (DYSF). Cardiopulmonary exercise testing (CPET) has been validated in the stratification of patients with diastolic heart failure (DHF), and its combination with stress echo showed a great potential in unmasking DHF. However, the relationship between CPET and stress echo parameters still remained undetermined.

Objective: To analyse the parameters of combined stress echo CPET in patients with hypertension, exertional dyspnea with normal resting LVSF and LVDV in the early detection of DHF.

Methodology: We examined 82 pts with hypertension, exertional dyspnea and normal resting LVSF and LVDV. All pts performed combined stress echo CPET (supine bicycle, ramp protocol, 15W/min increments). Standard M-mode and 2-D echo measurements at rest, continuous echo monitoring (to exclude myocardial ischemia) and DFF assessment at the top of the exercise, have been performed. We measured transmural flow with pulsed doppler, and annular mitral velocities (e' and a' using TDI) according to guidelines using E/e' as a main echo determinant DFF. We included patients ≥65 years old in order to decrease the influence of age on LV diastolic properties.

Results: DFF (E/e' ≥15) was found in 7/82 pts (8.5%) during combined CPET stress echo test. There was no significant difference in LV EF in pts with and without DHF. Patients with DHF had lower peak VO2 (14.8±2.2 vs 20.3±5.5 ml/kg/min; p=0.021), and VO2 at the VAT (p=0.035), lower O2 pulse (p=0.04) and impaired ventilatory reserve with higher VE/VCO2 slope (p=0.033), and lower VCO2 (p=0.021). However, there was no statistically significant difference in double product and circulatory power in pts with and without DHF. Multivariate analysis showed that VE/VCO2 slope was an independent predictor of DFF (HR 3.7 with 95% CI: 1.3-9.04). There was a strong correlation between VE/VCO2 slope and E/e' (r=0.69; p<0.0001). Value of VE/VCO2 best predictive for DHF in this group of pts according to ROC curve was 32.9 (Sn 100%, Sp 91%).

Conclusion: Combined stress echo CPET has very high accuracy to detect DHF early phase in the presence of normal resting echo values. The exercise unmask defective impaired ventricular response in patients with dyspnea with excellent correlation between VE/VCO2 slope and E/e' relationship confirming the need for assessment the diastolic properties during the effort even in patients with normal resting LV function.
tion) and 41 age-matched healthy controls. Cardiopulmonary exercise testing with echocardiographic assessment of myocardial function, including measurement of E/e' ratio approximating LV filling pressure, at rest and post-exercise were undertaken. Blood sampled including Gal-3 and BNP. According to the response of LV filling pressure to exercise, pts with HFpEF were stratified into 2 groups: with and without exertional increase in E/e' > 13.

Results: Higher Gal-3 and lower exercise capacity were found in both subgroups with HFpEF, whereas higher BNP and resting E/e' and ΔE/e' (change from rest to peak exercise) only in pts with post-exercise E/e' > 13 HFpEF pts with post-exercise E/e' > 13 had higher Gal-3 and lower exercise capacity than their peers with E/e' < 13. In multivariable analysis, apart from patient age, BMI, LV mass, and presence of hypertension and diabetes, Gal-3 was an independent correlate of peak VO2 (β = −0.17P < 0.01), MET (β = 0.15, P = 0.02), E/e' at rest (β = 0.19, P = 0.01) and post exercise (β = 0.15, P = 0.03) as well as ΔE/e' (β = 0.15, P = 0.04).

Conclusions: Increased Gal-3 is associated with reduced exercise capacity and increased LV filling pressure response to exercise in HFpEF, which underpins the contribution of myocardial fibrosis to the pathophysiology of this disease state. The detrimental clinical effect of fibrotic activation is particularly evident in pts with LV hypertrophy and other confounding variables. Leptin may be one of the mechanistic links explaining the development of congestive heart failure of obese subjects.

P6566 | BENCH
The cardiac protease-activated receptor 2 expression is essential for the maintenance of the cardiac function in the aged heart
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Introduction: Elderly patients often suffer from left ventricular hypertrophy and diastolic dysfunction with preserved systolic function resulting from ongoing cardiac remodeling, loss and cardiac fibroses. The protease activated receptor (PAR) 2 is known to be a pro-fibrotic mediator. In a mouse model of myocardial infarction PAR2 overexpression in cardiomyocytes led to the development of fibrosis. In this study we examine the role of PAR2 in the aged heart regarding fibrosis and heart function.

Methods: 8 weeks (wks) and 1 year (yr) old wild-type (wt) and PAR2 knockout (ko) mice underwent hemodynamic measurements with a 12F microconductance catheter and hearts were collected for histological and biochemical analysis. Collagen release and Smad2 phosphorylation were determined with western blots and the ROS activity was analysed with a DCF dependent immunofluorescence assay on adult cardiac fibroblasts. The PAR2 gene expression was determined in myocardial biopsies from HFPEF patients.

Results: 1 year old PAR2ko mice suffered from a left ventricular dysfunction with preserved systolic function, which was accompanied by an age dependent fibrosis. In hearts of 8 wks old wt and PAR2ko mice no differences in collagen expression were present. In contrast, 1 yr old PAR2ko mice showed collagen deposition in the heart and the collagen I/ III ratio revealed a fibrosis in PAR2ko mice but not in wt mice (p < 0.05). Moreover, adult cardiac PAR2 fibroblasts also showed an increased collagen I release into the supernatant compared to wt fibroblasts. Furthermore, the TGFβ-dependent Smad2 phosphorylation was stronger in PAR2ko fibroblasts compared to wt fibroblasts. Oxidative stress in the heart often triggers cardiac dysfunction. After treatment with H2O2, PAR2ko fibroblasts exhibited higher ROS levels than wt fibroblasts (wt vs PAR2ko: 4.26±1.78 vs. 6.42±5.35, p < 0.05). The GSH / GSSG ratio in hearts of 1yr hearts pointed also to an increased oxidative stress in PAR2ko mice compared to wt mice (par 1yr vs wt: 0.53 vs. 0.89,p < 0.05). These results suggest a lower capacity of the heart associated with a higher oxidative stress, which leads to fibrosis and an impaired heart function. In HFPEF patients a decreased PAR2 expression was associated with severe diastolic dysfunction and vice versa.

Conclusion: The cardiac PAR2 expression is essential for the maintenance of heart function in the aged heart. The loss of PAR2 results in increased oxidative stress, an age-dependent cardiac fibrosis and a left ventricular diastolic dysfunction.
sectional area (MCSA); a measure of cardiomyocyte hypertrophy, and volume fraction of interstitial fibrosis (VFIF) were assessed in LV free wall by histomorphometry. Protein levels of SERCA-2a were measured in LV homogenate using Western blotting and quantified in densitometric units (du). Results: Compared to NL, HF-Controls showed significantly larger MCSA (410±10 vs. 678±15 μm², p<0.05), significantly greater VFIF (3.7±0.1 vs. 11.8±0.5%, p<0.05) and significantly lower protein levels of SERCA-2a (0.57±0.06 vs. 0.22±0.02 du, p<0.05). These abnormalities were associated with reduced indexes of LV diastolic function in HF-Controls compared to NL. Treatment with valsartan ameliorated the increase in MCSA (600±4 μm² vs. p<0.05), significantly reduced VFIF (9.7±1.4%, p<0.05) and significantly increased protein levels of SERCA-2a (0.42±0.05 du, p<0.05) compared to HF-Controls. The benefits were associated with improved LV global indexes of diastolic function. Conclusions: Therapy with valsartan ameliorates several key mal-adaptations implicated in diastolic dysfunction of the failing LV. These findings support the continued development of Bendavia as a potential therapy for patients with HF and LV diastolic dysfunction.

P6566 | BEDSIDE Left atrial strain rate during isovolumic contraction predicts pulmonary capillary wedge pressure in patients with left ventricular systolic dysfunction

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Aim: The purpose of this study was to test the hypothesis that tissue Doppler (TD) derived left atrial strain rate (SR) during left ventricular (LV) isovolumic contraction predicts pulmonary capillary wedge pressure (PCWP) in LV systolic dysfunction, and to compare left atrial SR between patients with heart failure and normal subjects.

Methods: Forty consecutive heart failure patients (56±8 years, 10 females (25%), all sinus), and 10 healthy controls were studied. Patients had undergone cardiology immediately before invasive catheter measurement of PCWP. TD derived left atrial strain rate during LV isovolumic contraction (SR-IC), LV ejection (SR-EJ), LV early diastole (SR-ED), and LV late diastole (SR-LD), were measured. Patients were classified according to their LV ejection fraction (EF) to 21 with EF<55%, and 19 with EF≥55%.

Results: All SR values were lower in the patient groups compared to controls (SR-IC: 1.46±0.62 vs. 4.23±0.37 ±1/s, p=0.001, SR-EJ: 1.91±0.77 vs. 3.75±0.85 ±1/s, p=0.001, SR-ED: 1.9±0.02 vs. 5.1±0.73 ±1/s, p=0.001, SR-LD: 2.54±1.02 vs. 3.7±0.81 ±1/s, p=0.009). Moreover, patients with EF<55% had the lowest SR-IC and SR-EJ compared to patients with EF≥55% (1.25±0.5 vs. 1.7±0.57 and 5.1±0.2 vs. 4.22±0.1 ±1/s, p=0.04, and 0.001) and controls (p<0.001), while SR-ED was not different between patients with EF<55% vs. EF≥55%, despite both being lower than that in the controls, and SR-LD was lower in EF<55% vs. controls, while was similar between EF≥55% and controls. Interestingly, the only variable that could overall significantly correlate with PCWP was SR-IC (r=0.567, p=0.001), while SR-EJ showed a weaker correlation (r=0.329, p=0.053), and SR-ED and SR-LD correlate with PCWP. SR-IC correlation with PCWP became excellent in EF<55% (r=0.715, p=0.001), while it was lost in EF≥55% (r=0.161, p=0.553). Other echocardiographic correlates with PCWP in EF<55% were: E/E' (r=0.523, p=0.013), left atrial volume (r=0.087, p=0.001), and mitral flow vpeak (r=0.585, p=0.008). Multivariate regression analysis revealed that SR-IC was the only variable that could independently predict PCWP in EF<55% (adjusted r2=0.552, beta=−0.469, p=0.04). ROC-curve suggested that SR-IC effectively predicts PCWP in EF<55% (AUC=0.9).

Conclusions: Left atrial SR values are impaired in all patients with heart failure symptoms, irrespective of the systolic function. SR-IC and SR-EJ are especially further impaired in patients with LV systolic dysfunction compared to those without. Our observations indicate that left ventricular diastolic dysfunction II

P6567 | BEDSIDE Lysyl oxidase-like-2 is expressed in patients with heart failure and preserved ejection fraction and correlated with the degree of fibrosis and inflammation in the heart

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Purpose: Lysyl oxidase-like-2 (LOXL2) belongs to the family of lysyl oxidase (LOX) and LOX-like proteins and promote cross-linking of fibrillar collagen I and fibrin. Heart failure with preserved ejection fraction (HFPEF) is characterised by increased myocardial stiffness due to several mechanisms, among others due to increased collagen deposition and cross-linking of collagen fibers in the myocardium. We sought to examine the role of LOXL2 in HFPEF.

Methods: We investigated 41 patients (mean age 49±11.5) with normal ejection fraction (mean EF 59±9.5) whose endomycocardial biopsies were taken previously. Assessment of diastolic function was performed by mitral-flow and tissue Doppler measurements. Immunohistostaining was performed to determine collagen I, cross-linking, LOXL2, LFA-1, ICAM-1 and VCAM-1 expression and CD3+ and MAC-1+ cells number.

Results: Twenty patients with HFPEF and diastolic dysfunction showed a significant increase in collagen I expression (30% higher, p=0.009) compared with that of 15 controls. LOXL2-expression was 2.5times higher in HFPEF patients compared to controls (p=0.023). This was associated with significantly higher cross-linking of collagen fibers in HFPEF patients by 1.7times (p=0.03) compared to controls. Furthermore, HFPEF patients showed increased inflammation as measured by 2times higher CD3+ cells (p=0.04), 1.7times higher ICAM-1 expression (p=0.03), 3times higher VCAM-1 expression (p=0.015) and 2times higher LFA 1 expression (p=0.035). There was no significant difference in the expression of MAC-1+ cells between the groups.

The expression of LOXL2 correlated significantly with the protein expression of collagen I (r=0.49, p=0.033), the amount of cross-linking (r=0.67, p=0.0078), the amount of CD3+ cells (r=0.47, p=0.04) and LFA-1 (r=0.5, p=0.017) but not with the MAC-1+ cells. LOXL2 was significantly higher in patients with HFPEF compared with patients without HFPEF and correlated with the degree of myocardial fibrosis and inflammation. LOXL2 might be a new target for reduction of fibrosis and inflammation in HFPEF patients.

Conclusions: LOXL2 shows a significantly higher expression in the myocardium of patients with HFPEF compared with patients without HFPEF and correlated with the amount of myocardial fibrosis and inflammation. LOXL2 might be a new target for reduction of fibrosis and inflammation in HFPEF patients.

P6568 | BENCH Non-redox-independent protective effects of GTP cyclohydrolase 1 (GCH1) overexpression and tetrahydrobiopterin (BH4) in diabetic cardiomyopathy


Purpose: Diabetic cardiomyopathy is characterised by the early onset of significant left ventricular (LV) diastolic dysfunction, the origin of which remains poorly understood. Oxidative stress and reduced nitric oxide (NO) bioavailability secondary to BH4 reduction underlie the endothehial dysfunction observed in all types of diabetes; however, whether an altered myocardial NO-redox balance accounts for the diabetic cardiomyopathy phenotype remains to be established. We addressed these issues in a murine model of type 1 diabetes and evaluated the effects of BH4 on cardiac myofibril-specific gene expression in BH4 in the development of LV dysfunction

Methods: Diabetes was induced by streptozotocin injection (43mg/kg; for 5 days). After 12 weeks we evaluated vasomotor function in aortic rings by wire myo-
Impaired LV diastolic function in diabetic mice can be prevented that increasing myocardial BH4 preserved LV diastolic function without preventing was significantly increased in both WT and mGCH1Tg diabetic mice, indicating increased oxidative stress, suggesting that GCH1/BH4 protect the diabetic myocardium by myocardial GCH1 overexpression in the absence of NOS dysfunction or inflammation which was prevented in diabetic mGCH1Tg (t=0.1 in ms, diabetic vs control: 105.3 ± 4.0 vs 118.6 ± 2.8 in mGCH1Tg and 77.3 ± 3.5 vs 73.3 ± 2.4 in mGCH1Tg, t=25.46, P < 0.05 for the interaction between genotype and diabetes). LV collagen content was significantly increased in both WT and mGCH1Tg diabetic mice, indicating that increasing myocardial BH4 preserved LV diastolic function without preventing the development of fibrosis.

**Conclusions:** Impaired LV diastolic function in diabetic mice can be prevented by increasing myocardial BH4 content by transgenic overexpression of human GCH1/BH4.

**P6573 | BEDSIDE**

**Elevation of circulating fatty acid-binding protein 4 is associated with left ventricular diastolic dysfunction in a general population**

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**Purpose:** Fatty acid-binding protein 4 (FABP4) is expressed in both adipocytes and macrophages. Recent studies have shown secretion of FABP4 from adipocytes and association of elevated serum FABP4 level with obesity, insulin resistance, and atherosclerosis. However, little is known about role of FABP4 in cardiac dysfunction.

**Methods:** From database of the Tanno-Sobetsu study, data for 190 subjects (male/female: 82/108) who were treated with no medication and underwent echocardiography in 2011 or 2012 were retrieved for analyses of relationships between serum FABP4 concentration, metabolic markers and parameters of echocardiography.

**Results:** Serum FABP4 level was positively correlated with age, body mass index (BMI), blood pressure (BP), LDL cholesterol and homocysteine level and negatively correlated with HDL cholesterol, estimated glomerular filtration rate (eGFR) and total cholesterol level. Multivariate regression analysis with BMI, eGFR, brain natriuretic peptide (BNP), FABP4, and metabolic markers. Multivariate regression analysis adjusted by HOMA-R, BMI, eGFR, BNP or left ventricular wall thickness in addition to age, gender and BP revealed that serum FABP4 concentration was independently correlated with eGFR.

**Conclusions:** Elevation of circulating FABP4 may contribute to LV diastolic dysfunction via a hypertrophy-independent mechanism in a general population.

**P6574 | BEDSIDE**

**Association of obstructive sleep apnea with diastolic dysfunction with elevated left ventricular filling pressure in coronary artery disease patients with preserved ejection fraction**

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**Purpose:** We addressed if diastolic dysfunction with elevated left ventricular (LV) filling pressure was associated with obstructive sleep apnoea (OSA) in a cohort of patients with coronary artery disease (CAD) and preserved LV ejection fraction. The study was carried out within the framework of a randomized controlled trial (PAPI). The primary aim was to study the impact of OSA on cardiovascular outcomes in CAD patients with concomitant OSA.

**Methods:** Baseline sleep study recordings and echocardiographic measurements of 431 revascularized patients with CAD (age 63.7 ± 8.8 yrs; 82.5% men) with LV ejection fraction ≥ 50% were evaluated. OSA patients (n=331) had Apnea-Hypopnea-Index (AHI) > 15 events/h, and non-OSA patients (n=100) had AHI ≤ 5 events/h. Diastolic dysfunction with elevated LV filling pressure was defined as peak flow velocity in early diastole (E')/Tissue Doppler of early diastolic ventricular filling velocity was defined as ≥ 9 cm/s for women, or E'/E ≥ 9 and a left atrium diameter of ≥ 40 mm for men.

**Results:** Diastolic dysfunction with elevated LV filling pressure was more common among the OSA group (54.4% vs 41.0%, p=0.019). In a multivariate analysis, OSA was associated with diastolic dysfunction with elevated LV filling pressure (odds ratio [OR] 1.90, 95% confidence interval [CI] 1.13;3.18) adjusted for female gender (OR 2.28, 95% CI 1.28;4.07), hypertension (OR 1.84, 95% CI 2.01;2.82), diabetes mellitus (OR 2.45, 95% CI 1.42;2.43), age >60 yrs (n.s.), obesity (n.s.) and current smoking (n.s.).

**Conclusions:** In this CAD cohort with preserved LV ejection fraction, diastolic dysfunction with elevated LV filling pressure was associated with OSA independent of the traditionally recognized risk indicators.

**P6575 | BEDSIDE**

A good left ventricular diastolic performance is predictive of better outcome in young subjects in early phase of hypertension

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**Objective:** Echocardiographic data are important predictors of outcome in hypertensive but it is not clear which echocardiographic parameters have better prognostic capacity in particular in young subjects in stage I hypertension. In the present study we assessed the predictive value of structural and functional echocardiographic parameters for the development of hypertension in a cohort of young-to-middle-age subjects from the HARVEST study.

**Methods:** 674 adults (501 men, age=33.8±8.8 years) screened for stage I hypertension were considered. Patients were seen every six months to determine which subjects developed hypertension during the observation period (HT). Echocardiography and ambulatory blood pressure (BP) monitoring were performed at entry. Left ventricular (LV) mass index, relative wall thickness, LV stress, LV ejection fraction, and the E/A ratio as a measure of LV diastolic function were calculated. The predictive value of echocardiographic data was assessed in multivariable Cox analyses, adjusting for age, gender, body mass index, 24-hour systolic or diastolic BP, and lifestyle factors.

**Results:** During a median follow-up of 13.5 years 64.5% of the subjects developed HT. In a multi-variable Cox analysis, 24-h systolic BP (p=0.0009), 24-h diastolic BP (p=0.0005), coffee consumption (p=0.008), and the E/A ratio (inverse association, p=0.004) were independent predictors of outcome. None of the other echocardiographic parameters were associated with the risk of HT. In the subjects developing HT, the quintiles of E/A ratio, an increase in the rate of HT was observed going from the top (52%) to the bottom (70%, p for trend=0.0006) E/A quintile with a tendency to an inverted L-shaped relationship. Having an E/A ratio ≥ 1.68 (lower limit of the top quintile) showed a protective effect on the risk of HT compared to the subjects of the bottom quintile (hazard ratio= 0.57, 95%CI = 0.41–0.80, p=0.001).

**Conclusions:** These data show that a good LV diastolic performance is a better predictor of outcome in young subjects screened for stage 1 hypertension on the other hand structural and functional echocardiographic parameters are not predictive of outcome in this setting.

**P6576 | BEDSIDE**

**Relationship between left atrial volume and diastolic dysfunction in Nigerian hypertensives**

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**Purpose:** This study was designed to determine the usefulness of left atrial volume index (LAVI) as a surrogate marker of left ventricular diastolic dysfunction in Nigerian hypertensives.

**Methods:** Hypertensive subjects attending a cardiology practice in South Western Nigeria who were in sinus rhythm without a history of atrial arrhythmia or valvular heart disease and age and sex matched normotensive controls were recruited for the study. Transthoracic echocardiography was conducted for all the participants. Doppler indices of diastolic function were assessed and left atrial volume was measured using the biplane area length method and further indexed to body surface area. Associations between LAVI and diastolic dysfunction were examined.

**Results:** There were 200 subjects and 100 controls (age 55.8±11.4 vs 55.7±11.0yrs, p=0.92). The subjects had higher systolic blood pressure (SBP) and diastolic blood pressure (DBP). 141.1±23.6 vs 112.6±6.6mmHg and 84.8±14.9 vs 71.4±6.7mmHg, p<0.0001 respectively. The subjects also had significantly higher BMI than the controls, 27.3±5.0 vs 25.7±5.1, p=0.004. Among Nigerian hypertensives, height was a significant positive predictor of left atrial volume index by 0.6 mL/m2/p=0.001. Among Nigerian hypertensives, height was a significant positive predictor of left atrial volume index by 0.0006 mL/m2/p<0.0001. In this CAD cohort with preserved LV ejection fraction, diastolic dysfunction with elevated LV filling pressure was associated with OSA independent of the traditionally recognized risk indicators.

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LAVI to detect grade I, grade II, and grade III to IV DD was 0.70, 0.75 and 0.87 respectively, showing a progressive increase with worsening DD. Left atrial volume index performed better than LA linear M-mode dimensions in the detection of diastolic dysfunction.

**Conclusions:** Diastolic dysfunction is common in Nigerian hypertensives and LAVI to detect left atrial involvement with diastolic dysfunction. Left atrial volume index predicts the presence of diastolic dysfunction and has a graded increase with worsening diastolic dysfunction in Nigerian hypertensives.

### P6577 | BEDSIDE

High resting heart rate as a risk factor of recurrent hospitalisations in heart failure with preserved ejection fraction: results of the Preserved-DATA-HELP registry

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**Background:** High resting heart rate (HR) is common in patients with systolic heart failure (HF) and associated with poor outcome. Its reduction due to both β-adrenergic and I(f) current blockade has provided survival benefits in these patients. We investigated the prevalence of high resting HR in patients with HF with preserved ejection fraction (HFPEF), as well as links with clinical profile, applied treatment and hospitalisation rates.

**Methods:** During the DATA-HELP registry performed in 2009 in Poland among cardiologist and general practitioners outpatient clinics, we collected the data on 488 patients with HFPEF in a sinus rhythm with available resting HR (age: 67±11 yrs, men: 52%, BMI: 28.5±4.0 kg/m², LVEF: 52±15%, NYHA class III-IV: 17%, CCS class III-IV: 15%, previous MI: 45%, hypertension: 75%, diabetes: 32%).

**Results:** Among patients with HFPEF, a mean resting HR was 75±12 bpm with a median (lower and upper quartiles) of 75 (68-80) bpm. High resting HR (>70 bpm and ≥75 bpm) were found in 71% and 51% of patients, respectively, regardless on NYHA class (p<0.001) and although 96% of them received β-blockers. Treatment with either β-blockers or Ca2+ channel blockers did not differentiate resting HR (all p>0.2). Moreover, there were no associations between resting HR, and daily doses of particular β-blockers and Ca2+ channel blockers (all p>0.2). Lower CCS class, higher systolic blood pressure, jugular venous dilation, female gender and the treatment by general practitioner were independent predictors of high resting HR (all p<0.05). The higher the number of urgent cardiovascular hospitalisations during recent 12 months, the higher resting HR (for 0, 1-3 and ≥4 hospitalisations: - mean HR: 74±10, 75±12 and 87±17 bpm - p<0.001, HR>75 bpm: 45%, 54% and 88%, p=0.03). Also, the higher the number of other elective hospitalisations during recent 12 months, the higher resting HR (for 0, 1-3 and ≥4 hospitalisations: - mean HR: 75±10, 76±14 and 91±9 bpm - p<0.001, HR>75 bpm: 51%, 49% and 91%, p<0.003).

**Conclusions:** High resting HR is found in the majority of patients with HFPEF, regardless of NYHA class and therapies with β-blockers or Ca2+ channel blockers. High resting HR is associated with increased recent hospitalisation rates. Given these findings, HR reducing therapies and their effects on hospitalisation rates could be considered in patients with HFPEF.

### P6578 | BEDSIDE

Left ventricular involvement in type I gaucher disease

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**Purpose:** Type I Gaucher Disease (GD) is an autosomal recessive lysosomal storage disease characterized by multi-organ involvement. Right ventricular overload due to pulmonary hypertension is the most frequent cardiac manifestation, whereas a clear-cut left ventricular (LV) involvement has been reported only in a few cases of advanced disease stages. Accordingly, aim of the study was to evaluate LV geometry and function in a series of patients with GD.

**Methods:** Seventeen patients with Type I Gaucher Disease (GD) (median age = 46 yrs, interquartile range = 39–50), 17 age and sex-matched normal controls (NC) and 17 age and sex-matched hypertensive patients (HT) were compared by standard echo-Doppler examination. LV mass index (g/m²²), relative wall thickness and ejection fraction (%) were determined by 2D echo. Transmural E/A ratio, deceleration time of E velocity (DT, ms), atrial filling fraction (AFF = velocity time integral of A velocity / velocity time integral of total diastole x 100), E/e’ ratio and left atrial volume index (LAVI, ml/m²) were measured as indicators of LV diastolic function. Between-group comparison was carried out using Kruskal-Wallis test and ANCOVA.

**Results:** The 3 groups were comparable for body mass index, whereas heart rates were higher in HT (p<0.05). Eight GD patients showed higher resting HR ≥75 bpm were found in 71% and 51% of patients, respectively, regardless on NYHA class (p<0.001) and although 96% of them received β-blockers. Treatment with either β-blockers or Ca2+ channel blockers did not differentiate resting HR (all p>0.2). Moreover, there were no associations between resting HR, and daily doses of particular β-blockers and Ca2+ channel blockers (all p>0.2). Lower CCS class, higher systolic blood pressure, jugular venous dilation, female gender and the treatment by general practitioner were independent predictors of high resting HR (all p<0.05). The higher the number of urgent cardiovascular hospitalisations during recent 12 months, the higher resting HR (for 0, 1-3 and ≥4 hospitalisations: - mean HR: 74±10, 75±12 and 87±17 bpm - p<0.001, HR>75 bpm: 45%, 54% and 88%, p=0.03). Also, the higher the number of other elective hospitalisations during recent 12 months, the higher resting HR (for 0, 1-3 and ≥4 hospitalisations: - mean HR: 75±10, 76±14 and 91±9 bpm - p<0.001, HR>75 bpm: 51%, 49% and 91%, p<0.003).

**Conclusions:** High resting HR is found in the majority of patients with HFPEF, regardless of NYHA class and therapies with β-blockers or Ca2+ channel blockers. High resting HR is associated with increased recent hospitalisation rates. Given these findings, HR reducing therapies and their effects on hospitalisation rates could be considered in patients with HFPEF.

### P6579 | BEDSIDE

Value of diastolic function indexes during exercise echocardiography to predict outcome when mitral regurgitation information is available

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The ratio of left ventricular (LV) inflow early wave and tissue Doppler annulus early myocardial wave (E/e’) is a subrogate of LV filling pressures that can be assessed during exercise (Ex). Previous work has demonstrated the value of the increase of this ratio with Ex to predict outcome. We sought to assess the relative value of E/e’ during Ex-echocardiography (ExE) to predict outcome when information about intracardiac filling pressure with exercise (ExE) is available.

**Methods:** ExE with assessment of MR, LV inflow patterns and E/e’ at rest and at exercise were performed in 470 patients (298 men; age 62±2 years). An exercise Ps pattern was defined as the persistence of a resting Ps pattern, or a change from a normal/relaxed alteration pattern to a Ps pattern. Considered hard events were non-fatal myocardial infarction (MI) and overall mortality, and considered combined events were a hard event, stroke or late revascularization.[≥3 months after ExE] Cox regression analysis was performed to assess predictors of the end-points by a time to first event basis.

**Results:** There were 63 hard events (34 non-fatal MI and 29 deaths) and 85 combined events during a mean follow-up of 1.8±2.2 years. Independent predictors of combined events were a history of coronary artery disease (hazard ratio [HR]=1.88, 95% confidence interval [95CI]= CI=1.19-2.98, p=0.007), treatment with digoxin (HR=10.41, 95% CI=2.42-44.89, p=0.002), resting MR (HR=1.10, 95% CI=1.03-1.17, p=0.003), achieved workload in METs (HR=0.90, 95% CI=0.84-0.98, p=0.009), clinical symptoms during ExE (HR=1.94, 95% CI=1.16-3.24, p=0.007), positive ECG (HR=1.94, 95% CI=1.16-3.24, p=0.007) and increase in rate was higher in HT (p<0.05). Eight GD patients showed higher resting HR (≥75 bpm: 45%, 54% and 88%, p=0.03). Also, the higher the number of other elective hospitalisations during recent 12 months, the higher resting HR (for 0, 1-3 and ≥4 hospitalisations: mean HR: 75±10, 76±14 and 91±9 bpm - p<0.001, HR>75 bpm: 51%, 49% and 91%, p<0.003).

**Conclusions:** In conclusion, the diagnostic value of LV diastolic indexes for predicting outcome seems limited when strong information based on MR is available during ExE.