LONG-TERM OUTCOME AFTER PCI

2007 | BEDSIDE
Predictors of long-term outcomes following saphenous vein graft intervention: an observational analysis of 1,310 patients from the British Columbia Cardiac Registry

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Background: Saphenous vein grafts (SVG) intervention is associated with worse clinical outcomes compared with intervention of native coronary arteries. The use of a distal protection device (DPD) is a Class I indication, and whilst it enhances procedural safety, its effect on long-term outcomes is unknown. Data on the benefit of drug-eluting (DES) in these patients is conflicting. We evaluated whether DPD or DES use was associated with improved long-term outcomes.

Methods: We analyzed 1,310 patients undergoing isolated SVG intervention between 2008–2013 in the British Columbia Cardiac Registry, and analyzed mortality and target vessel revascularization (TVR) at 3 years. Multivariable models were used to determine independent predictors for outcomes.

Results: The overall mortality and TVR at 3 years was 19% and 25%. A DPD was used in 7.3% and DES in 63% (first-generation DES (F-DES) in 25% and second-generation DES (S-DES) in 75%). Multivariable analyses identified increasing age, diabetes, renal disease, cardiogenic shock, IABP use, peripheral vascular disease, ACS presentation, reduced post-procedural TIMI flow and bare metal stent (BMS) use as predictors of increased mortality. Although DPD use was a strong predictor for post-procedural TIMI 3 flow (OR=2.10, 95% CI: 1.31–3.33, p=0.001), it did not confer a mortality benefit (HR=1.16, 95% CI: 0.69–2.01, p=0.620). DES use was not associated with a reduction in TVR (HR=1.16, 95% CI: 0.89–1.51, p=0.621), and Kaplan-Meier analyses demonstrated comparable TVR for BMS, F-DES and S-DES.

Conclusions: This study represents the largest reported study with longest follow-up following SVG intervention. The use of DPD was not a predictor for long-term survival. Whilst DES use was a predictor for long-term survival, its use was not associated with reduced TVR.

2008 | BEDSIDE
Very long-term (10 to 14 years) outcomes after implantation of bare-metal stent

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Background: Long-term outcomes (≥10 years) after BMS implantation have not been well characterized from large-scale randomized registries.

Methods: The CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome study in Kyoto) registry is a multicenter registry enrolling consecutive patients undergoing first coronary revascularization between January 2000 and December 2002, excluding those with acute myocardial infarction within a week before the index procedure. A total of 5313 consecutive patients comprised of the current long-term (≥10 years) follow-up study.

Results: Mean follow-up duration for the survivors was 10.3±3.1 years (median 11.3 years, interquartile range 10.3–12.2 years, range 0.0–14.1 years). Late clinical follow-up information was obtained in 4901 (92.2%) patients at 5 years, and 4515 (85.0%) patients at 10 years. The all-cause mortality was 28% at 10 years. The incidences of myocardial infarction, definite stent thrombosis (ST) and target lesion revascularization (TLR) were 2.2%, 1.2% and 27% at 1 year; 4.8%, 1.4% and 32% at 5 years; and 8.8%, 2.1% and 36%, respectively. The steady rate of very late ST (>1 year) and TLR beyond 1 year were 0.1%/year and 1.0%/year, respectively, without any evidence of a plateau beyond 10 years (Figure). Multivariable Cox regression analysis showed younger age, male gender, and total stent length ≥28mm were independent risk factors for late TLR (>5 years), while current smoking habits at the time of index procedure was an independent predictor for definite ST beyond 5 years.

Conclusions: TLR beyond 1 year and very late ST (>1 year) after BMS implantation continued to occur without attenuation beyond 5 years.

Acknowledgement/Funding: the Research Institute for Production Development (Kyoto, Japan).

2009 | BEDSIDE
Long-term clinical outcomes of STEMI patients treated with BVS

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Background: Bioresorbable vascular scaffolds (BVS) are the newest interventional treatment for coronary artery disease. However BVS usage for patients presenting with ST-segment elevation myocardial infarction (STEMI) is still considered investigational.

Purpose: To examine the performance and feasibility of BVS usage in STEMI patients.

Methods: This is a prospective, single-arm, single-center study reporting data after implantation of a BVS in STEMI patients. Quantitative coronary angiography (QCA) data was evaluated and clinical events were reported. STEMI patients with age > 18 years and a culprit lesion in vessels between 2.0mm and 3.8mm (by online QCA) were included. Major exclusion criteria were known intolerance to contrast medium, previous CABG, previous PCI with the implantation of a metal stent, and age > 75 years.

Results: From November 2012 until December 2014, 160 STEMI patients underwent PCI with placement of one or more BVS. Mean age was 55.8 years, 73.1% was male, 10% had diabetes mellitus, 71.9% presented with single vessel disease. In <50% of the patients, the culprit lesion was located in the LAD. Thrombectomy was used in 79.4%. Predilatation was performed in 62.5%; post-dilatation in 42.5%. Clinical device success was 94.5%. Post-procedural TIMI III flow was achieved in 94.6%. Mean post-procedural %DS was 14%. Epifibatide was given in 33.8% of the patients. Survival status was available in 100%. 36 patients were excluded from further follow-up because of protocol-related exclusion criteria. 30/36 patients refused study related follow-up. In 109/ 124 (87.9%) patients, there was follow-up >30 days available. During a median follow-up time of 369 days (IQR 190–540), there were three cases of all-cause mortality, 9 cases of myocardial infarction (MI), 5 definite scaffold thrombosis (ST) (3 acute, 1 subacute and 1 very late), 5 target lesion revascularization (TLR), 7 target vessel revascularization (TVR) and 8 non-target vessel revascularization (non-TVR). Conclusions: BVS for primary PCI resulted in good procedural outcome, but the unexpected high number of definite stent thrombosis drives the search for optimal implantation strategy during primary PCI.

Acknowledgement/Funding: The institution Erasmus MC received research grants from Abbott. Robert-Jan van Geuns and Nicolas van Mieghem have received speakers fees from Abbott.

2010 | BEDSIDE
Long-term prognosis after exenatide treatment in patients with ST-segment elevation myocardial infarction

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Background: Treatment with the glucagon-like peptide-1 analogue exenatide administered at the time of reperfusion increases myocardial salvage in a population of ST-elevation myocardial infarction patients treated with primary percutaneous coronary intervention. Whether this effect will translate into improved clinical outcome remains unknown.

Purpose: In a post-hoc analysis we wanted to test if the cardioprotective effect of exenatide would have a beneficial effect on long-term outcome.

Methods: This is a post-hoc analysis of a randomized, double blind, placebo-controlled trial evaluating the cardioprotective effect of exenatide treatment per- formed at two university hospitals in Denmark. Outcome data were collected from Danish nationwide medical registries. All patients were followed from date of inclusion until death or December 2014. The primary endpoint was major adverse cardiac events (MACE), which was a composite of all-cause mortality and admis-
sion for heart failure. The secondary endpoints were admission for heart failure and all-cause mortality, respectively.

Results: A total of 334 patients with a first acute ST-elevation myocardial infarction were included in the present study and were randomized to receive exenatide (n=175) or placebo (n=159) in adjunct to primary percutaneous coronary intervention. Patient follow-up was a median of 5.2 years. MACE occurred in 95 (25%) patients with no difference between groups (24% versus 27%; p=0.52). However, admission for heart failure was significantly lower in patients treated with exenatide (11%) compared to patients treated with placebo (20%), yielding a hazard ratio of 0.53 (confidence interval: 0.30–0.93; p=0.042). There was no difference in all-cause mortality (14% versus 9%; p=0.18).

Conclusions: In ST-elevation myocardial infarction patients treated with primary percutaneous coronary intervention additional treatment with exenatide at the time of reperfusion reduced the rate of admission for heart failure, but did not reduce all-cause mortality or a composite endpoint of the two. Owing to small sample size these findings may only be considered hypothesis generating, but may encourage a larger multicenter study.

2011 | BEDSIDE
The longest available clinical follow-up of a cohort of real-world patients treated exclusively with drug-eluting stents

Background: There is still uncertainty about the durability of the results of drug-eluting stents (DES) in real-world complex patients (pts). We sought to provide the longest clinical follow-up data on outcomes of unselected patients treated solely with DES.

Methods: The DESIRE registry is a prospective, single-center registry encompassing all consecutive patients treated solely with DES since May 2002. The primary goal is the very long-term occurrence of MACE and stent thrombosis (ST). Patients were clinically followed at 1, 6 and 12 months and then annually. A multivariate model was built to determine independent predictors of MACE and ST.

Results: A total of 5,614 pts (8,825 lesions/9,980 DES) were included. The mean age was 64±11 years. DM was detected in 31.5% and 41.8% presented with acute coronary syndrome (STEMI) represented 16.8% of the cohort. Follow-up was obtained in 98.4% of the patients (median 5.9 years). Currently, 78.9% of the population is free of any MACE. Ischemia-driven TLR was performed in 7.3% of the patients. Q-wave MI rate was only 1.7% while cumulative incidence of definite/probable ST was 4.1%. Independent predictors of MACE were initial presentation as ACS (HR 1.4; 95% CI, 1.1 to 1.7, p=0.001), lesion length <20mm (HR 1.4; 95% CI, 1.2 to 1.6, p<0.001), residual stenosis (HR 1.02; 95% CI, 1.01 to 1.03, p<0.001), DM (HR 1.6; 95% CI, 1.1 to 2.2, p=0.005) and severe coronary calcification (HR 1.4; 95% CI, 1.1 to 1.8, p=0.004) while use of 2nd generation DES was protective (HR 0.7; 95% CI, 0.5 to 0.9, p=0.007). Independent predictors of ST were PCI for STEMI (HR 2.6; 95% CI, 1.6 to 4.3, p<0.001) and treatment of small vessels (HR 2.0; 95% CI, 1.3 to 3.3, p=0.002).

Conclusion: In our single center experience, the use of DES was associated with a long-term safety and effectiveness with acceptable low rates of adverse clinical events, including ST. Treatment of patients with ACS, in particular STEMI, increase the risk of adverse events while use of 2nd generation DES might be contraindicated.

2012 | BEDSIDE
Differential prognostic impact between 1st and 2nd generation drug-eluting stents in coronary bifurcation lesions: pooled analysis of the COBIS II, Excellent, and Resolute-Korea registries
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Purpose: To investigate the differential clinical outcomes after percutaneous intervention (PCI) for coronary bifurcation lesions with 1-stenting or 2-stenting techniques with the use of 1st or 2nd generation drug-eluting stent (DES).

Methods: Pooled analysis was performed with patients undergoing PCI using 1st or 2nd generation DES for bifurcation lesions with side branch diameter <2.3 mm from dedicated bifurcation PCI registry (COBIS II) and the largest 2nd generation DES registry (EXCELLENT, RESOLUTE-Korea registry) in Korea. The 3-year clinical outcomes were compared between 1- and 2-stenting techniques, stratified by the type of DES (1st or 2nd generation).

Conclusions: We identified 7 variables independently associated with late outcome following PCI with DES in a real-world population. CKD and insulin-treated diabetes were the strongest predictors. Accurate knowledge of clinically identifiable risk factors for ICTE events may be useful in individualizing potency and duration of DAPT after PCI.

Acknowledgement/Funding: Bristol-Myers Squibb and Sanofi - Aventis.
Background: There are no whole country studies of survival following percutaneous coronary intervention (PCI) to the unprotected left main stem (UPLMS) which account for background mortality.

Methods: We identified 11079 cases with ST-elevation myocardial infarction (STEMI), non ST-elevation acute coronary syndrome (NSTEACS) and elective chronic stable angina (CSA) who received UPLMS PCI, 2005 to 2014. We used age, sex, and calendar year-specific population mortality rates for England and Wales to calculate expected survival, and 5-year cumulative relative survival rate ratios (RSRR) using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR) for key covariates of interest.

Results: One and 5-year RSRRs were better in CSA group (97.5% versus 93.8%) compared to STEMI (64.1% versus 75.7%) and NSTEACS (84.6% versus 73.1%) (Fig 1). EMRR mortality increased significantly with age. For STEMI, EMRR was 2.18% (95% CI; 1.67 to 2.78) and 2.01 (95% CI; 1.47 to 2.76) for STEACS. For CSA, EMRR was associated with diabetes 2.21 (95% CI; 1.44 to 3.38), previous AMI 2.27 (95% CI; 1.39 to 3.71) and poor left ventricular ejection fraction (LVEF) 2.50 (95% CI; 1.44 to 4.35). For NSTEACS, EMRR was associated with renal failure 2.71 (95% CI; 2.28 to 3.22), moderate 2.20 (95% CI; 1.74 to 2.78) and poor LVEF 3.25 (95% CI; 2.58 to 4.10) while for STEMI EMRR was associated with renal failure 2.16 (95% CI; 1.47 to 3.19) and cardiogenic shock 6.96 (95% CI; 5.75–8.42).

Conclusion: Survival after UPLMS PCI for CSA is excellent and contrasts with STEMI and NSTEACS where patient characteristics are significantly associated with excess mortality. These phenotype-specific differences have implications for clinical risk assessment, patient prognosis, and future treatment strategies.

2915 | BEDSIDE

The optimal duration of dual antiplatelet therapy in patients receiving percutaneous coronary intervention with drug-eluting stents

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Background: The optimal duration of dual antiplatelet therapy (DAPT) following drug-eluting stent (DES) implantation remains a subject of ongoing debate.

Methods: We identified 11079 cases with ST-elevation myocardial infarction (STEMI), non ST-elevation acute coronary syndrome (NSTEACS) and elective chronic stable angina (CSA) who received UPLMS PCI, 2005 to 2014. We used age, sex, and calendar year-specific population mortality rates for England and Wales to calculate expected survival, and 5-year cumulative relative survival rate ratios (RSRR) using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR) for key covariates of interest.

Results: One and 5-year RSRRs were better in CSA group (97.5% versus 93.8%) compared to STEMI (64.1% versus 75.7%) and NSTEACS (84.6% versus 73.1%) (Fig 1). EMRR mortality increased significantly with age. For STEMI, EMRR was 2.18% (95% CI; 1.67 to 2.58) and 2.01 (95% CI; 1.47 to 2.76) for STEACS. For CSA, EMRR was associated with diabetes 2.21 (95% CI; 1.44 to 3.38), previous AMI 2.27 (95% CI; 1.39 to 3.71) and poor left ventricular ejection fraction (LVEF) 2.50 (95% CI; 1.44 to 4.35). For NSTEACS, EMRR was associated with renal failure 2.71 (95% CI; 2.28 to 3.22), moderate 2.20 (95% CI; 1.74 to 2.78) and poor LVEF 3.25 (95% CI; 2.58 to 4.10) while for STEMI EMRR was associated with renal failure 2.16 (95% CI; 1.47 to 3.19) and cardiogenic shock 6.96 (95% CI; 5.75–8.42).

Conclusion: Survival after UPLMS PCI for CSA is excellent and contrasts with STEMI and NSTEACS where patient characteristics are significantly associated with excess mortality. These phenotype-specific differences have implications for clinical risk assessment, patient prognosis, and future treatment strategies.

2916 | BEDSIDE

1-year angiographic and 5-year clinical outcomes of cobalt-chromium everolimus-eluting versus zotarolimus-eluting coronary stents in patients with multivessel CAD

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Objective: We aimed to compare angiographic and clinical outcomes after the implantation of cobalt-chromium everolimus-eluting, and zotarolimus-eluting (ZES) stents in patients with multivessel CAD.

Background: There are limited data on long-term outcome after EES vs ZES implantation in MVD patients.

Methods: We randomized 426 patients with multivessel coronary artery disease to EES (n=216) or ZES (n=210) implantation. Angiographic follow-up was performed 12 months after the index procedure and all patients were followed clinically for 5 years. The primary endpoint was angiographic in-stent late luminal loss at 12-month follow-up. Secondary endpoints included angiographic restenosis rate, the need for target lesion revascularization (TLR) and major adverse cardiac events (MACE; defined as cardiac death, myocardial infarction, definite stent thrombosis, or TLR) at 5-year follow-up.

Results: At 12-month angiographic follow-up, in-stent late lumen loss was 0.20±0.49 mm and 0.13±0.49 mm (p=0.16), and angiographic restenosis rate was 4.4% and 6.0% (p=0.57) in the EES and ZES groups, respectively. At 5-year clinical follow-up, MACE had occurred in 44 (20.4%) patients in the EES group and 50 (23.8%) patients in ZES group (HR 0.84, 95% CI 0.57–1.29; p=0.65), with TLR performed in 12 (5.6%) and 20 (9.5%) patients in the two groups [HR 0.38, 95% CI 0.30–1.33; p=0.21].

Conclusion: EES and ZES had comparable 12-month angiographic and 5-year clinical outcomes in patients with multivessel (2VD or 3VD) coronary artery disease.
tions as in the second Marfell group i.e. septal defects, coarctation of aorta, patent ductus arteriosus and Ebstein’s anomaly, the mortality was still nearly 10 times greater than in controls.

Conclusions: Despite the increased rate of survival in patients with congenital heart disease, the mortality risk in children and young adults is still high compared to general population. Our results stress the importance for further research about underlying mechanisms of death in this group of young patients.

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2926 | SPOTLIGHT
Down syndrome and congenital heart disease: surgical therapy, development of Eisenmenger syndrome and survival in 1,549 patients from the German national register for congenital heart defects
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Background and introduction: Patients with Trisomy 21 (Down syndrome, DS) are frequently affected by congenital heart disease (CHD) and are at higher risk for developing pulmonary hypertension and Eisenmenger syndrome (ES).

Purpose: To characterize DS patients based on the data of the German National Register for Congenital Heart Defects (NRCHD), to identify temporal changes in therapeutic strategies over the last decades and to analyze the impact of medical progress on developing ES as well as DS patients’ overall survival.

Methods: Inclusion of all patients in the NRCHD diagnosed with DS. Results: Overall, 1,549 DS patients were identified (53.2% female, mean age 14.4±10.4 years; leading diagnoses: AVSD [53.2%], VSD [25.8%], ASD [10.1%]). N=797 patients (50.3%) have been operated or treated interventionaly before the age of seven years. The likelihood of being treated with curative intention increased significantly over time (OR 1.013, [95% CI 1.004 – 1.024], p=0.006).

In parallel the likelihood of developing an ES, decreased over time (OR 0.872 [95% CI 0.849–0.893], p<0.0001). Comparing the rate of ES we found that 46.7% of patients in the birth cohort 1960–1969 had ES compared to only 0.25% for the birth cohort 2000–2009 (p<0.0001). Overall survival after 1, 10, 20 and 40 years was 98%, 96%, 94% and 79%, respectively. Patients with an ES had a significantly worse survival compared to those without an ES (HR 25.9 [95% CI 11.0–60.8], p<0.0001).

Conclusion: Preliminary data show no adverse event among ACHD using NOACs for prevention of thromboembolism. Distribution of CHD

2928 | BEDSIDE
Prognostic value of NT-proBNP after atrial redirection surgery
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Background: In systemic morphological right ventricles after atrial redirection surgery, NT-proBNP is correlated with NYHA-class, ventricular function and subaortic AV-valve regurgitation (TR).

Purpose: To assess the impact of NT-proBNP on adverse clinical events: This prospectively designed, longitudinal, observational study evaluated NT-proBNP in 116 patients (24.9±12.4 years old, NYHA class I/III 97/18/1, 71 men) relative to all cardiac causes of hospitalisation, heart failure, transplantation and death.

Results: The mean observation time was 7.3±2.4 years. In univariate Cox proportion analysis, the predictors for all causes of hospitalisation (n=41; 35.5%) were NT-proBNP (HR: 5.99; 95% CI: 3.21–11.18), NYHA class (HR: 2.98; 95% CI: 1.62–5.5), ventricular function (HR: 1.96; 95% CI: 1.27–3.02), TR (HR: 2.39; 95% CI: 1.48–3.59), ventricular septal defect repair (HR: 1.29; 95% CI: 1.08–1.53) and a history of supraventricular tachycardia (SVT) (HR: 7.13; 95% CI: 3.74–13.59). In multivariate Cox proportion analysis, NT-proBNP (HR: 3.71; 95% CI: 1.82–7.57), TR (HR: 2.09; 95% CI: 1.06–4.12) and SVT (HR: 8.00; 95% CI: 1.62–5.5) were independent predictors for all causes of hospitalisation (n=41; 35.5%). For heart failure, transplantation and death, the single predictors were NT-proBNP (HR: 20.67; 95% CI: 4.69–91.78), NYHA class (HR: 6.45; 95% CI: 2.75–15.14), ventricular function (HR: 2.70; 95% CI: 1.48–4.92), TR (HR: 4.11; 95% CI: 1.99–8.87), SVT (HR: 1.62–1.15), NYHA class (HR: 6.79; 95% CI: 1.75–26.28). Using ROC curves, the ability of NT-proBNP to detect patients at risk was greater for heart failure, transplantation and death (AUC: 0.94; 95% CI: 0.90–0.988) than for all causes of hospitalisation (AUC: 0.8; 95% CI: 0.713–0.887).

Conclusion: In systemic right ventricles, NT-proBNP is a useful risk predictor for all causes of hospitalisation and, in particular, for heart failure, transplantation and death. It therefore might be a useful tool for risk assessment in this patient population.

2927 | BEDSIDE
NOACs, Are they safe in congenital heart disease? First results of an international multicenter registry
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Purpose: Adults with congenital heart disease (ACHD) and non-valvular atrial amythymia (AA) have higher incidence of bleeding under the use of vitamin K antagonists (VKA) than adults with acquired heart disease. The Non-vitamin K antagonist oral anticoagulants (NOACs) for thromboembolic prevention (NOTE) registry was designed to evaluate the safety of NOACs among ACHD.

Methods: This is a multicenter prospective registry of ACHD using NOAC for the prevention of thromboembolism. At baseline, patient characteristics and medical history concerning anticoagulation, thromboembolic and bleeding events are collected. Patients are followed every 6 months to register efficacy and safety events (primary endpoints) as well as quality of life using Qol survey (SF-36) and adherence using Morisky-8 scale (secondary endpoints).

Results: So far 81 adults (mean age 50±14 years, 40% male) with various CHD using NOACs have been included. Indication for prevention of thromboembolism was non-valvular AA. Previously, 62% used vitamin K antagonist and 16% used anti-platelet agents. The mean CHA2DS2-VASc score was 1.8±1.3 and the median HASBLED score was 1 (IQR 0–1). General medication adherence in Morisky-8 scale consisted of low, medium and high adherence rate of 14.6%, 34.2% and 51.2% respectively. Mean Qol SF-36 physical score and mental score were impaired (45±11 and 48±11 respectively). During a cumulative follow-up of 32 patient years, no thromboembolism or major bleeding event occurred. Two patients switched back to VKA due to presumed side-effects such as dizziness and fatigue.
2929 | BEDSIDE
Cardiopulmonary adaptation to short-term high altitude exposure in adult Fontan patients
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Introduction: In Fontan patients, even a mild increase in pulmonary artery pressure can decrease cardiac preload and circulatory output. Nowadays, Fontan patients can easily travel to high altitude (3500 m) during holidays or for leisure activities. High altitude induced hypoxia mediates pulmonary vasoconstriction. Whether Fontan patients tolerate hemodynamically short-term high altitude exposure is unknown.

Methods: 17 adult Fontan patients and 15 healthy controls underwent cardiopulmonary exercise testing with measurement of pulmonary blood flow (PBF) with an inert gas rebreathing system in Bern (at 540 m above sea level; low altitude) and at an altitude of 2187 m (high altitude). All tests were performed within 12 weeks. Endpoints were the change in PBF at rest and during submaximal exercise between low and high altitude, and the respective change in exercise capacity measured as peak VO2.

Results: Fontan patients and controls were matched for age (28±7 years) and gender (56% female). Fontan patients had at any time lower oxygen saturations than controls (low altitude: 92±2% vs. 96%, high altitude: 85±3% vs. 88%).

Effective PBF at rest and at exercise was higher in controls than in Fontans, both at low and high altitude (figure 1). PBF increased 2-fold in Fontan patients and 2.5-fold in the control group during exercise, with no difference from low to high altitude (p=0.209). The relative reduction in peak VO2 at high altitude compared to baseline was more pronounced in the healthy control group than the Fontan patients (17±8% vs. 9±12%, p=0.005).

Conclusion: Short term high altitude exposure did not affect PBF in Fontan patients at rest and during exercise. High altitude related reduction of exercise capacity is more pronounced in healthy controls than Fontan patients.

2030 | BEDSIDE
Does fontan circulation engender progressive liver dysfunction?
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Introduction: Total cavopulmonary connection (TCP) forces systemic venous blood into the lungs, equalizing caval and pulmonary pressure. Chronic hepatic stasis generates a progressive liver dysfunction, eventually leading to cirrhosis.

Purpose: To investigate prospectively the hemodynamic changes and the liver status after TCP.

Methods: From March 2013 to December 2014, 64 TCP patients (pts) underwent cardiac catheterization and liver examination (blood tests, ultrasound and gastroscopy) at our center.

Results: Median age was 10 (5–32) yrs, median distance from TCP 10 (1–19) yrs. Catheterization showed the following data: pulmonary arterial pressure (PAP) 11±6 mm Hg, ventricular end-diastolic pressure (VEDP) 6.6±2.58 mm Hg, hepatic stiffness 16.63±5.96 KPa and/or inhomogeneous in 10 and 35 pts. Stiffness was 16.63±5.96 KPa and significantly related to time from TCP (r=0.33, p=0.01). A subgroup of patients showed a negative trend very early after TCP.

Conclusions: This is the largest prospective series showing that TCP engenders a progressive decrease of QSI and increase in VEDP, with a tendency to PAP and PVR to raise. This is balanced by the progressive development of venous collateral vessels, from both caval and hepatic systems. The hepatic stiffness increases with time, but cirrhosis and esophageal varices are found in few patients. Only a multidisciplinary approach will be able to identify patients at risk.

2931 | BEDSIDE
Left ventricular function as a predictor for long-term outcomes in marfan syndrome
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Background: Risk stratification in Marfan syndrome (MFS) has identified aortic diameter and family history as adverse factors. Left ventricular (LV) function may also be impaired in MFS, but the impact on prognosis is not yet defined.

Aims: This study examined the contribution of left ventricular function with other risk factors for adverse prognosis.

Methods: From 1988 to 2014, all adult MFS patients were enrolled in a prospective cohort study with annual echocardiographic imaging. Linear and Cox regression models were used to examine risk factors associated with progressive aortic dilatation, aortic dissection and mortality.

Results: The cohort of 224 MFS patients (age 28±13.3 years, 55% male) was followed for a median of 9.5 years (interquartile range 4–17 years, total 2488 patient-years). Baseline maximum aortic root diameter was 41±6±8.5 mm (Z-score = 2.6±2.1). Baseline systolic LV fractional shortening (FS) was 36±7±6.8% with an LV end-diastolic diameter of 53±2±7.8 mm and a LV end-systolic diameter of 34.0±6.7 mm.

During follow-up, 44 patients died and 41 patients experienced an aortic dissection. Both LV FS and aortic Z-score were independent predictors for mortality when controlled for age (respectively hazard ratio (HR) 0.89, 95% CI 0.80–0.96, p=0.003 and HR 1.35, 95% CI 1.09–1.66; p=0.006). The only independent predictor for aortic dissection was baseline aortic dilatation (HR 0.84, 95% CI 1.5–34.1; p=0.01), whereas annual aortic progression was trending (HR 1.4, 95% CI 0.9–2.1; p=0.072). Neither mortality nor dissection was associated to gender, family history or any of the systemic features in the revised Ghent nosology. Aortic dilatation progression rate was 1.04±1.1 mm/year, and did not correlate with baseline aortic diameter (r=0.04, p=0.678), Z-score (r=0.04; p=0.692) or age (r=-0.05; p=0.577).

Conclusions: The most important predictors of long-term mortality in MFS patients are baseline LV function and aortic diameter. Patients with a baseline aortic diameter >40 mm were 7 times more likely to suffer aortic dissection. The LV systolic function should be included in future risk stratification models. Phenotypic severity, according the revised Ghent nosology systemic score, is unrelated to the risk of death or dissection.

2932 | BEDSIDE
Super flexible replicas of complicated congenital heart disease employing with stereolithography and vacuum casting -a reliable simulator for surgical operation
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Background: Precise understanding of 3-dimensional anatomical structure is crucial for successful surgical operation in complicated congenital heart diseases (CHDs). Here we introduce a new technology that reproduces extremely flexible polyurethane biomodels of complicated CHDs by employing with stereolithography followed by vacuum casting.

Methods: The diagnosis of the 22 patients who needs heart replicas included tetralogy of Fallot with pulmonary atresia, double outlet right ventricle with non-committed ventricular septal defect, hypoplastic left heart syndrome, tricuspid atresia, total anomalous pulmonary venous drainage, and congenitally corrected transposition of the great arteries. Three-dimensional volumetric datasets of CHSTs were used to examine risk factors associated with progressive aortic dilatation, aortic dissection and mortality.

Results: During follow-up, 44 patients died and 41 patients experienced an aortic dissection. Both LV FS and aortic Z-score were independent predictors for mortality when controlled for age (respectively hazard ratio (HR) 0.89, 95% CI 0.80–0.96, p=0.003 and HR 1.35, 95% CI 1.09–1.66; p=0.006). The only independent predictor for aortic dissection was baseline aortic dilatation (HR 0.84, 95% CI 1.5–34.1; p=0.01), whereas annual aortic progression was trending (HR 1.4, 95% CI 0.9–2.1; p=0.072). Neither mortality nor dissection was associated to gender, family history or any of the systemic features in the revised Ghent nosology. Aortic dilatation progression rate was 1.04±1.1 mm/year, and did not correlate with baseline aortic diameter (r=0.04, p=0.678), Z-score (r=0.04; p=0.692) or age (r=-0.05; p=0.577).

Conclusions: The most important predictors of long-term mortality in MFS patients are baseline LV function and aortic diameter. Patients with a baseline aortic diameter >40 mm were 7 times more likely to suffer aortic dissection. The LV systolic function should be included in future risk stratification models. Phenotypic severity, according the revised Ghent nosology systemic score, is unrelated to the risk of death or dissection.

Figure 1
and reproducibility of the replicas was evaluated by pediatric cardiologists and cardiac surgeons using questionnaires.

Results and conclusions: Wide variety of biomodels of complicated CHDs from neonates to adults was reproduced. Pediatric cardiologists and cardiac surgeons highly evaluated these biomodels as reliable simulators for cardiac surgery. This technology allowed surgeons to precisely understand the internal chambers of the heart and allowed them to perform surgery simulation by way of cutting and suturing like a real heart tissue. These polyurethane biomodels were instructive for medical students, young surgeons, patients and parents to understand the complex structures and hemodynamics of the disease.

Acknowledgement/Funding: Japanese Ministry of Health Welfare and Labor

2933 | BEDSIDE
Right atrial flow patterns in the normal heart - a new clue in the patent foramen ovale and cryptogenic stroke


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Background: 40% of ischaemic strokes in those under 55 are termed cryptogenic (no identifiable cause). Frequency of patent foramen ovale (PFO) is twice that of the general population in this group (50%-55%). 4D flow MRI may reveal haemodynamic clues to the nature of this relationship.

Aim: To determine the nature of right atrial flow in PFO and cryptogenic stroke versus controls.

Methods: 12 pairs of objects (40-79 years, 7male) with cryptogenic stroke and PFO on TOE and 12 controls (40±7 years, 6male) underwent 4D flow MRI at 3T (retrospective ECG-gated, respiratory-gated TFE, venc: 150/5ms, spatial res: 3mm², temporal res: 50-55ms, SENSE 2). The right atrium was manually defined and flow visualised with streamlines. Peak and average velocity were assessed. Controls were positioned orthogonal to the SVC and IVC to assess flow and spatial arrangement. 8 subjects underwent repeat scans for reproducibility.

Results: BMI, heart rate and systolic BP compared between groups. Diastolic BP was higher in PFO group (90±16 vs. 81±17, p<0.05). A spectrum of right atrial flow patterns were seen (vortex, helico-vortical, helix, multiple vortices). Absence of the “standard” vortex was notable in the stroke group (table). Helico-vortical flow was associated with a trend to reduced IVC flow (p=0.06) and reduced atrial velocities (p<0.06). In the right-left plane the IVC was more medial to the SVC in the stroke group (105±5mm vs. 3±11, p=0.002). This corresponded to flow patterns (table). The antero-posterior relationship of the vena cava was constant. Flow patterns were consistent in all repeated scans. Reproducibility of SVC and IVC flow was 5–10% and 10–15% and peak and average atrial velocity were 10–15% and 5%.

Table 1

<table>
<thead>
<tr>
<th>Controls</th>
<th>PFO/Stroke</th>
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<tbody>
<tr>
<td>Vortex</td>
<td>8</td>
</tr>
<tr>
<td>Other patterns</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Right atrial flow patterns</th>
<th>Controls</th>
<th>PFO/Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vortex</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Helico-vortical</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Helix</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Multiple Vortices</td>
<td>4</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Conclusion: A spectrum of right atrial flow patterns occur in the normal heart. Non-vortical patterns are more frequent in cryptogenic stroke with PFO. The relative position of the vena cava appears to be influential in their generation. The mechanistic implications of this warrants further investigation.

2934 | BEDSIDE
Lifelong endocarditis prophylaxis for congenital heart disease patients with prosthetic material?

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Background: Risk for infective endocarditis (IE) in adult congenital heart disease (ACHD), determined in retrospective studies, is found to be increased. This is largely attributed to prosthetic material used for repair or palliation, complex defects and residue. Guidelines recommend IE prophylaxis up to six months after complete repair of congenital heart disease with prosthetic material. Whether this is sufficient has never been determined in a prospective study.

Purpose: To prospectively determine incidence of and risk factors for IE in a large ACHD cohort.

Methods: We selected all patients included in a large registry of adult congenital heart disease. Incidence of IE was determined using Poisson regression. Predictors for IE were identified using time-dependent Cox regression.

Results: During a cumulative follow-up of 108499 patient-years in 15284 patients (51% female, median age 34 years), 83 IE episodes occurred in 77 patients. 556 (3.6%) patients had a currently cyanotic defect, 5878 (38.5%) had prosthetic material implanted. IE incidence was 0.76 episodes/1000 person-years (95% CI: 0.61–0.94), and did not differ between before and after the new ESC IE-prophylaxis guidelines of 2009. In multivariable Cox regression, male sex (HR=1.88; 95% CI: 1.19–2.99), history of IE (4.17; 2.27–7.65) and prosthetic material (2.84; 1.77–4.57) independently predicted IE. Complex cyanotic ACHD did not (1.29; 0.50–3.23).

Conclusions: The incidence rate of IE in ACHD patients is 0.76/1000 patient years, which is ~15 times the general risk. Prosthetic material is an important risk factor, imposing ~3 times greater risk. These findings suggest IE prophylaxis may be warranted in all ACHD patients with prosthetic material.

Acknowledgement/Funding: The work described in this study was carried out in the context of the Parelinsor Institute (PSI).

THE INCREASING EVIDENCE FOR CARDIAC REHABILITATION

2935 | BEDSIDE
Is cardiac rehabilitation (CR) safe and useful in octogenarians after transcatheter aortic valve implantation (TAVI) compared to surgical aortic valve replacement (sAVR) for aortic stenosis?

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Purpose: To prospectively determine incidence of and risk factors for IE in a large ACHD cohort.

Methods: From January 2010 to June 2013 58 consecutive TAVI (27% male, age 86±5, 25 Edwards, 33 CoreValve) and 52 consecutive AVR (44% male, age 82±4) aged >80 years were enrolled in a 3-week intensive CR program (walking, up to 30 minutes of cycling or treadmill session twice daily, respiratory training).

Results: Compared to AVR, TAVI patients had a frail index (FI) at discharge which were assessed; a frail index (FI) at discharge was defined as the presence of at least two of the following: 6MWT <200m, BI <75, MFS >30.

Table 1

<table>
<thead>
<tr>
<th>TAVI</th>
<th>AVR</th>
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<tbody>
<tr>
<td>CIRS-CI (M±SD)</td>
<td>4.6±1.5</td>
</tr>
<tr>
<td>BI discharge (M±SD)</td>
<td>84.15</td>
</tr>
<tr>
<td>MFS discharge (M±SD)</td>
<td>32.16</td>
</tr>
<tr>
<td>Training on 10W or 1,5 km/h twice/d (%)</td>
<td>91.16</td>
</tr>
<tr>
<td>6MWT discharge (M±SD)</td>
<td>168.131</td>
</tr>
<tr>
<td>FI (%)</td>
<td>16 (27)</td>
</tr>
<tr>
<td>AP (M±SD)</td>
<td>1.20±0.8</td>
</tr>
<tr>
<td>Death at follow up (%)</td>
<td>19 (33)</td>
</tr>
</tbody>
</table>

Conclusion: In octogenarians after TAVI, as in patients after AVR CR is safe and useful because it leads to disability and functional capacity recovering favoring the probability of safe discharge at home. However, compared to sAVR TAVI tolerated reduced training workloads and maintained at discharge a higher FI which is expected to have influenced survival at follow up.
2936 | BESIDE
Secondary prevention after myocardial infarction widens health disparities between Swedish and immigrant patients
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Background and introduction: Immigrants bear a disproportionate burden of poor cardiovascular health. Secondary prevention programs are essential for patients with a recent myocardial infarction (MI) as modification of risk factors favorably impacts their health. However, little is known about whether disparities in cardiovascular health are influenced by secondary prevention.

Purpose: The purpose of this study was to determine if secondary prevention interventions narrowed disparities in cardiovascular health between Swedish and immigrant MI patients.

Methods: A cohort of 400 MI patients (58.6±8 years) was followed for two years, 292 Swedish and 108 immigrants (71% men). During the first year after MI patients participated in a secondary prevention program. The average number of six selected risk factors, before and two years post MI was evaluated and the mean change in risk burden from baseline calculated. The risk factors were current smoking, BMI ~30 kg/m², total cholesterol >4.5 or LDL >2.5 mmol/l (in accordance with reference values at the time of the study), HDL ~1.0 mmol/l, blood pressure >140/90 mmHg and HbA1c ~45 mmol/mol (>52 mmol/mol for diabetic patients).

Results: There were significant differences in risk factor exposure between Swedes and immigrants among men (p<0.005) and women (p<0.003) two years after MI. Among MI patients aged 65 years or more, a beneficial effect was seen. CO2 peak at four months (24.3 ml/kg/min versus 20.7 ml/kg/min, p<0.004) and the explorative outcomes (six minute walking test (591.5 meters versus 576.3 meters, p<0.02) and sit-to-stand (16.0 times versus 15.5 times, p<0.004). However, we found no significant effect on the Short-Form 36 mental component score at six months (53.8 versus 51.9 points, p=0.20). We found no significant differences between the cardiac rehabilitation and control group in self-reported AF symptoms at six months (p=0.55). Self-reported adverse events were registered by 18 patients in the rehabilitation group and 7 in the control group (p=0.02). Two serious adverse events (atrial fibrillation in relation to physical exercise and death (not assessed as related to rehabilitation)) occurred in the intervention group and one patient died in the control group (not assessed as related to rehabilitation) (p=0.56).

Conclusion(s): Participating in six months comprehensive cardiac rehabilitation has a positive effect on physical capacity compared with control, but shows no effect on mental health. Moreover, cardiac rehabilitation caused more adverse events. This calls for more attention towards rehabilitation for patients with atrial fibrillation and the need for a prioritization of health and exploring events.

Acknowledgement/Funding: the Danish Strategic Research Council. The Heat centre, Rigshospitalet, Dk. Metropolitan University College, Dk. The Lundbeck Foundation, Dk.

2937 | BESIDE
Optimizing patient benefit from CRT response with the addition of high intensity interval training - a randomized controlled trial
R. Pinto1, A. Abreu2, V. Santos1, X. Melo1, P. Cunha1, M. Oliveira1, R. Soares1, R. Ferreira1, B. Fernhali1, H. Santa Clara1, 1University of Lisbon, Faculty of Human Kinetics, Lisbon, Portugal, 2Hospital Santa Marta, Department of Cardiology, Lisbon, Portugal

Background: Cardiac resynchronization therapy (CRT) improves prognosis, leading to reverse remodeling with a reduction in left ventricular (LV) size, improvement in the LV ejection fraction (LVEF) and systolic volume. However, 30–40% of patients who underwent CRT are non-responders. The addition of aerobic training to CRT may provide further benefit. Moderate aerobic exercise training (MAE) has been tested in CRT patients resulting in improvements in functional hemodynamics, exercise capacity and quality of life, but data on high intensity interval training (HIIT) effects are scarce. HIIT is more effective than MAE for improving exercise capacity in stable patients with heart failure. It is unknown whether the beneficial effects of HIIT may be observed in patients following CRT with less functional impairment.

Purpose: Evaluate the effect of a 6 month combining CRT and HIIT on exercise capacity, cardiac remodeling parameters and functional capacity.

Methods: Participants were recruited at the University Hospital of Coimbra and randomized into two groups: (A) a combination of CRT and HIIT or (B) CRT only. HIIT consisted of eight 4-min intervals on a cycle ergometer (200 W, 30 s interval). Participants were asked to maintain a heart rate above 75% of maximum. The primary outcome was VO2 peak measured by exercise testing. The secondary outcomes plus usual care (intervention group) or usual care alone (control group) stratified by type of atrial fibrillation (paroxysmal or persistent) and sex. The primary outcome was VO2 peak measured by exercise testing. The secondary outcome was mental health measured by Short-Form 36. The explorative outcomes included six minute walk test and sit to stand test.

Results: Based on sample size calculation, 210 patients were included. 74% were men, the mean age was 59 years, 72% had paroxysmal, and 28% had persistent atrial fibrillation prior to ablation. Cardiac rehabilitation compared with usual care showed a significant benefit of VO2 peak at four months (24.3 ml/kg/min versus 20.7 ml/kg/min, p<0.004) and the explorative outcomes (six minute walking test (591.5 meters versus 576.3 meters, p<0.02) and sit-to-stand (16.0 times versus 15.5 times, p<0.004). However, we found no significant effect on the Short-Form 36 mental component score at six months (53.8 versus 51.9 points, p=0.20). We found no significant differences between the cardiac rehabilitation and control group in self-reported AF symptoms at six months (p=0.55). Self-reported adverse events were registered by 18 patients in the rehabilitation group and 7 in the control group (p=0.02). Two serious adverse events (atrial fibrillation in relation to physical exercise and death (not assessed as related to rehabilitation)) occurred in the intervention group and one patient died in the control group (not assessed as related to rehabilitation) (p=0.56).

Conclusion(s): Participating in six months comprehensive cardiac rehabilitation has a positive effect on physical capacity compared with control, but shows no effect on mental health. Moreover, cardiac rehabilitation caused more adverse events. This calls for more attention towards rehabilitation for patients with atrial fibrillation and the need for a prioritization of health and exploring events.

Acknowledgement/Funding: the Danish Strategic Research Council. The Heat centre, Rigshospitalet, Dk. Metropolitan University College, Dk. The Lundbeck Foundation, Dk.

2938 | BESIDE
Comprehensive rehabilitation for patients treated for atrial fibrillation with ablation; Results from the CopenHeartRFA randomized trial
S.S. Rison1, A.D.Z. Zwiers2, J.H.S. Swendsen1, T.B.R. Rasmussen1, K.L.S. Siblitz1, T.L.S.M. Madsen2, C.G. Glud3, J.L. Lindschou2, P.W. Winkel1, S.K.B. Berg1 on behalf of The CopenHeart Group, 1Rigshospitalet - Copenhagen University Hospital, Dept of Cardiology, Odense, Dk. Metropolitan University College, Copenhagen, Denmark, 2Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark

Background: Ablation for atrial fibrillation is an invasive treatment with a success rate of around 70%. Even so patients often report lower physical activity levels and perceived health compared to the general population. In order to try to increase physical activity and perceived health we conducted a randomized clinical trial.

Purpose: To assess the effect of comprehensive cardiac rehabilitation versus usual care for patients treated for atrial fibrillation with ablation.

Methods: The participants were randomized 1:1 to 6 months cardiac rehabilitation consisting of 12 weeks of education, feedback, video consultations plus usual care (intervention group) or usual care alone (control group) stratified by type of atrial fibrillation (paroxysmal or persistent) and sex. The primary outcome was VO2 peak measured by exercise testing. The secondary outcome was mental health measured by Short Form-36. The explorative outcomes included six minute walk test and sit to stand test.

Results: Based on sample size calculation, 210 patients were included. 74% were men, the mean age was 59 years, 72% had paroxysmal, and 28% had persistent atrial fibrillation prior to ablation. Cardiac rehabilitation compared with usual care showed a significant benefit of VO2 peak at four months (24.3 ml/kg/min versus 20.7 ml/kg/min, p<0.004) and the explorative outcomes (six minute walking test (591.5 meters versus 576.3 meters, p<0.02) and sit-to-stand (16.0 times versus 15.5 times, p<0.004)). However, we found no significant effect on the Short-Form 36 mental component score at six months (53.8 versus 51.9 points, p=0.20). We found no significant differences between the cardiac rehabilitation and control group in self-reported AF symptoms at six months (p=0.55). Self-reported adverse events were registered by 18 patients in the rehabilitation group and 7 in the control group (p=0.02). Two serious adverse events (atrial fibrillation in relation to physical exercise and death (not assessed as related to rehabilitation)) occurred in the intervention group and one patient died in the control group (not assessed as related to rehabilitation) (p=0.56).

Conclusion(s): Participating in six months comprehensive cardiac rehabilitation has a positive effect on physical capacity compared with control, but shows no effect on mental health. Moreover, cardiac rehabilitation caused more adverse events. This calls for more attention towards rehabilitation for patients with atrial fibrillation and the need for a prioritization of health and exploring events.

Acknowledgement/Funding: the Danish Strategic Research Council. The Heat centre, Rigshospitalet, Dk. Metropolitan University College, Dk. The Lundbeck Foundation, Dk.
Conclusions: CR as provided in Denmark can be considered cost neutral and with a high participation rate. CR is associated with more outpatient visits however no significant differences occurred in terms of overall total cost. Further studies should investigate the benefits of CR to heart valve surgery patients on patient reported outcomes e.g. health-related quality of life as part of a formal cost-utility analysis.

2940 | BEDSIDE
Effectiveness of cardiac rehabilitation in patients with type 2 diabetes mellitus after percutaneous coronary intervention

Introduction: Patients with diabetes mellitus are at increased risk of recurrent cardiovascular events after percutaneous coronary intervention.

Purpose: The aim of this study was to assess if cardiac rehabilitation decreases mortality and recurrence of cardiovascular events in this subgroup of patients after percutaneous coronary intervention.

Methods: We performed a retrospective cohort study of 318 consecutive patients with type 2 diabetes mellitus who underwent percutaneous coronary intervention in our hospital between September 2004 and January 2011. We classified the patients in two cohorts according to their participation (n=154) or not (n=164) in a cardiac rehabilitation programme. Events occurring in the first 2 years of follow-up were recorded.

Results: CR was associated with a significant decrease in all-cause mortality (OR 0.105 [95% CI: 0.31–0.356]; p<0.001) and cardiac mortality (OR 0.107 [95% CI: 0.24–0.468]; p<0.001) over a two year follow-up. No significant differences were observed in nonfatal myocardial infarction, stent restenosis and nonfatal stroke.

Conclusion: Participation in a CR programme after percutaneous coronary intervention is associated with a significant reduction in cardiac mortality and all-cause mortality rates in type 2 diabetic patients.

2943 | BEDSIDE
Clinical predictors of exercise-induced regression of coronary atherosclerosis: a serial intravascular ultrasonography study
1 Norwegian University of Science and Technology, Department of Circulation and Medical Imaging, Trondheim, Norway; 2 Norwegian University of Science and Technology, Department of Laboratory Medicine, Children’s and Women’s Health, Trondheim, Norway; 3 St. Olav’s Hospital, Department of Cardiology, Trondheim, Norway

Background: Aerobic exercise induces beneficial changes in coronary atherosclerosis via reduced necrotic core (NC) and plaque burden (PB). The purpose of the study was to identify potential clinical predictors of regression of coronary atherosclerosis following aerobic exercise.

Methods: Post-hoc analysis of associations between baseline clinical variables and reductions in coronary NC and PB following aerobic exercise intervention. Plaque characteristics were measured with grayscale and radiofrequency intravascular ultrasound in 36 patients (median age 58.5 years, 7 women) with stable coronary artery disease (SCAD) or non-ST-elevation acute coronary syndrome (NSTE-ACS). Screening of variables was performed with random forest analysis followed by multivariate linear regression.

Results: The only significant variable for NC reduction was clinical presentation of disease (SCAD vs. NSTE-ACS, p=0.011). The change in NC was 4.94 (−10.33; −1.33) mm³ in patients with SCAD, and 1.03 (−4.29; 3.71) mm³ in patients with NSTE-ACS (p=0.01). NC was reduced in 17 patients (94%) with SCAD and 8 patients (44%) with NSTE-ACS (p=0.01, Figure). R-squared for the model including baseline clinical presentation and baseline NC volume was 0.96. There were no significant explanatory variables for PB reduction.

Conclusions: Exercise-induced plaque stabilization via reduced NC may be strongly dependent on clinical presentation of disease. We hypothesize that an increased pro-inflammatory load renders patients with NSTE-ACS more resistant to exercise-induced plaque stabilization than patients with SCAD. Furthermore, aerobic exercise may have a particular potential for inducing beneficial effects on coronary atherosclerosis in patients with SCAD compared to patients in the early phase following an acute coronary syndrome.

2944 | BEDSIDE
Effect of exercise training on functional capacity and oxygen uptake kinetics in patients with restrictive cardiomyopathy

Introduction: Restrictive cardiomyopathy (endomyocardial fibrosis-EMF) is characterized by fibrotic process in the endocardium of one/or both ventricles. This results in ventricular walls thickening, which leads to diastolic dysfunction. EMF patients have reduced functional capacity which is associated with increased mortality. However, it is still unknown if exercise could improve functional capacity and oxygen uptake kinetics (ΔVO2peak/ΔWatts) in this patients.

Conclusions: SDB is prevalent in CR patients and is independently predicted by aging and obesity. The association between SDB and poorer exercise capacity may be explained by age, gender, and waist circumference.
**Purpose:** The aim of this study was to evaluate the effect of exercise training on:
1. oxygen consumption (VO2peak).
2. ΔVO2peak/ΔWatts.
3. oxygen pulse (ΔVO2peak/ΔHR).
4. quality of life in patients with EMF.

**Methods:** 19 patients were allocated: sedentary EMF (Sed-EMF; n=11) and training EMF (Tr-EMF; n=8). VO2peak, ΔVO2peak/ΔWatts and VO2peak/ΔHR, by cardiopulmonary exercise testing, and quality of life by Minnesota Living with Heart Failure Questionnaire were evaluated. Left ventricle ejection fraction (LVEF) were evaluated by echocardiography (Simpson). Exercise training were performed for 4 months, 3 times/week, each session: 40 minutes of cycling (intensity between anaerobic threshold and respiratory compensation point) and strength training (mild to moderate intensity).

**Results:** There were no differences between groups for age (57±2 vs 55±3 years, p=0.79, respectively), gender (female=7/male=1 vs. female=9/male=2ex, p=0.64, respectively), and LVEF (55±4 vs 53±3, p=0.70, respectively). After 4 months, VO2peak did not change in Tr-EMF (18±1.1 to 19±1.3 vs. 15.5±0.8 to 15.4±0.7 ml/kg/min; p=0.38, respectively). VO2peak/HR increased in Tr-EMF (9.20±0.79 to 10.17±0.84 vs. 9.17±0.58 to 8.84±0.34 ml/kg/min; p=0.04, respectively). Peak heart rate did not change (128±5 to 114±7 vs. 122±5 to 129±5 beats; p=0.64, respectively). Tr-EMF increased power output (61±6 to 86±7 vs. 56±4 to 56±5 Watts; p=0.001, respectively). ΔVO2peak/ΔWatts decreased in Tr-EMF (12.47±0.85 to 9.89±0.52 ml/min/Watts; p=0.05) and it showed a significant improvement when compared to Sed-EMF (12.29±0.69 to 12.37±0.55 ml/min/Watts; p=0.04, respectively). Quality of life improved in Tr-EMF (47±28 vs 27±6 vs. 49±5 vs 46±26 score; p=0.04, respectively).

**Conclusion:** Exercise training in patients with EMF improved the oxygen consumption distribution in the exercised muscle (oxygen uptake kinetics) with improved tissue perfusion and additional information to the VO2peak, suggesting that other variables of cardiac adaptation to exercise compared to male counterparts with lesser wall thickness is a common phenotype, it should raise suspicion of underlying cardiomyopathy patients.

**SPORTS CARDIOLOGY IN DEVELOPMENT**

**2966 | BEDSIDE**

High aerobic capacity is associated with increased survival. A 44 years follow-up of the study of men born in 1913

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**Background:** Previous studies have shown an association between high aerobic capacity and increased survival during short and intermediate follow-up. However, the predictive power of aerobic capacity regarding survival over 44 years of follow-up is unknown.

**Purpose:** To study the predictive power of aerobic capacity regarding survival over 44 years of follow-up.

**Methods:** The study is part of “The Study of Men born in 1913”, a longitudinal prospective study of men, living in a city in Sweden. A random sample of 855 men was followed from 50 to 98 years of age with repeated examinations and by linkage to the National Hospital Discharge and Cause of Death registers. In 1967, at the age of 54, 792 men participated in a bicycle exercise test of whom 656 (83%) performed maximum exercise. Predicted VO2max was based on measurements in a subsample of participants. Risk factor levels were assessed at clinical examination.

**Results:** High VO2max during maximum exercise, no smoking, low serum cholesterol and low mean arterial blood pressure at rest were all significantly associated with survival in a Cox regression analysis (p<0.001 for all). In multivariable analysis including body height as a variance reducer, the association between VO2max tertiles and survival was independent of established risk factors; Hazard Ratio (HR) 0.79 (0.71–0.89) (p=0.001) for VO2maxHR, 1.01 (1.02–1.02), (p=0.01) for mean arterial blood pressure at rest, HR 1.13 (1.04–1.22), (p<0.005) for serum cholesterol and HR 1.58 (1.34–1.85) (p<0.001) for smoking. The variable impactful (Wald’s c2) of maximum VO2 tertiles (15.3) was secondary only to that of smoking habits (31.4). The benefit of high VO2max was confirmed through four decades of follow-up after exercise testing.

**Conclusion:** In a Swedish sample of middle-aged men, high aerobic capacity versus a low one, was associated with increased survival during more than forty years of follow-up. This effect was independent of traditional risk factors including smoking, blood pressure and serum cholesterol.

**Acknowledgement/Funding:** Insurance company Förensade Liv

**2967 | BEDSIDE**

Effect of gender and sporting discipline on left ventricular adaptation to exercise


**Purpose:** Studies in female athletes indicate that they exhibit limited cardiovascular adaptation to exercise compared to male counterparts with lesser wall thick-
Results: We evaluated 112 veteran athletes (M=81, F=31, mean age=55.9±1.6) and 18 healthy aged matched sedentary controls (M=10, F=8). The lowest incidence of significant CAC was observed in athletes running <20 miles per week and finishing marathons in 2:45–3:15h for males and running 20–30 miles per week and finishing marathons in 3–3:30h for females (see diagram). Running more or less than those mileages and running slower or faster than these marathon times conferred unfavourable CAC. Male athletes who run faster and longer than those ranges had a 2–3 fold increase in CAC after 70 centile (39% vs 13%, p=0.037 for weekly mileage).

Conclusion: These data indicate a U shaped relationship between the dose of exercise and coronary artery calcification in both male and female veteran athletes. Running at modest duration and intensity is more beneficial than no exercise and coronary artery calcification in both male and female veteran athletes. Running at modest duration and intensity is more beneficial than no exercise and coronary artery calcification in both male and female veteran athletes.

GENETICS ASPECTS OF ARRHYTHMIAS

2897 | BEDSIDE
Role of electrophysiological study for risk stratification of asymptomatic patients with Brugada syndrome: a meta-analysis
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Introduction: Brugada syndrome (BrS) is an inherited channelopathy associated with an increased risk of sudden cardiac death. An implantable cardioverter defibrillator (ICD) may be considered for patients with BrS. The available evidence does not support a significant role of EPS for risk stratification of asymptomatic patients with BrS. We performed a meta-analysis of published trials to examine the role of electrophysiological study (EPS) for risk stratification of asymptomatic patients with BrS.

Methods: We searched MEDLINE and EMBASE databases for studies evaluating the predictive accuracy of EPS in patients with BrS. Trials which reported outcomes in asymptomatic patients were included. Among studies pertaining to the same patient cohort, only the largest study was retained to avoid duplication of data. Risk ratios (RR) with 95% confidence interval (CI) were calculated using a random effects modeling approach.

Results: Sixteen studies involving 2,997 patients with BrS were included. Of those, 1,278 (43%) patients were asymptomatic and underwent an EPS. EPS was positive in 540 of 1,278 (42%) asymptomatic patients. During a median follow up of 34 months, 38 (3%) asymptomatic patients had an arrhythmic event. Based on the pooled estimate across the 16 studies, inducibility of ventricular tachycardia/arrhythmia (VT) during EPS failed to predict arrhythmic events during follow up (RR 1.50, 95% CI 0.77 to 2.91, p=0.23. Figure).

Conclusion: Inducibility of VT during EPS does not predict future arrhythmic events in asymptomatic patients with BrS. The available evidence does not support a significant role of EPS for risk stratification of asymptomatic patients with BrS.

2988 | BEDSIDE
Worldwide experience with the S-ICD in patients with congenital long QT
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Introduction: Long-QT syndrome patients (pts) with an ICD indication are young individuals likely to survive many generator changes. Transvenous (TV) leads carry a risk of complication as they increase over time. The subcutaneous inappropriate shocks were caused by oversensing and were corrected by vector reprogramming in all patients. Rates of inappropriate shocks were equivalent in the 2 patient groups.

Conclusion: The S-ICD IDE and EFFORTLESS studies were sponsored by Boston Scientific.

ANTITHROMBOTIC DRUGS – AN ONGOING RESEARCH

3030 | BEDSIDE
Effect of time to intervention on NSTE-ACS outcomes in PLATO
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Background: Ticagrelor (Ticag) has a faster onset of antplatelet activity than clopidogrel (Clo). Early use of more potent antplatelet therapy would be expected to have benefit, although the use of another potent antplatelet prior to angiography was seen to have no benefit and increased bleeding.

Purpose: We investigated efficacy and safety outcomes of Ticag vs Clo in the PLATO trial in NSTE-ACS pts undergoing early vs. late diagnostic angiography (DA) during the index hospitalisation.

Results: 6792 NSTE-ACS pts underwent DA ≥72 hours of randomisation. Adjusted Cox proportional hazards models evaluated the interaction between timing of DA and randomisation to antplatelet treatment “early” (<3h) or “late” (≥3h) on outcomes following DA.

Conclusion: Median time to DA was 2.7h (0.6–21.15 h). There were 3486 pts in the early cohort (1749 Ticag and 1737 Clo) and 3306 in the late cohort (1697 Ticag and 1609 Clo). Initial planned treatment approach was invasive in 95% of early subjects; 73% in late subjects. In multivariate adjusted analyses, there were no differences in outcomes for efficacy endpoints, with similar benefit with Ticag vs Clo on CV death/MI/stroke and mortality. An interaction was observed for major bleeding, with no difference in the early DA group, but higher bleeding with Ticag at 7 days in the late DA group (Table). In pts with NSTE-ACS in PLATO, the clinical benefit of Ticag over Clo was consistent in those undergoing early and late DA. In early DA pts, the benefit was consistent with outcomes at 7, 30 and 360 days, with no increase in the risk of major bleeding. In late DA pts, consistent efficacy benefit was seen with Ticag, but Ticag was associated with increased bleeding compared to Clo.
RF (P-trend=0.4, Figure 1B) however, minor bleeding increased with worsening risk. The relative risk of TIMI Major bleeding was similar across categories of risk reduction in ischemic events with T was similar by category of eGFR (P-int=NS). The relative risk of ischemic events and bleeding in PEGASUS-TIMI 54 by RF and whether T required adapted management strategies. Registries are tools to verify in real life the guidelines indications; reperfusion therapy is indicated in all patients <12 h from symptom onset.

**Purpose:** To analyse the outcomes of ACS patients receiving OAC enrolled in the EPICOR study.

**Methods:** EPICOR (prospective, multicentre, observational, longitudinal cohort study) included ACS patients within 24 h of symptom onset and follow-up to 2 years. The analysis was in STEMI and UA/NSTEMI groups.

**Results:** The study enrolled 10,568 patients at 555 sites in 20 countries. Among them, 345 (3.3%) patients were on OAC (77 [22.3%] STEMI and 268 [77.7%] UA/NSTEMI) (Table). Only 44 (65.7%) STEMI patients had pPCI and 51 (28.2%) UA/NSTEMI patients had PCI. Two-year mortality in the total OAC group was 45/345 (13.0%).

**Background:** The number of ACS patients receiving OAC as chronic medication is increasing. Triple therapy increases risk of haemorrhagic complications (Huber K et al. Am Heart J 2014;168:611–621). Patients receiving OAC may require adapted management strategies. Registries are tools to verify in real life the guidelines indications; reperfusion therapy is indicated in all patients <12 h from symptom onset.

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3050 | BEDSIDE
BAV morphology in relation to coronary dominance and outcome
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Purpose: Variable coronary anatomy has been described in patients with bicuspid aortic valves (BAVs). Prognostic relevance of coronary dominance in this patient group is unclear and was never specified to BAV morphology. The purpose of this study was to evaluate BAV morphology in relation to coronary dominance and outcome in patients with isolated BAV and with associated aortic coarctation (CoA).

Methods: Valve morphology of 189 BAV patients (141 men (79.2%), 51±14 years) was evaluated retrospectively by echocardiography. Coronary anatomy and coronary artery disease (CAD) were assessed by computed tomography or coronary angiography.

Results: Strictly bicuspid valves (without raphe) with left-right cusp orientation, more often had left dominance than BAVs with left-right cusp orientation with a raphe (48% vs 27.3%, p=0.047). In general, strictly bicuspid BAVs more often had significant CAD (36.4% vs 21.9%, p=0.029) and coronary events (25.9% vs 40%, p=0.029) than BAVs with a raphe. Strictly bicuspid valves with left-right cusp orientation had more significant CAD than left-right oriented BAVs with a raphe (37.5% vs 3.8%, p=0.047). Patients with associated CoA more often had a strictly bicuspid valve and showed more left dominance than the non-CoA group (resp. 31.8% vs 17%, p=0.501 and 65.2% vs 24.1%, p=0.05).

Conclusion: Strictly bicuspid aortic valves, especially with left-right cusp orientation, more often have a left dominant coronary artery system and are at risk of developing significant CAD. In patients with CoA, left dominance is more common, indicating these patients might be more at risk for developing CAD.

3051 | SPOTLIGHT
NOTCH1 polymorphisms as a predictor of aortic insufficiency in patients with bicuspid aortic valve

Objectives: To establish the contribution of NOTCH1 polymorphisms on the development of a combined BAV and CoA.

Methods: The study included 34 patients; the control group consisted of 200 people without CHD. We applied a targeted screening of 10 exons and the adjoining introns of NOTCH1, previously described in association with LVOT malformations.

Results: In 12 of 34 patients with a combination of CoA and BAV observed AR of varying degrees. Typical CoA was examined in all cases. Average peak presystolic gradient between the zones before and after the constriction of the aorta was 46.3 mm. Hg. We identified 26 polymorphic variants, both reported and new and found that exon SNPs were more common in patients with AR, whereas intronic SNPs were more common in the groups of normal BAV and controls. For example, 4 out of 12 (33.3%) patients with AR substitution in exon 34 (g.49602 A/G, R2179H) or in exon 33 (g.39006 G/A, R1279H) and exon 34 (g.48602 G/A, D2185S), while patients with normal functioning of the BAV variant in exon 34 (g.48930 G/A, L2294L) was patients (8.3%) with AR and BAV (8.3%), whereas variants in exon 34 (g.49393 G/A, L2294L) substitutions or combinations of exons 23 (g.39006 G/A, R1279H) and 34 (g.48602 G/A, D2185S), on the contrary, they were more common (33.3%). In the control group similar exon combination practically met (1%) in patients with normal function BAV and CoA observed in a very low percentage (4.5%).

Conclusions: Thus, intronic NOTCH1 SNPs, probably are less associated with BAV development, but have a greater impact on remodeling type and AR.

3065 | BENCH
Proximal titin A-band truncation causes dilated cardiomyopathy in response to increased afterload in mice
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Purpose: Approximately 20% of dilated cardiomyopathy (DCM) patients carry heterozygous truncating mutations in the giant protein titin (TTN). Titin spans the cardiomyocyte sarcomere from Z-disc to M-line and is important for assembly, contraction, relaxation and signaling. Truncating mutations are overrepresented in particular in dilated cardiomyopathy (DCM). Moreover, animal models with truncating NOTCH1 mutations have a more severe phenotype than one with titin A-band truncation (TTN A) and associated cardiomyopathy, function, and transcriptional profile.

Results: To generate TTN A mouse we introduced lox-P sites flanking exons 276–277 and 34 into a titin A-band knockout (TMT A) mouse, causing fractionation and a premature stop codon in the proximal A-Band. 28 heterozygous intercrosses produced 120 pups: none were homozygous TTN A (p=6.10–10). Genotyping (n=125) revealed homozygous embryos at E5.5-E10.5, with fetal demise at E10.5. Heterozygous male and female mice (age 8–60 weeks) were viable, fertile and not different from wildtype (WT) in appearance, activity, or echocardiographic phenotype. Digital PCR of RNA from TTN A hearts (n=3) showed mutant transcripts levels 0.4-fold that of WT allele, and gels and immunoblots detected no mutant titin protein. TTN A and WT mice (n=5–6 per study) were stressed for ten weeks by voluntary cage-wheel running and two weeks of ischemoreperfusion, evoking no difference in echocardiographic phenotypes. Compound TTN A/LMNA mutation mice showed no exacerbation of DCM compared to LMNA mice (LVIDd 4.02mm vs. 3.97mm, both p=0.05 vs. WT). By contrast, TTN A mouse treated for two weeks of ANGII infusion showed hypertrophy with exacerbated diastolic dysfunction (longitudinal strain rate 12.3s–1 vs. WT: 9.6s –1, p=0.004). Substitutions not observed in any of the 22 people, and simultaneous substitution in exon 23 (g.49602 G/A, R2179H) and exon 34 (g.48602 A/G, D2185S), while in patients with normal function of CoA the BAV variant in exon 34 (g.48930 G/A, L2294L) was patients (8.3%) with AR and BAV (8.3%), whereas variants in exon 34 (g.49393 G/A, L2294L) substitutions or combinations of exons 23 (g.39006 G/A, R1279H) and 34 (g.48602 G/A, D2185S), on the contrary, they were more common (33.3%). In the control group similar exon combination practically met (1%) in patients with normal function BAV and CoA observed in a very low percentage (4.5%).

Conclusions: Thus, intronic NOTCH1 SNPs, probably are less associated with BAV development, but have a greater impact on remodeling type and AR.

3066 | BENCH
AAV9-mediated gene transfer of desmin restores cytoskeletal integrity and attenuates development of cardiomyopathy in desmin-deficient mice
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Desmin is a type III intermediate filament, which is mainly expressed in muscle cells comprising 2% of the cardiac muscle’s total protein mass. Its ability to form a filamentous network is crucial to maintaining the structural integrity of skeletal and heart muscle cells. Patients with dysfunctional desmin develop progressive cardiomyopathy and cardiomyopathy. Frequently, cardiac complications determine life expectancy of these patients and therefore comprehensive treatment strategies are needed. In recent studies desmin deficient (DKO) mice were used as an animal model for desminopathy and cardiomyopathy. Aim of this study was to investigate the effect of adeno-associated virus (AAV) mediated gene transfer of wild type desmin (DES)-cDNA on the development of cardiomyopathy in DKO-mice. Two month-old DKO (B6.129S2/Sv-Destm1Cba/Orl) mice were randomised to treatment with an AAV vector expressing DES cDNA (AAV-DES) or a luciferase control vector (AAV-LUC). Healthy wild type littermates (WT) were used as controls. Left ventricular function was assessed using transthoracic echocardiography before vector application and every three months during treatment. Additionally pressure volume loops were measured 10 months after vector application. Desmin expression was quantified by qPCR and western blot analysis. Vector-mediated desmin expression attained 4.0±0.6% on mRNA level and...
22±9.8% on protein level yielding a typical distribution pattern characterized by cross striation and signal accumulation at the intercalated discs. Reconstitution of the desmin filamentous network also enabled syncoolin to form a proper filamentous network. AAV-DES treated mice revealed significantly reduced heart weight to tibia length ratios compared to AAV-LUC-treated animals. Cardiomyocyte cross-sectional areas were also decreased, confirming a reduced hypertrophy in AAV-DES treated animals. Masson's trichrome stained OCT sections revealed large fibrotic areas in AAV-LUC animals which were not present in AAV-DES animals or wild type controls. Follow up echocardiography revealed a significantly smaller decrease in FS (p<0.03) and practically no increase in LVEDD. Maximal rate of pressure development was also increased compared to AAV-LUC controls (p<0.003).

In summary, our data show that AAV-mediated gene transfer of the wild type desmin cDNA is an effective method to reduce desmin filamentous in desmin deficient mice. Reconstitution of syncoolin filamentous, reduced fibrosis and hypertrophy as well as ameliorated contracture function underlines the potential use of this approach for treating the cardiomyopathy associated with desminopathy.

3067 | BEDSIDE
Performance of the copy number variant (CNV) screening using next generation sequencing in a cohort of inherited cardiac disease patients

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Background: Inherited cardiac disease are as a group a prevalent condition usually associated with high morbidity and mortality. Previous genetic screenings in the literature report a responsible mutation in a portion of patients between 16 and 25% depending on the population and disease. The remaining patients remain genetically undetermined.

Copy number variants (CNVs) are the major type of structural variation in human genome and are important sources of human genetic and phenotypic variation. CNVs have been associated to predisposition to human diseases. Next generation sequencing (NGS), unlike traditional Sanger sequencing, allows the detection of structural variants. Our aim was to describe the performance of CNV screening in a cohort of patients with inherited cardiac disease.

Methods: One thousand and eight patients were sent to our laboratory to be sequenced using HiSeq NGS with a 214 gene panel. Analyses were focused in the genes previously associated with each pathology. CNVs were explored using comparison of sequencing coverage after normalization for total coverage in each region. Each region was analyzed using absolute coverage and deviation from the median.

Results: The two commonest phenotypes were hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM). N=338 and 171 respectively. Fifty percent of the probands were males. Mean age of diagnosis was 39±24 years. Thirty CNVs were found (2.97% of patients), 17 were considered responsible for disease (1.68% of patients). Positivity of CNV ranged from 0 in RCM or CPVT to 5.8% in ARVC (See Table 1). Four CNVs were found in ARVC probands, all considered associated with disease. CNVs represent 10% of ARVC associated genetic disease in 3% of the hypertrophic probands. Four CNVs were identified in aortic disease probands representing 5.2% of the population, 3 of them were considered associated with the disease. CNVs are 8% of the mutations associated with aortic disease and explain the phenotype in 9.3% of the cases.

Conclusion: This is the first cohort to define the performance of CNV analyses across a big cohort of cardiac inherited disease. CNVs detection using NGS coverage analysis is a reliable tool during genetic diagnosis of inherited cardiac disease. CNVs could explain 3% of the inherited cardiac disease cases. CNVs are a common cause of disease in genotype negative patients, especially in ARVC and aortic inherited disease. CNV analysis should be routinely performed during genetic test of inherited cardiac disease.

Acknowledgement/Funding: Health in Code

3068 | BENCH
The Eya4/Six1 signalling cascade is activated in acquired heart disease

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Rationale: We previously identified a mutation in the human transcriptional co-factor Eya4 as cause of familial dilated cardiomyopathy (DCM). We now provide evidence that the Eya4/Six1 signalling cascade also is crucial in acquired heart disease.

Hypothesis: We hypothesize that the transcriptional complex Eya4/Six1 regulates targets relevant in normal cardiac function. We speculate that Eya4/Six1 complexes, amongst others, regulates the expression of p27kip1 (p27), a known inhibitor of hyper trophy in adult cardiomyocytes, upon hypertrophic stimuli.

Methods and results: We first examined the correlation of Eya4 and p27 in regards to phosphorylation and cellular distribution in cryosections of failing and normal human hearts. Immunocytochemical analysis revealed Eya4 is mainly distributed in the cytoplasm while p27 predominantly resides in the nucleus of healthy myocardial tissue. In sections of failing human hearts, Eya4 was accumulated in the perinuclear and nuclear region; nuclear p27 levels were significantly diminished, phosphorylated p27 was evenly distributed in the cytoplasm. In a murine model of MI, immunofluorescence staining showed Eya4 is translocated to the nucleus in a time-dependent manner. 16 min after experimental MI there is a strong perinuclear accumulation of Eya4 in cardiomyocytes; translation to the nucleus was detectable 24h post infarction compared to the cytoplasmic distribution in control heart tissue. WB analyses for p27 showed an age dependent decrease in p27 protein levels upon experimental MI compared to control littermates, respectively.

In addition, we generated transgenic mice with constitutive myocardial overexpression of Eya4 and/or E193 overexpression. Eya4 and/or E193 overexpression of Eya4 resulted in decreased contractile function underlines the potential use of this approach for treating the cardiomyopathy associated with desminopathy.

3069 | BENCH
Immunomodulatory microRNAs expressed in the myocardium predict individual antiviral capacity in human entero viral heart disease


Background: The impact of the human noncoding genome upon several important cardiovascular diseases is increasingly appreciated. We investigated myocardial microRNA (miR) expression patterns in a cardiomyopathy caused by the single-stranded RNA virus Cosackievirus B3 (CVB3). Here we show immunomodulatory functions of four miRs differentially expressed between patients spontaneously eliminating their virus (CVB3-ELIM) vs. those with progressive deterioration and virus persistence (CVB3-PERS).

Methods and results: Transcriptome mapping of CVB3 cardiomyopathy patients revealed cardiac miR patterns associated with differential clinical courses. Profiling of 754 miRs in endomyocardiac biopsies (EMBs) of test cohorts was performed at initial presentation, revealing highly significant differences of 16 miRs in CVB3-ELIM vs. CVB3-PERS hearts. This distinctive miR pattern was confirmed in validation cohorts and multivariate ROC analysis confirmed it as highly predictive for disease course (AUC 0.89±0.071, 95% CI 0.758–1.000). Eight miRs which are undetectable in healthy human hearts, and also in CVB3-ELIM hearts, were strongly induced in CVB3-PERS (miRs 135b, 155, 190, 422a, 489, 590, 601, 1290) only. They thus constitute possible targets for antiviral therapeutics drugs aiming at suppression of miRs associated with virus persistence and ad- vancing clinical outcome.

To further assess therapeutic potential we used locked nucleic acid (LNA) antisenes oligonucleotide (ASO)-mediated ablation of miRs 135b, 190, 422a, and 590 in human monocytes and macrophages. Strongest immunomodulating effects were observed in miR-190 knockdown human monocytes with induction of FASLG (22.1-fold), IL-6 (14.5-fold), TNF (4.6-fold) and CCR5 (2.4-fold). These data suggest important immune control functions of miR-590 in macrophages: enhanced FASLG enhances cytokine resistance against PAS expressing cells, IL-6 enhances lymphocyte activation, and CCR5 enhances immune cell migration and antiviral defense via interaction with CCL5 (RANTES), CCL4 (MIP-1b), and CCL3 (MIP-1a). FASLG was also induced by miR-135b and 190a ablation (5.1- and 13.3-fold), and miR-135b ablation additionally induced chemokine receptor CCR7.

Conclusions: miR profiling is valuable to assess the risk of virus persistence and disease progression in CVB3 cardiomyopathy. Beyond this use of miRs as clinical predictive markers, the observed immunomodulating effects achieved by miR ablation in monocytes-macrophages suggest therapeutic potential via enhancement of antiviral capacity.

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3070 | SPOTLIGHT
Can differences in genetic background explain differences in extent of clinical expression of a disease causing mutation?

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Background: Single gene mutations are known to cause hereditary cardiac dis-
ease. It is unknown why there is considerable variability in the extent and severity of cardiac disease even between carriers of an identical mutation. The most common explanation is that genetic variation modifies the clinical expression of a disease causing mutation.

**Purpose:** We aimed to estimate the genomic contribution to most often used clinical traits in hereditary heart disease.

**Methods:** We compared 90 monzygotic twins (MZ) with a mutation causing dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) or long QT syndrome type 1 or 2 in at least one twin. We also included 21 same-sex siblings (S) and 21 opposite-sex siblings (O) with a mutation causing DCM. We compared first available data on: left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVDD) in DCM; diastolic interventricular thickness (IVSd) in HCM; LVEF, LVDD, right ventricular ejection fraction (RVEF) and right ventricular end-diastolic diameter (RVEDD) in ARVC; QTc-time in LQTS 1 and 2. In a LQTS 3 pedigree (118 mutation carriers and 108 non-carriers) we studied PR- and QTc-time. We estimated narrow-range heritability (h²) using Structural Equations Modeling, which decomposes phenotypic variance into additive genetic and common environmental effects and estimates which model explains phenotypic variance best.

**Results:** In DCM (18 MZ, 36 C) we estimated 34.3% h² (95% CI 0.9–94.6%) for LVEF and 44.5% h² (0.0–89.4%) for LVDD. In HCM (34 MZ, 36 C), we estimated 0.0% h² for IVSd (0.0–43.6%) and a significant environmental effect (65.6%, 20.1–83.4%). In ARVC (24 MZ, 24 C), we estimated 0.0% h² for LVEF (0.0–68.2%) and RVEF (0.0–89.3%), and 65.1% h² (0.0–98.8%) for LVDD. In LQTS 1 and 2 (14 MZ, 34 C) we estimated 62.6% h² (0.0–94.0%) for QTc-time. The best model for explaining variance of LVEF (DCM and ARVC) and QTc-time in LQTS 1 and 2, included additive genetic effects. The best model for IVSd in HCM included common environmental effects. In the pedigree study, we estimated 33.7% h² (8.0–57.4%) for PR-time and 18.1% h² (0.0–38.3%) for QTc-time.

**Conclusions:** Disease causing mutations do not cause concordant cardiomyopathies in monzygotic twins, with no significant h² for structural traits and a significant common environmental effect on IVSd variability in HCM. We found non-significant h² for QTc-time in LQTS1, 2 and 3 and significant h² for PR-time in LQTS 3. Our results suggest that heritability for structural traits is low, but that additive genetic effects have an important influence on electrical trait variability.

**3071 | BEDSIDE**

**Genotype impacts survival in marfan syndrome**

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**Background:** Patients with Marfan’s syndrome often have severe cardiovascular disease leading to early death. Previous studies suggest that cardiovascular phenotype may depend on the effect of the FBN1 mutation on the fibrillin-1 protein.

**Purpose:** The purpose was to assess the impact of FBN1 mutation type upon survival and dissection-free survival in patients with Marfan’s syndrome.

**Methods:** We collected clinical and genetic data from all adults with Marfan’s syndrome who had been included in the Dutch CONCOR registry since the start in 2001. All pathogenic FBN1 mutations were classified into mutations with a dominant negative effect (DN, abnormal fibrillin-1 protein) and mutations with a haploinsufficient effect (HI, reduced fibrillin-1 protein).

**Results:** 570 patients with a mean age of 36 years (51% male, 29% prior aortic surgery, 8% prior aortic dissection) were prospectively followed for a median duration of 8.2 years (Q1-Q3: 5–11 years). After ten-year follow-up, cumulative survival was 94% and complication-free survival was 69%. A pathogenic FBN1 mutation was known in 355 patients, of whom 130 patients were positive for a mutation causing haploinsufficiency (37%) and 225 for a dominant negative mutation was known (35%). Patients with a haploinsufficient mutation had a 3-fold higher risk of aortic surgery compared to patients with a dominant negative mutation (p=0.004).

**Conclusions:** FBN1 mutation type has a major impact on survival and aortic dissection in adults with Marfan’s syndrome.

**3072 | BENCH**

**Comprehensive sequencing of dilated cardiomyopathy genes reveals additive effects of multiple genes on disease risk and severity**

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**Introduction:** Over 60 genes have been associated with dilated cardiomyopathy (DCM). However, a comprehensive assessment of rare, protein-altering variants associated on DCM susceptibility or severity, accounting for the background variation rate in ethnically matched and phenotypically evaluated healthy controls, has not been performed.

**Purpose:** To robustly measure the contribution of rare coding variants in DCM alone in isolation or combined with DCM risk and myocardial phenotype, by comparing rare variation burdens in DCM cases and phenotypically characterized healthy controls.

**Methods:** We sequenced and analysed 64 cardiomyopathy genes in 332 Caucasian DCM patients and in 319 ethnically matched healthy volunteers who volunteered to have cardiomyopathy gene sequencing. Targeted next-generation sequencing of DCM genes was performed, and variants were called after mapping data to the HG19 human genome reference. Burden testing for rare (minor allele frequency <0.1%), coding variants was performed for each gene, and regressed modelling was used to assess the effects of genetic variation on the disease phenotype and the additive effect of multiple variant genes on disease risk and severity.

**Results:** As compared to controls, 38 of the 64 genes were enriched for variation in DCM patients. At the gene level the highest enrichment was found for TTN (p=8.5E-8), coding variants in MYH6, previously reported to play an important role in DCM, were not enriched in patients at all by burden testing (12.2% DCM, 2.2% controls). A significant additive effect of the number of variant genes on DCM risk was identified by logistic regression modelling (p=5.7E-4), demonstrating a multi-genic capacity for DCM in some cases. Genotype-phenotype analyses also highlighted an additive effect of multiple variant genes on left-ventricle (LV) wall thinning in DCM (p=1.2E-3), with TTN and variants in MYH7 being the strongest contributors.

**Conclusions:** Our data show that, of all DCM genes and variant classes, TTN is alone significantly associated with DCM by burden testing when compared to a matched population control cohort. We show that a multi-genic effect underlies DCM risk, proving a long-held suspicion of this genetic architecture in DCM. Our data also show an additive effect of variant sarcomeric genes on LV wall thinning that is associated with increased wall stress and adverse outcomes. Together, these data inform diagnostic strategies and suggest disease mechanisms.

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carriers less often developed left ventricular ejection fraction (LVEF) below 35% (HR=0.50, p<0.02 for probands), and had better outcome (HR=0.10, p<0.001 for probands; HR=0.21, p<0.02 for relatives) compared to LMNA mutation carriers but also when compared to TTN/LMNAneg DCM patients (HR=0.33, p<0.05). Comparisons of only truncating TTN A-band mutation carriers to LMNA patients maintained significance, which was lost in the comparison to TTN/LMNAneg DCM patients.

Strikingly, an LVEF increase of at least 10% occurred in 50.0% of the TTN subjects after initiation of standard heart failure treatment, while this only occurred in 6.3% of LMNA subjects (p<0.001) and 22.2% of TTN/LMNAneg DCM subjects (p=0.03). These results remained significant when only comparing truncating TTN A-band mutation carriers.

**Conclusions:** This study shows that truncating mutations in TTN induce a DCM that is less severe at presentation and more potent to standard therapy than either LMNA mutation induced DCM or TTN/LMNAneg DCM.

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**3074 | BEDSIDE**

**Genetics of noncompaction cardiomyopathy (NCCM)**

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**Introduction:** Noncompaction cardiomyopathy (NCCM) is a genetic cardiomyopathy, characterized by hypertrabeculations with deep recesses of the left ventricular wall. We present the results of genetic analysis of a large NCCM cohort.

**Methods:** All NCCM index patients fulfilling the diagnostic criteria for NCCM diagnosis in our medical center were included. Molecular testing was performed using next generation sequencing of a panel of 48 cardiomyopathy genes. Genetic sequence variants in the cardiomyopathy genes were classified for pathogenic effect according to the current five category diagnostic criteria.

**Results:** The study included 128 index patients. Pathogenic or likely pathogenic variants (class 4 and 5) were identified in 40% (49/128) of the patients, including 8% (4/49) with two or more (likely) pathogenic variants. MYH7 mutations were the most frequent, affecting 16% (21/128) of the patients. The Titin gene also appeared as an important cause of NCCM with truncating variants classified as likely pathogenic in 10% (7/67) of the tested patients. In two patients (2/67) the MIBI gene, known to regulate embryologic compaction of the ventricular wall, was involved. Variants of unknown clinical significance (class 3) were observed in 30% (38/128).

**Conclusion:** Next generation sequencing detected a (likely) pathogenic variant in 40% of NCCM and variants of unknown clinical significance in an additional 30%. The improving molecular diagnostics for cardiomyopathies have a profound impact on counseling and screening of families of NCCM patients. Further studies are needed to understand the contribution of genetic factors to this disease.

**Acknowledgement/Granting:** Jaap Schouten Foundation

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**DIFFERENT ASPECTS IN MANAGEMENT OF ATRIAL FIBRILLATION**

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**P3070 | BEDSIDE**

**How common is normal renal function among patients with atrial fibrillation?**

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**Background:** Recent studies have found that the safety and efficacy of some non-vitamin K oral anticoagulants relative to warfarin varies by renal function. For example, edoxaban has recently received an FDA warning for use among atrial fibrillation (AF) patients with estimated creatinine clearance (eCrCl) < 55mL/min.

**Purpose:** We evaluated the frequency and characteristics of those with normal renal function and normal renal function among a community dwelling AF population.

**Methods:** Using data from the ORBIT AF registry, a US registry of AF patients, we examined 10,135 AF patients from 176 clinic sites from June 2010 through August 2011. We analyzed the characteristics of patients with available baseline eCrCl calculated by Cockcroft-Gault.

**Results:** Among 9,315 AF patients, the median eCrCl was 70mL/min (25th, 75th; 50; 95), while 26% had an eCrCl < 95mL/min (Figure). Patients with eCrCl < 95mL/min were younger (median 64 vs 76 years, p<0.001), male patients (74% vs 52%, p<0.0001) of greater weight (median 109 vs 80 kg, p<0.0001). The median CHA2DS2-VASc score among patients with eCrCl < 95mL/min was 3 (25th, 75th; 2, 4), and 94% of these patients had a CHA2DS2-VASc ≥ 1 and 77% ≥ 2.

**Conclusions:** Approximately 1 in 4 AF patients in US clinical practice have normal renal function and may be affected by a recent FDA warning. By ESC guidelines, nearly all patients with eCrCl > 55mL/min have a guideline indication for oral anticoagulation.
categorized as moderate/severe. Patients with perm-AF had more frequently any degree of CI (50% vs 38%), moderate/severe CI (13% vs 7%), and showed lower scores in MMSE (24.6±4.4 vs 23.7±4.8) and Pfeiffer (1.72±3.2 vs 1.3±1.8) tests (p<0.05 for all). In univariable analysis, CI was associated with an older age, female gender, a history of diabetes, and perm-AF. The same variables were confirmed to be independently associated with CI in the multivariable analysis (table).

Conclusions: In our series of patients with CHF, perm-AF showed a discrete but independent association with CI. Other variables such as age, female gender and a history of diabetes showed a stronger association with CI in this population.

P3078 | BEDSIDE Progression to asymptomatic atrial fibrillation as a prognostic index: the Euro Heart Study
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Background: Atrial fibrillation (AF) is associated with a wide variety of clinical presentations. The available data do not conclusively define whether a progression towards asymptomatic AF after clinical treatment could impact on prognosis, and what risk factors are implied. 

Purpose: To investigate clinical and instrumental parameters predictive for developing asymptomatic AF and to determine if patients developing asymptomatic AF have a lower incidence of mortality and cardiovascular (CV) events compared to those who remain symptomatic despite therapy.

Methods: The Euro Heart Survey on Atrial Fibrillation included 5333 consecutive patients with documented AF on ECG or Holter recording. We compared risk of all-cause mortality and CV events between patients who develop asymptomatic AF (n=1556) and those who remain symptomatic (n=896) over 1-year follow-up.

Results: Developing asymptomatic AF was associated with a lower risk of mortality and CV events (Table 1). AF recurrence during follow-up was associated with an increased risk of persistent symptoms despite clinical treatment (ORs 4.32, 2.41, and 2.40 for permanent, persistent and paroxysmal respectively; all p<0.001 vs no AF detection). Hypothyroidism (OR, 1.98; P=0.004), chronic heart failure (OR, 1.83; p<0.001), and chronic obstructive pulmonary disease (COPD, OR, 1.48; p<0.001), were also independently associated with an increased risk of persistent symptoms, whereas an AF considered cured by the clinician over 1-year was strongly associated with developing asymptomatic AF (OR 0.13; p<0.001).

Conclusions: Patients who develop asymptomatic AF after diagnosis have higher survival rates and experience less CV events during a 1-year follow-up. AF recurrence, along with hypothyroidism, COPD and chronic heart failure significantly associate with persistence of symptomatic AF.

P3079 | BEDSIDE Relationship between reduced left atrial function and electro-anatomical remodeling in patients undergoing atrial fibrillation ablation
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Background: Areas with reduced atrial electrogram amplitude ("low voltage areas", LVAs) are considered to represent fibrotic remodeling. We assessed the incidence of LVAs in patients undergoing catheter ablation of atrial fibrillation (AF).

Objective: We analyzed the relationship between LVAs with left atrial function determined by echocardiography.

Methods: In 36 patients with paroxysmal AF, myocardial function of the left atrium was assessed on the day prior to ablation by using 2-dimensional speckle-tracking echocardiography in sinus rhythm. LA voltage maps were created during sinus rhythm before ablation. LVAs were defined as areas presenting with a bipolar electrogram amplitude of <0.5 mV. Percentage of LVAs in relation to the whole LA surface was compared between patients with reduced LA function (LA strain <15%) and patients with normal LA function (LA strain ≥15%).

Results: In the whole group, mean percentage of LVAs was 4% ± 8 (min/max: 0/34%) and mean LA strain was 24% ± 6 (min/max: 12/38%). Reduced LA function (LA strain <15%) was found in 5 patients (14.0%) with a mean LA strain of 15% ± 3. Percentage of LVAs in these patients was significantly higher than in patients without LA dysfunction (15% ± 7 vs. 2% ± 5%; p=0.001, respectively).

Table 1. Patient characteristics and left atrial function

<table>
<thead>
<tr>
<th>Total population</th>
<th>LA strain &lt;15%</th>
<th>LA strain ≥15%</th>
<th>p valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=36</td>
<td>n=896</td>
<td>n=2700</td>
<td></td>
</tr>
<tr>
<td>Mean age (in years)</td>
<td>63 (10)</td>
<td>62 (8)</td>
<td>0.32</td>
</tr>
<tr>
<td>Male (group %)</td>
<td>19 (53)</td>
<td>17 (55)</td>
<td>0.38</td>
</tr>
<tr>
<td>CAD (group %)</td>
<td>6 (17)</td>
<td>4 (13)</td>
<td>0.40</td>
</tr>
<tr>
<td>CHA2DS2VASc score</td>
<td>26 (72)</td>
<td>23 (74)</td>
<td>0.43</td>
</tr>
<tr>
<td>LVEF, % (SD)</td>
<td>56 (9)</td>
<td>59 (5)</td>
<td>0.02</td>
</tr>
<tr>
<td>LA-diaphragm mr (SD)</td>
<td>41 (5)</td>
<td>41 (5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Baseline LA strain % (SD)</td>
<td>24 (6)</td>
<td>26 (5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low voltage area, % (SD)</td>
<td>4 (8)</td>
<td>2 (5)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusions: This is the first study showing the relationship between left atrial dysfunction determined by echocardiography and the extent of areas with reduced atrial electrogram amplitude. Our data further support the hypothesis, that reduced LA function determined by speckle tracking echocardiography represents left atrial structural remodeling.
Purpose: We compared the efficacy of peri-operative ivabradine, bisoprolol, or both for the prevention of post-operative atrial fibrillation (AF) at 30-day follow-up in patients undergoing coronary artery bypass grafting (CABG).

Methods: We enrolled 740 consecutive patients scheduled for elective CABG with or without valve surgery. Patients were assigned to one of three protocols: 1) ivabradine (given peri-operatively in the same previous dose plus bisoprolol at a dose of 5 mg once daily) (group 2), 2) or both drugs given peri-operatively (ivabradine in the same previous dose plus bisoprolol at a dose of 5 mg twice daily) (group 3). We excluded patients in whom the heart rate drops below 50/min during the first 48 hours. Cardiac rhythm was continuously monitored for 16 days after surgery by a transcutaneous automatic ECG recorder. Clinical follow-up for the occurrence of arrhythmias was performed for the next 14 days by office visits. The primary endpoint was the incidence of AF at 30-day follow-up.

Results: The mean age of the study cohort was 56.5±8.9 years; 30.5% were females; 80% diabetic. All patients completed 30-day follow-up. AF occurred in 10.4% of the whole cohort. Of the whole cohort, 212 (26.8%) received ivabradine alone, 288 (38.9%) received bisoprolol alone, and 240 (32.4%) received both drugs. The 3 groups were matched for baseline characteristics and operative data (p <0.05). All the incidence of AF was significantly lower in group 3 (4.2%), compared with group 1 (15.5%), and group 2 (12.2%), (p<0.05). The incidence of AF was not significantly lower in group 3 (4.2%), compared with group 1 (15.5%), and group 2 (12.2%), (p =0.001).

Conclusions: Our findings suggest, TN-C aggravates the deterioration of LV function due to MI partly by regulating inflammation at acute phase.

EXPERIMENTAL AND CLINICAL RESEARCH IN MYOCARDIAL ISCHAEMIA


Purpose: We investigated the effects of TN-C on LV remodeling and the biological function of TN-C during the acute phase of inflammatory responses after myocardial infarction.

Methods: The 8 to 10 weeks old male wild type (WT) and TN-C knock-out (KO) mice were subjected to 30 min isc and 3-hour rep and were divided into 8 groups: 1) Control, no further intervention, 2) PostC with 8 cycles of 30-sec isc/rep, 3) NTG treated animals subjected to the above interventions up to 10th min of rep when tissue samples were collected for determination of eNOS and Akt and of myocardial ROS by DHE fluorescence. Co-administration of L-NAME or Wor along with NTG eliminated the reduction of TN-C during the acute phase of inflammatory responses after myocardial infarction. We investigated the effects of TN-C on LV remodeling and the biological function of TN-C during the acute phase of inflammatory responses after myocardial infarction.

Conclusion: NTG protects through a CypD-dependent mPTP function. NTG administration. NTG had no effect on %I/R in eNOS(−/−) mice compared to Control and NTG-L+NAME groups. To further investigate the role of eNOS on NTG-mediated protection, wild type and eNOS(−/−) mice underwent isc-rep with NTG administration. NTG had no effect on %I/R in eNOS(−/−) mice compared to wild type. The increases of TN-C are mediated by eNOS phosphorylation and CypD, and the extent of fibrosis in the remote area revealed no significant difference between the two groups. By RT-PCR analysis, WT+M group showed significantly higher expression of atrial natriuretic peptide at the border including infarcted areas than that of KO+MI at chronic MI phase. At acute phase, fluorescence activated cell sorting analysis showed that ratio of CD45+, CD11b+, Ly6G high pro-inflammatory monocyte were significantly decreased, whereas CD45+, F4/80+, CD206+, anti-inflammatory M2 macrophage were significantly increased in KO+MI compared with WT+M group 7 days after MI. RT-PCR analysis showed that the expression of IL (interleukin)-10 was significantly decreased (Mannose receptor, C type I) was significantly higher in KO+MI than WT+M. These findings suggest, TN-C aggravates the deterioration of LV function due to MI partly by regulating inflammation at acute phase.


Purpose: We enrolled 740 consecutive patients scheduled for elective CABG

Methods: We investigated the effects of TN-C on LV remodeling and the biological function of TN-C during the acute phase of inflammatory responses after myocardial infarction.


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Purpose: Diabetes mellitus (DM) is accompanied with increased susceptibility to myocardial ischemia-reperfusion (IR) injury due to altered metabolic processes
and decreased bioavailability of nitric oxide (NO). Increased arginase activity in the heart and red blood cells (RBCs) has emerged as a possible factor for reduced NO bioavailability by competing for the substrate L-arginine. The aim of the present study was to investigate if inhibition of arginase protects from IR injury in rats with type 1 diabetes mellitus (T1DM).

**Methods:** T1DM was induced by iv injection of streptozotocin (55 mg/kg) to male Sprague-Dawley rats at least 4 weeks before further experiments. Age-matched non-diabetic rats were used as controls. Two groups of diabetic rats (n=9) and controls (n=8) were euthanized to collect hearts and RBCs for analysis of arginase expression and activity. Additional groups were anesthetized and subjected to 30 min left coronary artery occlusion and 2 h reperfusion. The animals were randomized to one of the following treatments given iv 15 min before ischemia: (1) saline (n=14 diabetic rats and n=7 controls); (2) the arginase inhibitor nor-NOHA (100 mg/kg, n=11 diabetic rats and n=8 controls); (3) the NO synthase (NOS) inhibitor NG-nitro-L-arginine monomethyl ester (L-NAME, 10 mg/kg; n=7 diabetic rats and n=5 controls) and nor-NOHA. Area at risk and infarct size (IS) were determined. Data are presented as mean±SE. Groups were compared using Student’s t-test or one-way ANOVA and Newman-Keuls post test.

**Results:** Basal arginase activity in the myocardium and in RBCs was significantly higher in diabetic rats than in controls. Arginase 2 expression was 1.8 fold higher in myocardium of diabetic rats vs controls (P<0.001) while arginase 1 expression did not differ significantly. Compared to saline-treated rats, IS was reduced (65±3%, resp.). Basal arginase activity in the myocardium and RBCs and increased expression of myocardial arginase 2. Arginase inhibition protects the diabetic heart from IR injury via a NOS-dependent mechanism. The decreased anticoagulation by arginase inhibition is comparable to that in healthy animals. Targeting arginase may be a promising therapeutic strategy for the protection against IR injury in DM.

**P3086 | BEDSIDE**

**Inflammatory activity of pericoronary adipose tissue in prediabetic patients with NSTE-ACS**

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**Purpose:** Paracrine activity of pericoronary adipose tissue (PCAT) may adversely affect coronary lesions formation and plaque stability. Maximal standardized uptake value (SUV) of 18-fluorodeoxyglucose (FDG) measurement by positron emission tomography has been proved to be an efficient tool to evaluate paracrine inflammatory activity of different tissues. In patients with stable coronary artery disease it correlated with % of coronary stenosis. We sought to investigate, whether PCAT influenced plaque composition in Non-ST elevation Acute Coronary Syndromes (NSTE-ACS) patients.

**Methods:** 30 patients (98 coronary arteries: LM, RCA, LCX, LAD) have been investigated in subjects without history of diabetes mellitus with moderate/low risk NSTE-ACS (GRACE <140). SUV was measured in PCAT surrounding arteries on the sections corresponding to coronary plaques detected by gray scale intravascular ultrasound and virtual histology (VI-US) during routine coronaryography. Additionally SUV was measured in subcutaneous fat (SC), visceral thoracic fat (VAT) and sublingual vein (EPV). Qualitative (calcified, fibrous, fibrofatty, or necrotic core) and quantitative analyses of plaques were performed, and further correlated with PCAT SUV. In all patients fasting blood glucose (FBG), 2 hour glucose tolerance (GTT) test and HbA1C were analyzed. Prediabetes was diagnosed according to WHO/ADA criteria.

**Results:** PVAT SUV in NSTE-ACS patients was significantly greater than in other fat locations (LM SUV: 1.60; RCA SUV: 1.47; LCX SUV: 1.89; LAD SUV: 2.30 vs SC SUV: 0.59; VS SUV: 0.78; EPI SUV: 0.99, p<0.001; ANOVA). PCAT SUV positively correlated with necrotic core plaque rate (r=0.61, p<0.05), and negatively correlated with fibrous plaque rate (r=-0.52, p<0.05), which was more prevalent in pts with IFG and/or IGT (r=-0.72, p=0.05 r=-0.57, p=0.05, respectively). There was also positive correlation between PCAT SUV and % plaque volume (r=0.45, p=0.05).

**Conclusions:** Inflammatory activity of PCAT is greater than in subcutaneous, visceral thoracic, or epicardial tissue in NSTE-ACS patients; PCAT SUV correlates with necrotic core component of coronary plaque and plaque volume in patients with NSTE-ACS, especially with IFG and/or IGT.
**P3091 | BEDSIDE**

Prognostic significance of global myocardial perfusion reserve measured using coronary sinus flow during stress cardiovascular magnetic resonance imaging

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**Background:** Coronary microvascular dysfunction has been implicated in a broad range of cardiac conditions. Current non-invasive techniques to measure coronary microvascular function are challenging for routine practice and limited to specialized research centers. We have recently shown the feasibility of rapidly assessing myocardial perfusion reserve (MPR) as a marker of coronary microvascular function by measuring coronary sinus (CS) flow during stress CMR. We therefore hypothesized that global abnormalities of coronary microvascular function as reflected in reduced coronary sinus derived MPR maybe of prognostic significance.

**Purpose:** To assess the prognostic value of coronary sinus-derived MPR for the prediction of major adverse cardiac events (MACE) in patients with known or suspected coronary artery disease.

**Methods:** 245 consecutive patients underwent a CMR stress-rest perfusion protocol. Perfusion imaging was performed at 1 and 15 minutes after administration of 0.4 mg regadenoson. CS through-plane flow was measured using a phase-contrast segmented gradient echo sequence at baseline (pre) and immediately after stress perfusion (peak). MPR was calculated as peak CS flow/pre CS flow.

Patients were followed for occurrence of MACE - death, nonfatal MI, chest pain or heart failure hospitalization, and late revascularization.

**Results:** The mean age of the population was 59 ± 14 years, with a mean ejec- tion fraction of 63% ± 13. 41 MACE occurred during a median follow-up of 12 months. Mean MPR for all patients was 2.75 ± 1.64. By Kaplan-Meier analysis, patients with CFR-mean estimates > 2.75 had significantly more adverse events than patients with CFR-mean estimates ≤ 2.75 (p = 0.0075) (Figure 1).

**Conclusions:** Reduced global MPR measured from coronary sinus flow during stress CMR is a significant predictor of MACE.

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**P3089 | BEDSIDE**

Impact of sleep apnea on severe microvascular dysfunction assessed by cardiovascular magnetic resonance after primary angioplasty in patients with acute myocardial infarction

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**Background:** Recent studies suggest that obstructive sleep apnea (OSA) is associated with impaired microvascular perfusion after primary percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction (STEMI). Non-invasive assessment of microvascular obstruction (MVO) and interstitial myocardial hemorrhage by cardiovascular magnetic resonance (CMR) provides a specific biomarker of severe microvascular dysfunction. However, the relationship between OSA and severe microvascular dysfunction has not been fully evaluated. The aim of this study was to determine whether OSA was related to the presence of severe microvascular dysfunction determined by CMR in patients with acute STEMI.

**Methods:** The study population consisted of 111 consecutive patients with a first STEMI successfully treated with PCI. CMR performed within 4 days after primary PCI was used to identify the presence of reperfusion hemorrhage and contrast enhancement was used to measure MVO. Recruited patients were scheduled to undergo an overnight sleep study week one after primary PCI. Sleep apnea was classified into 4 categories based on an apnea-hypopnea index (AHI): no (AHI < 5), mild (AHI 5-15), moderate (AHI 15-30), and severe sleep apnea (AHI >30). An AHI of ≥ 15 was considered diagnostic of OSA. We assessed the association between the degree of sleep apnea and microvascular dysfunction determined by CMR.

**Results:** Three OSA groups were analyzed: no, mild, moderate, and severe sleep apnea, respectively. An increasing AHI quartile was associated with increased odds of the frequency of MVO and hemorrhagic infarction (p values for trend < 0.01 and 0.027, respectively). Multiple logistic regression showed that OSA was associated with increased odds of MVO (odds ratio [OR] 3.68; 95% confidence interval [CI], 1.59–9.01, p = 0.0022) and hemorrhagic infarction (OR, 3.84; 95% CI, 1.50–10.7, p = 0.0045) compared with no OSA.

**Conclusion:** Undiagnosed OSA was associated with severe microvascular dysfunction after primary PCI in patients with STEMI.

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**P3090 | BEDSIDE**

Safety of anticoagulation withdrawal guided by magnetic resonance in STEMl patients with left ventricular thrombus


**Background:** Left ventricular thrombus (LVT) following STEMI increases the risk of stroke. Anticoagulation is usually prescribed on top of double antiplatelet therapy, adding a risk of bleeding in this setting. Imaging techniques play a key role in predicting subsequent clinical outcomes.

**Purpose:** To evaluate the role of cardiac magnetic resonance (CMR) to rule out persistent thrombus suspected by echocardiography acutely after STEMI, and to assess the safety of anticoagulation withdrawal according to CMR findings.

**Methods:** We included 349 patients (82% male) with their first STEMI treated with primary or rescue PCI. Both, TTE and CMR were performed during admission during a mean follow-up of 51±29 months.

**Results:** LVT was suspected by non-contrast bed-side transthoracic echocardiography (TTE) in 47 subjects (16%) to whom anticoagulation was prescribed. CMR confirmed LVT in 6 cases and identified LVT in another 2 patients with negative TTE (AHI 7%), in total p = 0.001. Consequently, CMR ruled out LVT in 41 cases with positive TTE (87%) and anticoagulation was withdrawn in 16. None of them suffered stroke during follow-up. Only 3 patients (0.8%) presented an ischaemic neurologic event beyond 6 months after the infarction. New-onset atrial fibrillation was detected in 1 case and LVT had not been detected previously in none of them, neither by TTE or CMR. One patient (0.3%), in whom a LVT was detected by TTE but not by MRI, and anticoagulation was not discontinued, suffered an intracranial bleeding two months after discharge while on vitamin K antagonists. No other major hemorrhages were detected.

All cases of LVT detected by CMR occurred in patients with anterior myocardial infarction, with lower ejection fraction (35±10% vs 46±10%, p = 0.05) and larger infarct size (38±8% vs 20±13%, p < 0.001).

**Conclusion:** CMR rules out LVT in a significant proportion of cases initially suspected by TTE and ongoing anticoagulation that can be safely discontinued.

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**Conclusion:** CMR rules out LVT in a significant proportion of cases initially suspected by TTE and ongoing anticoagulation that can be safely discontinued.
subsequent independent prognostic information on hard clinical events over a 12 months follow-up period.

P3090 | BEDSIDE
Subendocardial stress perfusion defects on cardiovascular magnetic resonance in patients with angina and unobstructed coronary arteries are frequent, especially in women. A cure with evidence based medical therapy is often not possible. Measurements of stress perfusion cardiovascular magnetic resonance (CMR) may be of diagnostic utility to risk stratify patients with angina and unobstructed coronary arteries.

Methods: Between 1996 and 2012 we consecutively recruited 125 patients (mean age 64±16 years, 64 (51%) male) with angina pectoris who underwent an exercise stress CMR study (inclusion crite- rion rest function, adenosine stress and rest perfusion and late gadolinium enhancement imaging) and invasive diagnostic coronary angiography because of suspected obstructive coronary artery disease. In all patients no relevant epicardial stenosis was found (<50% narrowing) and intracoronary ACH-testing was performed in search of functional coronary vasomotor abnormalities.

Results: Twenty-eight patients (22%) presented with effort-induced angina, 66 patients (53%) with resting angina and 31 patients (25%) had a balanced presentation of effort and rest angina. An adenosine-induced, reversible subendocardial perfusion defect was detected in 56 (45%) patients. ACH-testing revealed coronary microvascular dysfunction in 59 (47%) patients (reproduction of symptoms, ischemic ECG-changes and no epicardial spasm) while epicardial coronary spasm (>75% diameter reduction with reproduction of the patient’s symptoms) was seen in 28 (23%), 38 patients (30%) had an uneventful ACH-test. Patients with a reversible stress-induced perfusion defect had significantly more often a positive ACH-test (51/58; 88%) than those without a perfusion defect (36/67; 54%; p<0.0005).

Conclusion: Reversible perfusion defects on stress perfusion-CMR in patients with effort angina and unobstructed coronary arteries are frequent due to coronary vasomotor abnormalities. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treat- ment.

P3099 | BEDSIDE
Long term effect of pulmonary endarterectomy on right ventricular loading conditions in patients with chronic thromboembolic hypertension by cardiomyo- ry: A. Rol1, W. Kim1, S. Stein1, J. Rixe1, C. Liebetrau1, H. Moellmann1, H.M. Neff2, S. Guth3, E. Mayer4, C. Hamm1, A. Kerckhoff-Heart-Center, Bad Nauheim, Germany; 1Kerckhoff-Liège University-Gießen, Medical Clinic I. Cardiology, Gießen, Germany; 2Kerckhoff-Thorax-Center, Bad Nauheim, Germany.

Purpose: To study the natural history of RV adaptation to varying loading condi- tions in patients with chronic thromboembolic hypertension (CTEHP) from before pulmonary endarterectomy (PEA) to one year follow up.

Background: Nearly 4% of patients with pulmonary embolism develop CTEHP. To study the natural history of RV adaptation to varying loading conditions in patients with chronic thromboembolic hypertension (CTEHP) from before pulmonary endarterectomy (PEA) to one year follow up.

Results: Twenty-eight patients (mean age 41±12 years, 28 female) underwent CMR pre- and post-PEA. 44 were available for one year follow up. Ejection fraction (EF), end-diastolic (EDV), end-systolic (ESV), and stroke (SVI) volumes were indexed for body surface area. ESV-EDV was calculated as pulmonary artery mean pressure (mPAP)/ SVI, and ESV-RV_i as mPAP/ESV-RV.

Results: mPAP decreased from 47±12 to 25±9 mmHg, p=0.0001 and PVR de- creased from 646±286 to 334±225 dynes/s/cm5, p=0.0001. ESV-EDV_i was increased before PEA and normalized afterwards (2.8±2.1 vs. 0.8±0.4 mm3/m/m2, p=0.0001). ESV-RV_i was depressed before and after PEA (0.72±0.27 vs. 0.6±0.3 mm3/m/m2, p=0.13). EF improved from 25±12% to 46±10%, p=0.0001, because ventriculo-arterial coupling was restored (4.2±3 vs. 1.4±0.6, p=0.0001). EDV and ESV improved significantly (EDV 92±32 to 72±23 ml, p=0.0001; ESV-EDV_i 4.2±3 vs. 1.4±0.6, p=0.0001). All effects were sustained at one year follow up (PEA; 2.8±2.1 vs. 1.0±0.5, p=0.0001; ESV-EDV_i 0.72±0.27 vs. 0.56±0.2, p=0.03; ESV-ESV-RV_i 4.2±3 vs. 1.9±0.8; EDV 92±32 vs. 65±18 ml, p=0.0001; ESV 69±31 vs. 42±14 ml, p=0.0001; EF 25±12 vs. 37±9%, p=0.0001).

Conclusion: RV function is largely determined afterload and returns to normal once afterload is normalized. This is paralleled by a significant improvement of CMR indices of right ventricular remodelling. These effects are sustained at long term follow up one year after PEA.

NEW ADVANCES IN CARDIOVASCULAR GENETICS AND GENE THERAPY

P3096 | BENCH
PRKGR1 mutations and thoracic aortic disease: another candidate gene for hereditary genetic disease approach to non-syndromic cases

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Introduction: Thoracic aortic aneurysms and dissections are major disorders affecting the thoracic aorta. These potentially lethal manifestations can be or not part of Marfan, Loeys-Dietz or Ehlers-Danlos type IV connective tissue syn- dromes. When they appear isolated the patients are considered affected by non- syndromic aortic disease, a monogenic condition inherited as an autosomal dom- inant disorder with low penetrance and variable expression. Mutations in ACTA2, AN程, and COL3A1 have been reiteratively described to be causal, but there are still many unresolved familial cases suggesting the need for other candidate genes to be detected.

Purpose: To identify the genetic mutation causing non-syndromic aortic disease in a 4-generation Spanish family with multiple cases of aortic disease-sudden death at least 6 alive affected family member.

Methods: Customized targeted-sequencing of aortic disease candidate genes in the proband through 5500 SOLID System followed by whole-exome sequenc- ing of 4 affected (including the proband) and 2 unaffected family members using HiSeq 2000/2500 sequencing technology. All variants were filtered by location, frequency and functional significance using ESP6500 and 1000 Genomes Project’s individuals and in an internal database. The presence or absence of selected variants was confirmed through capillary electrophoresis sequencing.

Results: After the negative results obtained for the candidate aortic disease genes included in the customized targeted-sequencing assay, the analysis and filtering of whole-exome sequencing data, assuming an autosomal domi- nant inheritance model, brought out the c.575G>A; p.Arg192Gln PRKGR1 mutation (NM_006258) previously related with the development of thoracic aortic disease cases and already known to be causal. This mutation was common to the 4 af- fected and absent in the 2 unaffected family members. No other mutation was found in the remaining aortic disease candidate genes.

Conclusions: This new independent PRKGR1-thoracic aortic disease familial case
P3097 | BEDSIDE
Major histocompatibility complex risk haplotype predisposes to acute coronary syndrome


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Introduction: HLA-DRB1*01 allele of the human leucocyte antigen (HLA) class II gene on chromosome 6p21.3 has been associated with coronary artery disease in smaller case-control data sets while not in genome-wide association studies.

Purpose: We aimed to analyze HLA-DRB1*01 allele together with major histocompatibility complex (MHC) single nucleotide polymorphisms (SNP) to identify genetic risk loci for acute coronary syndrome with effective clinical implications.

Methods and results: We analyzed the copy numbers of HLA-DRB1*01 allele in 270 unrelated control subjects and 350 healthy controls. We found a disease associated haplotype containing SNPs from HLA-DRB1*01 allele in all four populations with odds ratios varying between 1.21 and 4.43. Subjects homozygous for disease-associated HLA-DRB1*01 allele also had higher BTNL2 mRNA levels in their coronary samples (r=0.760, P<0.0001). BTNL2 blocking increased CD4+FOXP3+ regulatory T cell proliferation significantly (blocking vs non-blocking, P<0.05) in T cell stimulation assays.

Conclusion: Our study suggests that BTNL2-HLA-DRA-HLA-DRB1*01-haplotype on chromosome 6p21.3 associates with acute coronary syndrome and seems to enhance immune reactions.

P3099 | BENCH
Gene transcription efficiencies, left ventricular function and fibrosis formation in mouse heart after direct intramyocardial gene transfers with aden-, adeno-associated- and lentiviral vectors

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Introduction: Gene therapy is a promising new treatment option for ischemic heart disease and viral vectors are used to deliver therapeutic genes into ischemic tissue. Adenoviruses (Ad) are currently the most used vectors for different gene therapy protocols.

The aim of this study was to compare adeno viral vectors to adeno-associated (AAV) and lentiviral (LeV) vectors in mouse heart regarding the transcription efficiency, effects on the left ventricular function, and fibrosis formation in order to find the most suitable and safe vector for cardiac gene therapy.

Methods: High-resolution echocardiography was used to guide the closed-chest injections of Ad-, AAV2-, AAV9- and LeV gene constructs into the anterior wall of the left ventricle (LV) of C57BL/6J mice. AAV9 was also studied by using i.v. injections of three different virus doses (10^9, 10^10 and 10^12 viral particles). Echocardiographic measurements were performed before (d0), 6 (d6) and 28 (d28) days after the gene transfers. Gene transcription efficiencies were induced with wild type and transgenic pigs via reduction stent graft in the circumflex artery. Retiniouss of rAAV T4 (5x10E12 viral particles) was performed at day 28. Global myocardial function (EF, LVEDP) was obtained at day 28 and 56. In addition subendocardial segment shortening (SSE) in the ischemic region and post mortem angiography (collateral growth) were examined on day 56. Histological analysis of PECAM-1 positive cells (capillaries/high power field (chpf)), and vessel maturation (pericyte coverage, NG-2 positive cells) was performed in the ischemic tissue.

Results: Analysis of non-ischemic wt and diabetic animals revealed capillary rarefaction in the myocardium (234±8 in wt vs. 163±14 chpf in diabetic hearts). Analysis of myocardial function in non-ischemic hearts detected a trend towards loss of ejection fraction in diabetic pigs. In chronic myocardial ischemia, rAAV.Tß4 overexpression in wt animals significantly enhanced capillary density (278±6 vs. 148±6 chpf) and collaterals (9±1 vs. 3±1) in the ischemic area compared to control wt animals. Furthermore, rAAV.Tß4 improved ejection fraction (47±4% vs. 29±3% in controls) as well as SES (at 150 beats/min: 73±5 vs. 10±6% in non-ischemic area). In diabetic pigs, blood glucose levels were elevated (305±12 mg/dL at day 28 and 353±10 mg/dL at day 56). Here, rAAV.Tß4 still induced angiogenesis (190±4 chpf (Tß4) vs. 120±5 chpf in wildtype hearts) as well as collateral growth (4±1 (Tß4) vs. 2±1 in control hearts). Moreover, EF increased in rAAV.Tß4 diabetic hearts (32±2% vs. 27±1% in controls).

Conclusion: HLA-B4 transduction induces therapeutic neovascularization and thereby improves the myocardial function in the presence of type I diabetic mice. Therefore, rAAV.Tß4 appears suitable for treatment of ischemic cardiomyopathy associated with this cardiovascular risk factor.

P3100 | BENCH
A deep phenotype and exome-sequencing based characterization of patients with non-compaction cardiomyopathy (NCCM)

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Left ventricular non-compaction cardiomyopathy (NCCM or LVNC) is an increasingly recognized cause of heart failure, arrhythmias, thromboembolic events, and sudden cardiac death. Advanced diagnostic methods, predominantly based on modern imaging techniques, including cardiac magnetic resonance imaging (cMRI) have resulted in considerably increased detection rates, enabling a collection of larger NCCM cohorts. Hence we were able to recruit 104 subjects (67 non-ischemic and 37 ischemic). With this large NCCM cohort we intended to lead to cause hypertrophic cardiomyopathy (HCM), 10 dilated cardiomyopathy (DCM) and 7 arrhythmogenic right ventricular cardiomyopathy (ARVC). Besides already known genetic causes, we identified a number of genes contributing to different pathophysiologic pathways, besides common NCCM-loci. By genomewide conformation and linkage analyses, we provide for the first time evidence for a gene that was previously not known to cause any human disease, Compactin1. In conclusion, we for the first time present a genetic screening of a large cohort of deeply
phenotyped NCCM patients, which will contribute to a better diagnosis, counseling of affected families and estimation of prognosis in future.

P3101 | BENCH
Targeted capture sequencing identifies a mutation in a substantial amount of prior genotype negative - phenotype positive patients with inherited primary arrhythmia syndrome or cardiomyopathy

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Background: In inherited primary arrhythmia syndromes (PAS) and cardiomyopathies (CMP) the yield of genetic testing varies between 20% and 75% in different diseases. These numbers are mainly derived from studies evaluating only the most frequently affected genes. Next generation sequencing (NGS) allowed us to design and validate a panel of 75 PAS and CMP susceptibility genes for targeted capture and massive parallel sequencing.

Purpose: We evaluated the additional yield of NGS based panel testing in PAS and CMP patients and determined if genetic testing was worthwhile in previously negative or positive - phenotype positive probands.

Methods: We examined the database of our hereditary heart disease clinic and selected patients with a clear phenotype who were genotype negative after genetic analysis of the main genes implicated in their specific phenotype. Targeted sequencing was performed on regions of 75 genes targeted in PAS and CMP was performed. Variant interpretation and classification was done according a stringent scoring system including different in-silico analyses, population frequencies and paralogous and orthologous conservation. Sanger sequencing was performed when the presence of the tested variants was unknown, and when enough data was available. Co-segregation was performed when DNA and clinical data of family members was available.

Results: 96 patients were included: 25 with LQTS, 8 with BrS, 4 with CPVT, 1 with SSS and familial sudden death, 1 with AF, 6 with idiopathic VF, 42 with HCM, 7 with DCM, 1 with restrictive CMP and 1 with ARVC. A total of 41 variants of class 3, 4 and 5 were identified. Co-segregation was performed on 20 variants. Three class 3/4 variants were downgraded to a benign variant due to lack of co-segregation. In contrast, 12 were upgraded to class 4 or 5 after critical evaluation of published functional studies or co-segregation analysis. In total we identified 22 variants of class 3 and 16 mutations (class 4/5) in 15 patients, resulting in a genetic yield of 16% (14% in CMP and 18% in PAS). The initial detection failures had several causes: detection of a mutation in a new gene in 8 cases, allele dropout with DHPLC in 2, not reported variant by an external lab in 2, functional and clinical reclassification in 1, heterozygous calling with failing sequenced in 1 and a wrong initial diagnosis in 1.

Conclusion: Genetic retesting in robust PAS and CMP cases, who were genotype negative after earlier sequencing, resulted in a diagnostic yield in up to 16% of the cases and clearly supports genetic testing with NGS based panels.

P3102 | BENCH
Targeted versus whole exome re-sequencing for clinical diagnostic application in inherited cardiac conditions

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Inherited cardiac conditions (ICC) are inherited cardiovascular diseases of the heart and circulation with a prevalence of ~1%. New sequencing technologies have enabled high-throughput sequencing of disease genes for clinical application where targeted and whole exome sequencing (WES) approaches are equally suggested for diagnostic use. Genomic DNA was extracted from patients (n=216) and three iterations of custom ICC gene panel were used to enrich 169 ICC genes using the Nextera Rapid Capture Enrichment kit. The libraries of pooled samples (n=6–12) were sequenced using Illumina Miseq paired-end 150bp reads V2 or V3 kit. Three versions of improved sequence captures (IICCv1, IICCv2 and IICCv3) and a non-custom WES panel (Nextera Rapid Capture Enrichment kit, HiSeq2000) were compared using stringent, “clinically grade” sequence depth and quality metrics. The proportion of bases covered adequately for variant calling (Callability) was proportional to the number of mapped reads per sample but each reached saturation at 4.5–5M reads/sample. The callability of ICC genes was improved in the ICCv2 panel by reducing the targeted region from 1.47Mb in IICCv1 (comprising exons and UTR) to 0.58Mb in IICCv2 (exons only). Difficult to capture regions in IICCv2 were targeted with additional capture probes in ICCv3 that reached the highest callability (~99.8% of target). WES performed as detailed by the manufacturer at ~40Gb/sample and achieved a callability of 95.2% for the ICC target. All SNPs deemed pathogenic using the IICCv1-v3 panels were confirmed by Sanger sequencing. Targeted re-sequencing enables comprehensive (>99.8% of targeted genes), rapid (5 days) and high throughput (169 genes) analysis of all targeted regions at low cost, while WES does not yet adequately capture ICC genes for clinical application.

ADVANCES IN ENDOCARDITIS

P3103 | BEDSIDE
Isolated right-sided infective endocarditis in cardiac device carriers: clinical profile and prognosis

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Introduction and objectives: Classically, right-sided infective endocarditis (RIE) occurred in the context of intravenous drugs use. However, due to the widespread indications for device implants in the last decade and the aging of the population, RIE epidemiology has dramatically changed, being nowadays cardiac device carriers the main affected group. Several works have been published regarding to device-related infections in general and cardiac device infective endocarditis (CDIE) in particular. However, the majority of these series included patients with concomitant left valve involvement, probably making the clinical profile somewhat different and overestimating in-hospital mortality rates. The aim of this work is to describe the epidemiology, clinical profile and outcomes of isolated right-sided infective endocarditis in cardiac device carriers.

Methods: Among 1,182 episodes of definitive infective endocarditis (IE) consecutively diagnosed in three tertiary centres from 1995 to 2014, 113 episodes occurred in cardiac device carriers (9.5%). Of them, 13 were excluded from the analysis due to concomitant left valve involvement. Therefore, our final study population is 100 patients with isolated right-sided IE (8.5%). An analysis of 85 variables has been performed.

Results: Mean age (±SD) was 67±14 years, 75% were males and 35% healthcare related. Local infection (29%) and indwelling catheter (14%) were the most frequent predisposing conditions. Comorbidities were common (46%), being diabetes (20%) and chronic renal failure (14%) the more frequently associated. Septic shock during hospitalization. Staphylococci species were the most causative microorganisms (coagulase negative 60%, aureus 31%) and one-third of the episodes were caused by methicillin-resistant strains. Tricuspid valve was affected in 22%. Cardiac devices were removed during antibiotic treatment in 90% of patients. Overall in-hospital mortality was 8%. Univariate analysis demonstrated that renal failure at admission (OR 8.16 [95% CI, 1.256–30.293]), septic shock at admission (OR 11.6 [95% CI, 1.651–47.907]), septic shock during clinical course (OR 8.9 [95% CI, 1.651–47.907]) and persistent infection (OR 19.42 [95% CI, 3.032–125.704]) increase in-hospital mortality, while device removal (OR 0.08 [95% CI, 0.017–0.389]) is related with better outcomes.

Conclusion: In-hospital mortality related to CDIE is lower than previously reported. Device removal is mandatory in patients with CDIE since decrease in-hospital mortality.

P3104 | BEDSIDE
Streptococcus bovis endocarditis revisited. A not so virulent microorganism

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Aim: Infective endocarditis (IE) due to S. bovis has been classically associated with elderly patients, frequently involving more than one valve, large vegetations and high embolic risk. This constellation of facts entails a high-risk patient group. Our aim is to analyze the clinical profile, and prognosis of S. bovis IE episodes, and to compare them with those episodes caused by viridans group streptococci and enterococci.

Methods: We analyzed 1242 consecutive episodes of IE prospectively recruited on an ongoing multipurpose database. Left-sided streptococcus and enterococcus episodes (n=294) form our study population and were classified into 3 groups: Group I (n=47), episodes of IE due to S. bovis, Group II (n=134), episodes due to...
viridans group streptococci, and Group III (n=113), those episodes due to enterococci.

**Results:** The incidence of enterococci IE have significantly increased in the last 2 decades (6.4% [1996–2004] vs 11.1% [2005–2013]; p<0.005), while the incidence of IE due to S. bovis and viridans streptococci has remained stable (4% and 10%, respectively). Patients with S. bovis and enterococci IE were older. Nosocomial acquisition was more frequent in Group III. Concerning comorbidity, diabetes mellitus (38.3% vs 9.0% vs 26.5%; p<0.001) was more common in S. bovis IE. Colorectal neoplasias were found in 70% of patients from this group. Vegetation detection was similar in the three groups. However, vegetation size was smaller in S. bovis IE (7.4 mm vs 11.6 mm vs 11 mm; p<0.001). During hospitalization, in-hospital complications and in-hospital mortality were higher in enterococci episodes (Table).

<table>
<thead>
<tr>
<th>In-hospital evolution</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
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<tbody>
<tr>
<td>CNS embolisms</td>
<td>5 (10.6%)</td>
<td>18 (13.5%)</td>
<td>12 (10.6%)</td>
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<tr>
<td>Heart failure</td>
<td>26 (55.6%)</td>
<td>63 (47.0%)</td>
<td>82 (73.2%)</td>
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<tr>
<td>Acute renal failure</td>
<td>18 (38.3%)</td>
<td>39 (29.3%)</td>
<td>60 (53.1%)</td>
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<tr>
<td>Septic shock</td>
<td>5 (10.9%)</td>
<td>10 (7.5%)</td>
<td>18 (15.9%)</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>30 (63.8%)</td>
<td>82 (61.2%)</td>
<td>61 (54.0%)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>9 (19.1%)</td>
<td>28 (21.2%)</td>
<td>41 (36.9%)</td>
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</tbody>
</table>

**Conclusions:** S. bovis IE is associated with a high prevalence of colonic tumours, and affect patients without pre-existing vascular disease. It is related to small vegetations and a low rate of in-hospital complications, including systemic embolisms. In-hospital mortality is similar to that of viridans group streptococci. Thus, S. bovis should not be considered a virulent microorganism.

**P3105 | BEDSIDE**

Dramatic decrease in Staphylococcus aureus infective endocarditis early mortality using a new strictly applied protocol


**Background:** S. aureus infective endocarditis (SAIE) is still associated with high mortality despite using recommended antibiotic protocols.

**Objectives:** To assess the effectiveness and safety of a new antibiotic protocol, using the association of high doses cotrimoxazole and clindamycin (C+C).

**Methods:** A prospective cohort of IE initiated in 2002 was used. All patients with a definitive SAIE according to DUKE criteria were included. Since 2012, combination therapy with rifampin and gentamicin was added if blood cultures were positive. Since 2014, patients were included in the study if they met the new criteria for comparison.

**Results:** Among 245 definite SAIE, 75 received C+C, 170 standard therapy. C+C was more effective than the vancomycin and gentamicin protocol in reducing the incidence of new embolic events (6% of incidence if absence of vegetation, 20% if vegetation size <10 mm, 74% if vegetation size >10 mm; p<0.001). S. aureus infection was also more frequent in patients with new embolic episodes (38.3% vs 21.0%; p<0.05). However, vegetation size was smaller in S. aureus IE (7.4 mm vs 11.6 mm vs 11 mm; p<0.001). During hospitalization, in-hospital complications and in-hospital mortality were higher in enterococci episodes (Table).

**Conclusions:** C+C was more effective than standard therapy in reducing the incidence of new embolic events (p=0.04). Prosthetic valve IE was more frequent in enterococcal IE. Infection due to viridans and S. bovis IE was associated with the rate of new systemic embolic events (6% of incidence if absence of vegetation, 20% if vegetation size <10 mm, 74% if vegetation size >10 mm; p<0.001). S. aureus infection was also more frequent in patients with new embolic episodes (38.3% vs 21.0%; p<0.05). However, vegetation size was smaller in S. aureus IE (7.4 mm vs 11.6 mm vs 11 mm; p<0.001). During hospitalization, in-hospital complications and in-hospital mortality were higher in enterococci episodes (Table).

**P3107 | BENCH**

The influence of radiological lesions on neurological outcome in endocarditis patients with preoperative stroke


**Objective:** Infective endocarditis (IE) is associated with high mortality (20–40%) and cerebrovascular complications (CVC). Although radiological brain lesions are important in decision making in IE, their impact on outcome is not clear. We analyzed the influence of different types of preoperative ischemic stroke on outcome.

**Methods:** Retrospectively reviewed all charts, brain imaging, and follow-up data from patients operated for left-sided endocarditis between Jan-07 and April-13. We performed Chi-Square, multivariate, and Cox-regression analyses.

**Results:** A total of 308 patients (age 62.0±13.9) underwent surgery for IE. The preoperative CVC were as follows: stroke in 91 patients (56 ischemic and 35 hemorrhagic), silent cerebral infarction in 27 patients and transient ischemic attack in 4 patients. In-hospital mortality was higher in patients with preoperative stroke than those without it. However, the difference was not statistically significant (27.5% vs. 22.6%, p=0.36). The incidence of death because of neurological complications (massive ischemic infarction or ICB) was 2.6% (n=8) and did not differ between patients with or without preoperative stroke (3.3% vs 2.3%, respectively; p=0.70). Cox-regression analysis showed that preoperative stroke did not affect long-term survival (hazard ratio 0.78, Confidence interval 0.53–1.13). Newly occurring postoperative stroke (n=14) was not associated with higher incidence of new symptomatic embolic events (6% of incidence if absence of vegetation, 20% if vegetation size <10 mm, 74% if vegetation size >10 mm; p=0.001). S. aureus infection was also more frequent in patients with new embolic episodes (38.3% vs 21.0%; p<0.05). However, vegetation size was smaller in S. aureus IE (7.4 mm vs 11.6 mm vs 11 mm; p<0.001). During hospitalization, in-hospital complications and in-hospital mortality were higher in enterococci episodes (Table).

**Conclusions:** This new antibiotic protocol, using the association of high doses cotrimoxazole and clindamycin, appears useful in the treatment of SAIE. A careful management-based approach, using only old unexpressive compounds with rapid shift to oral prescription, may lead to the best results ever founded in these severe patients.
Among the patients with NIE, 33 died during their hospital admission. The manipulation as predisposing procedure were independent clinical risk factors for the presence of a central intravenous catheter, hemodialysis, and genitourinary tract malignancies. On indication of cardiac surgery (but not done) 16 (18.2%) vs. 5.9%, p = 0.030. In contrast, both ATL and SAA-LDL significantly decreased from 3 months to 1 year after smoking cessation (from 1.9 μg/ml to 1.6 μg/ml, p < 0.008, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p < 0.019), and from baseline to 1 year after smoking cessation (AT-LDL: from 2.1 μg/ml to 1.6 μg/ml, p < 0.001, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p = 0.004). On multiple analysis, age, LC, cancer chemotherapy, presence of a central intravenous catheter, hemodialysis, and genitourinary tract manipulation as predisposing procedure were independent clinical risk factors for NIE. Among the patients with NIE, 33 died during their hospital admission. The independent risk factors for in-hospital death were older age (Adjusted Odds ratio [Adjusted OR], 1.04; 95% confidence interval [CI], 1.01–1.07; p = 0.037) and chemotherapy for malignancy (Adjusted OR, 3.89; 95% CI, 1.18–12.87; p = 0.026). Because of the considerable incidence of NIE and its poor prognosis, we should pay attention to early diagnosis and active management of NIE, especially for older patients and patients receiving chemotherapy.

**IMPACT OF SMOKING CESSION ON CARDIOVASCULAR PROGNOSIS: MYTHS AND REALITY**

**P3110 | BEDSIDE**

**Time course changes of atherosclerotic LDL complexes after smoking cessation**

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**Introduction:** Smoking cessation is associated with increase in body weight. While long-term (over 4 years) smoking cessation certainly reduces cardiovascular events, effects of smoking cessation-associated obesity on cardiovascular risks in an early period (within one year) are largely unknown. Serum alpha-1-antitrypsin LDL (AT-LDL) and amyloid A/LDL (SAA-LDL) are oxidatively modified LDL complexes which promote atherosclerosis. We have previously reported that the serum level of the AT-LDL is higher in smokers than in nonsmokers, and that the level decreases at 3 months after smoking cessation. We have also demonstrated that larger weight gain after smoking cessation perturbs such decrease at 3 months after the cessation.

**Purpose:** The present study investigated time-dependent changes in AT-LDL and SAA-LDL after smoking cessation and relationships of these changes with weight gain.

**Methods:** In 17 patients who had continued smoking cessation for one year, we measured serum AT-LDL and SAA-LDL levels by the enzyme-linked immunosorbent assay before smoking cessation, and at 3 months and 1 year after smoking cessation.

**Results:** Body mass index (BMI) significantly increased from baseline (pre-cessation) to 3 months after smoking cessation (from 23.0 kg/m² to 23.7 kg/m², p < 0.027). Serum AT-LDL and SAA-LDL tended to decrease at 3 months after smoking cessation from 2.4 μg/ml to 1.9 μg/ml, SAA-LDL: from 9.0 μg/ml to 9.0 μg/ml, while the decrease was insignificant in this number of patients. BMI further increased from 3 months to 1 year after smoking cessation (from 23.7 kg/m² to 24.1 kg/m², p < 0.038). In contrast, both AT-LDL and SAA-LDL significantly decreased from 3 months to 1 year after smoking cessation (AT-LDL: from 1.9 μg/ml to 1.6 μg/ml, p < 0.008, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p < 0.019), and from baseline to 1 year after smoking cessation (AT-LDL: from 2.1 μg/ml to 1.6 μg/ml, p < 0.001, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p < 0.004).

**Conclusion:** BMI and levels of two atherogenic lipoproteins, SAA-LDL and AT-LDL, time-dependently change after smoking cessation. While BMI progressively increased after smoking cessation, decrease in SAA-LDL and AT-LDL levels at 3 months after smoking cessation was insignificant. In contrast, the beneficial effect of non-smoking certainly overcomes potential cardiovascular risks by associated obesity at one year after the cessation.

**P3111 | BEDSIDE**

**Effect of smoking cessation on metabolic factors and the incidence of metabolic syndrome**

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**Purpose:** Smoking is one of the major risk factors for cardiovascular disease. Although smoking cessation is essential for good health, it might increase body weight and, thereby, have undesirable influence on metabolic factors. We investigated effects of smoking cessation on the incidence of metabolic syndrome (MetS) and its components in the Japanese general population.

**Methods:** Participants in our health checkup program were enrolled and followed up with the endpoint being the development of MetS. Past smokers (n = 1918) and participants who started smoking during the follow-up period (n = 88) were excluded from the study and the remaining 5072 participants (male 49.7%, 55.1±11.5 years old) were analyzed. MetS was diagnosed according to Japanese criteria.

**Abstract P3109 – Table 1**

<table>
<thead>
<tr>
<th>NIE</th>
<th>Survived (n=88)</th>
<th>Died (n=33)</th>
<th>p-value</th>
<th>Survived (n=413)</th>
<th>Died (n=26)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age (year) ≤ 60</td>
<td>58.08±15.72</td>
<td>64.24±11.36</td>
<td>0.020</td>
<td>50.34±17.62</td>
<td>66.54±17.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>52 (59.1%)</td>
<td>16 (56.4%)</td>
<td>0.040</td>
<td>266 (63.9%)</td>
<td>17 (65.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>20 (22.7%)</td>
<td>15 (51.5%)</td>
<td>0.023</td>
<td>15 (5.6%)</td>
<td>1 (3.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Malignancy</td>
<td>32 (36.4%)</td>
<td>20 (60.6%)</td>
<td>0.023</td>
<td>28 (6.8%)</td>
<td>14 (5.1%)</td>
<td>0.11</td>
</tr>
<tr>
<td>On indication of cardiac surgery (but not done)</td>
<td>16 (18.2%)</td>
<td>13 (39.4%)</td>
<td>0.68</td>
<td>127 (30.8%)</td>
<td>128 (38.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td>5 (5.7%)</td>
<td>3 (9.1%)</td>
<td>0.15</td>
<td>17 (4.1%)</td>
<td>15 (5.9%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Methylisothiazolin (MRSA)</td>
<td>17 (19.4%)</td>
<td>11 (33.3%)</td>
<td>0.946</td>
<td>1 (0.2%)</td>
<td>13 (4.8%)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/509/434476 by guest on 07 February 2019
Exposure to cigarette smoke and the morphology of atherosclerotic plaques in extracranial arteries assessed by computed tomography angiography in patients with essential hypertension

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Background: Exposure to cigarette smoke is one of the major health problems of the modern world. In recent years, an important aspect of the research is to evaluate the importance of atherosclerotic plaque morphology in the context of a variety of clinical conditions. The available literature lacks a sufficient amount of scientific evidence on the relationship between exposure to cigarette smoke and the morphology of atherosclerotic plaques in the extracranial arteries.

Purpose: The aim of this study was to determine the relationship between exposure to cigarette smoke and the incidence and morphology of atherosclerotic plaques in the extracranial arteries, as assessed by computed tomography angiography (CTA), in patients with essential hypertension.

Methods: The study included 61 hypertensive patients diagnosed and treated pharmacologically (mean age: 69.8±9.1 years). In the group of patients based on a survey three groups of patients were distinguished, varying in their exposure to tobacco smoke: 17 active smokers (group A), 18 non-smokers, declaring environmental exposure to tobacco smoke (group B) and 26 never smokers, not declaring exposure to cigarette smoke (group C). All the patients underwent CTA of extracranial arteries. CTA images obtained were analyzed in terms of the morphology of atherosclerotic plaques in the various segments of the arteries.

Results: In the whole group of patients plaques were visualized on average in 7.70±1.65 of the 10 segments evaluated, calcified plaques in 6.44±1.60 segments, non-calcified plaques in 2.28±1.77 segments, mixed plaques in 1.08±1.37 segments, calcified mixed plaques in 0.92±1.04 segments, and mixed calcified plaques in 0.56±0.72 segments. The number of segments with the plaques was significantly higher in group C compared to groups B and C (A: 8.88±1.76, B: 7.28±1.41, C: 7.23±1.37, pA-B <0.05, pA-C <0.001). The number of segments with non-calcified and mixed plaques was significantly higher in group A and group B than in group C (non-calcified plaques - A: 5.24±1.95, B: 4.83±1.54, C: 2.92±1.47, pA-C <0.001, pB-C <0.001; mixed plaques - A: 5.65±2.60, B: 5.22±2.02, C: 3.38±1.72, pA-C <0.001, pB-C <0.001). There was no significant difference in the number of segments with calcified plaques between groups A-C.

Conclusions: In patients with essential hypertension, exposure to cigarette smoke is associated with more severe atherosclerosis of extracranial arteries. Both active smoking and environmental exposure to tobacco smoke appear to increase the number of segments of extracranial arteries occupied by non-calcified and mixed atherosclerotic plaques.

P3113 | SPOTLIGHT

Association between tobacco smoking and pro-inflammatory humoral signalling in human epicardial adipose tissue: a prospective cohort study in patients undergoing major cardiac surgery

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Background: Epicardial adipose tissue (EAT) is a source of various pro- and anti-inflammatory cytokines. Studies to date suggest that certain EAT cytokines could act in pathogenesis of coronary artery disease (CAD). A potential relationship between known cardiovascular risk factors such as smoking or obesity and EAT humoral signalling (measured by tissue levels of cytokines) has not been fully elucidated.

Purpose: We designed and conducted a prospective study to determine whether smoking is related to the levels of cytokines in selected subcutaneous (SAT) and epicardial adipose tissue.

Methods: Samples of SAT and EAT were harvested from patients undergoing elective cardiac surgery. Tissue concentrations of tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), adipocyte fatty acid-binding protein (AFABP), leptin, and adiponectin were determined by sandwich ELISA tests, and adjusted for total protein content in the samples. Smoking (smokers vs. non-smokers), sex, age, body mass index (BMI), diabetes mellitus (DM), and obstructive pulmonary disease were used as confounders in stepwise backward regression analysis. ANOVA, and t-test with Bonferroni adjustment were used to compare across non-smoker/stop-smoker/active smoker groups.

Results: Samples from 141 patients were obtained. Information on smoking status was available in 133 patients (67.6%) of whom 76 (57.6%) were non-smokers, 34 (25.8%) stop-smokers, and 22 (16.7%) active smokers. TNF-α, and IL-6 concentrations in EAT and SAT levels of TNF-α were significantly higher in active smokers than in non-smokers, and stop-smokers. No difference was found between stop-smokers, and non-smokers. Higher BMI was associated with higher leptin levels in SAT, and SAT adiponectin was lower in DM patients. The other confounders were not predictive of higher/lower cytokine concentrations.

Conclusions: Smoking was independently associated with higher TNF-α and IL-6 concentrations in EAT, and higher SAT levels of TNF-α. A novel observation that pro-inflammatory cytokines are elevated in EAT in active smokers could represent an important mechanism in pathogenesis of CAD. No differences between EAT humoral signalling in non- and stop-smokers supports the results of previous epidemiological studies which demonstrated the importance of smoking cessation for cardiovascular risk reduction.
Impact of smoking cessation on cardiovascular prognosis: myths and reality / Management of procedural risks

P3115 | BEDSIDE
The combined effect of the 3872 A/G polymorphism on C-reactive protein gene with tobacco smoking on endothelial function, on inflammatory, thrombotic processes and the risk for coronary artery disease
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Background: Tobacco smoking is an established risk factor for coronary artery disease (CAD). Recent studies suggest that the 3872 A/G polymorphism on C-Reac-2(9.2±0.3 vs 4.7±1.1, p=0.007), hsCRP (1.69±0.78 vs 2.06±0.88, p=0.003), fibrinogen (397.3±114.3 vs 490.8±142.8, p<0.001) and D-dimers (425.5±577.2 vs 319.4±308.6, p=0.004) in non smokers. Impressively, the G allele carriers, compared to AA homozygotes, were correlated with significantly impaired endothelial function in the smoking group (4.8±2.9 vs 5.7±3.04, p<0.001), while no effect was observed among non-smokers (5.0±1.2 vs 4.3±2.2, p=0.24).

Conclusions: Our results demonstrate that the genetic predisposition of the G allele of rs1205 to increase the risk for CAD in smokers is mediated by inflammatory and thrombotic processes as well as the impairment of the endothelial function.

P3116 | BEDSIDE
Smoking versus healthy diet impact on left ventricular mass and diastolic performance in essential hypertension patients
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Background: Smoking and arterial hypertension are potent risk factors for the development of atherosclerosis. The Mediterranean diet (Med-Diet) assists in car-705

Purpose: To investigate whether left ventricular (LV) structural changes and diastolic performance in primary hypertension patients. Unfortunately smoking restricts that benefit. Our data emphasize the clinical value of a healthy lifestyle in essential hypertension population in order to maintain cardiac physiology.

Results: According to regression analysis, LV mass index and E/E' ratio, were positively associated with smoking status and negatively with the Med-Diet Score (all p<0.01), independently of age and blood pressure level. E/A ratio was significantly but negatively associated with smoking habit and positively with the Med-Diet Score. Subjects were further divided into subgroups according to smoking habit (current smokers/non smokers) and high/low Med-Diet Score. Non smokers with high Med-Diet Score (n=34) had significantly lower LV mass index and E/E' ratio and higher E/A ratio compared to all other smoking/Med-Diet subgroups (all p<0.05, figure).

Conclusions: High adherence to the Mediterranean diet confers a favorable impact on LV structure and diastolic function in primary hypertension patients. Unfortunately smoking restricts that benefit. Our data emphasize the clinical value of a healthy lifestyle in essential hypertension population in order to maintain cardiac physiology.

MANAGEMENT OF PROCEDURAL RISKS

P3117 | BEDSIDE
Transradial access for percutaneous coronary intervention (PCI) in British Columbia, Canada from 1999 to 2013: consistently lower mortality and transfusion rates in a large unselected patient cohort
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Background: Transradial access (TRA) for PCI has become more common in an effort to minimise procedural related complications such as bleeding. Despite this, significant variation remains in arterial access site used for PCI depending on operator experience and institutional practice. Using data from a large unselected patient cohort, we examined trends in the utilisation of TRA along with mortality and peri-procedural bleeding following PCI.

Methods: Data on all PCI cases from 1999 to 2013 for patients presenting with acute coronary syndrome (ACS) or stable angina (SA) from the British Columbia Cardiac Registry were linked to vital statistics mortality records. Linkage with the BC Central Transfusion Registry (CTR) was used to measure red blood cell (RBC) transfusions occurring in the 10 days following PCI as a surrogate safety marker.

Results: Between June 1, 1999 and May 31, 2013, 83,659 PCI cases were performed. There was an increase in the use of TRA for PCI in patients presenting with SA (20.4% to 41.7%, p=0.0001) and ACS (17.9% to 48.9%, p=0.0001) including those presenting with ST elevation MI (p=0.0001) and patients ≥80 years old (p=0.0001). Over the study period, peri-procedural transfusion rates following TRA remained stable (1.5% to 1.4% from 1999 to 2012; p=0.8) but increased within the femoral group (1.8% to 3.9%, p<0.0001). In a risk adjusted model, TRA independently predicted lower transfusion rates as well as 30-day mortality when adjusted for pre-procedural patient demographic and clinical characteristics including age, sex, procedural urgency, ejection fraction, cardiogenic shock, and renal dysfunction.

Conclusions: Using data from a large provincial registry, we report a sustained rise in the use of TRA for PCI cases over more than a decade of clinical practice. Compared to patients undergoing femoral access, transradial access is associated with lower peri-procedural bleeding as well as short and longer term mortality. Our data strongly support recent guidelines emphasising the clinical benefits of TRA for all patients undergoing PCI.

P3118 | BEDSIDE
The European and Chinese cardiac and renal remote ischaemic preconditioning study (EURO-CRIPS): a randomized controlled trial
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Aims: The potential protective effect of remote ischemic preconditioning (RIPC) on cardiac and renal induced nephropathy (CIN) after Percutaneous Coronary Intervention (PCI) remains to be defined.

Methods: A double-blind, randomized, placebo controlled multicenter study was performed. Patients were allocated 1:1 to RIPC or standard therapy if they were younger than 85 years old; with a renal clearance in the interval 30–60 ml/min/1.73m2 and candidate to PCI for all clinical indications except for primary PCI in ST segment elevation myocardial infarction (STEMI). Incidence of CIN was the primary end point, whilst incidence of peri-procedural myocardial infarction the secondary one. Diabetes mellitus was the only pre-specified exclusion.

Results: From February 2013 to April 2014 a total of 3108 patients scheduled for angiography were screened. 442 fulfilled the inclusion criteria, 223 received PCI and were randomized to sham RIPC (n=107) or treatment group (n=116). The
only pre-specified subgroup of diabetic patients presented 85 (38%) cases. RIPC significantly reduced AKI incidence in the overall population (12.1% vs. 26.1%, p<0.01, with a number needed to treat 9), in non diabetic patients (9.2% vs 25.0%, p<0.02) whilst diabetic subgroup showed no benefit (16.7% vs. 28.2%, p=0.21). A trend, although not significant, was reported for periprocedural myocardial infarction (Creatin Kinase MB more than 5 U/L: 8.4% vs 16.4%, p=0.07; Troponin T more than 5 U/L: 27% vs 38%, p=0.21).

Conclusions: Remote ischemic preconditioning significantly reduces the incidence of CIN in non diabetic patients undergoing PCI. Larger sample size is presumably needed to assess effect of RIPC for patients with diabetes mellitus.

P3119 | BEDSIDE
Contrast volume to creatinine clearance ratio for the prediction of contrast induced nephropathy in patients undergoing coronary angiography or percutaneous intervention
L. Barbieri1, M. Verdoia1, P. Marino1, H. Suryapranata2, G. De Luca1 on behalf of Novara Atherosclerosis Study Group (NAS), 1Maggiore Della Carita Hospital, Department of Cardiology, Novara, Italy; 2University HospitalNijmegen, Cardiology, Nijmegen, Netherlands

Background: Contrast Induced Nephropathy (CIN) is a complication of procedures that foresee the use of contrast media. The identification of high-risk patients and preventive optimal hydration are key points to reduce the incidence of CIN.

Purpose: Aim of this study was to evaluate the role of contrast volume/creatinine clearance ratio (V/CrCl) in the prediction of CIN after coronary angiography or percutaneous intervention (PCI).

Methods: Our population is represented by 2308 consecutive patients undergoing coronary angiography and/or PCI. The risk of CIN was evaluated across quartiles of V/CrCl. ROC curves were used to identify the best predictive value. CIN was defined as an absolute increase of 0.5mg/dL or a relative > 25% in creatinine levels at 24–48 hours after the procedure.

Results: The total incidence of CIN was 12.2% and was significantly higher in the fourth quartile (1st Quartile 8.8%, 2nd Quartile 8.9%, 3rd Quartile 11.6% and 4th Quartile 19.4%, p<0.001). By the use of ROC curves we identified a V/CrCl > 6.15 as the best discriminant value for the prediction of CIN, that occurred in 25.1% of patients with V/CrCl > 6.15 vs 9.7% in patients with V/CrCl <6.15 (OR [95% CI] = 3.12 [2.38–4.12], p<0.001). Patients with V/CrCl>6.15 were older, with family history of CAD, hypertension, diabetes, hypercholesterolemia and renal failure. They had more often a previous history of myocardial infarction, previous revascularization, previous cerebrovascular accident and they were more often in therapy with statins, nitrate, aspirin, calcium antagonist and diuretics at admission. V/CrCl>6.15 was more often associated with a lower level of red blood cells and haemoglobin, lower total and low density lipoprotein cholesterol, but higher uric acid, glycaemia and creatinine at admission. They had more often an acute coronary syndrome as indication for angiography with consequent higher prevalence of PCI and higher amount of contrast volume and preventive optimal hydration are key points to reduce the incidence of CIN.

Conclusions: A trend, although not significant, was reported for periprocedural myocardial infarction (Creatin Kinase MB more than 5 U/L: 8.4% vs 16.4%, p=0.07; Troponin T more than 5 U/L: 27% vs 38%, p=0.21).

P3120 | BEDSIDE
Disaster in the cath lab - cardiogenic shock induced by procedure: results from the EHS PCI registry
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Background: There is a large body of literature on acute myocardial infarction complicated by cardiogenic shock (CS). However, very little is known about initially hemodynamically stable patients that develop CS in the course of percutaneous coronary intervention (PCI).

Methods: Between 2005 and 2008 a total of 47,407 consecutive patients were prospectively enrolled into the PCI-Registry of the Euro Heart Survey Programme. Interventions with periprocedural complications that were classified as follows “shock induced by procedure” in the case report form were analysed. Clinical and interventional characteristics as well as hospital outcomes of initially hemodynamically stable patients that develop CS in the course of PCI were evaluated. Results: 68 patients (0.2%) developed CS. The majority of cases were acute coronary syndromes with complex lesions (table). Most patients had multi-vessel disease and known heart failure. Procedural success was low and hospital mortality was very high.

Conclusions: In this real-world registry the rate of initially hemodynamically stable patients that develop CS in the course of PCI was very low. Patients at a-priori high risk were more likely to be affected by this complication. Hospital mortality rate was very high.
radiation. A reduction in radiation doses as low as possible, maintaining the quality of procedures is essential.

**Purpose:** To analyze the results of a novel radiation reduction protocol (RRP) system for coronary angiography and interventional procedures and the determinants of radiation dose.

**Methods:** 960 consecutive procedures from a single catheterization laboratory [diagnostic coronary angiographies (CA) and percutaneous coronary interventions (PCI)] were analyzed. 283 were performed before RRP and 676 after it. RRP implementation consisted in reducing the number of ventriculographies and angiographies for cases with a clear indication, reducing number of cine runs, and using as much as possible low resolution fluoroscopy and last fluoroscopy hold (a software program that enables dynamic storage of last fluoroscopy sequences).

**Results:** There were no significant differences in clinical baseline features nor in the number of CA performed during the 2 periods (56.6% vs 54.9%; p=0.5). They had a similar complexity [multivessel or left main PCI (23.3% vs 19.6%; p=0.07); syntax score (16.6±12.2 vs 17.2±12.6; p=0.7); acute coronary syndromes (43.9% vs 45.2%; p=0.4); bifurcations (13.6% vs 17.6%; p=0.05)] apart from a double proportion of total chronic occlusions performed after the RRP implementation (5.3% vs 10.6%; p=0.01). The angiographic success was similar in both periods (98.3% vs 99.2%; P=0.6). After the implementation of RRP, there were no significant differences in median fluoroscopy time (13.3 vs 11.3 min; p=0.8) and duration of procedures (26.9 vs 23.4 min; p=0.14). A significant reduction of the percentage of procedures with ventriculography (80.9% vs 71.1%; p=0.001) or with angiography (15.4% vs 4.4%; p=0.001) was observed, as well as a significant reduction in cine runs (21.8 vs 6.9; p=0.001) and dose-area product (DAP) (165 vs 71 Gy cm²; p<0.0001).

**Conclusions:** With the implementation of a RRP, a highly significant 56.7% reduction of procedures. A RRP should be strongly considered among interventional cardiologists.
P3126 | BEDSIDE
Unmasking the prevalence of silent myocardial infarction, ischaemia and microvascular dysfunction in HFPEF with CMR
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Purpose: HFPEF (heart failure with preserved ejection fraction) is an increasingly recognized clinical entity, and its underlying aetiology remains unclear. This study aimed to assess which population with clinical features of HF and preserved LVEF (<50%) comprise the silent myocardial infarction (MI) group.

Methods: Comprehensive CMR of adenosine stress perfusion and late gadolinium enhancement (LGE) was undertaken as part of DIAMOND HFPEF (Developing Imaging And plasMa biomarkers IN Describing Heart Failure with Preserved Ejection Fraction) – a phenotyping, prospective, observational, cohort study. Inclusion criteria were: clinical features of HF and left ventricular ejection fraction (LVEF) of <50% as per echocardiography. Main exclusion criteria were: suspected or confirmed cardiomyopathy, pericardial constriction, non-cardiovascular late expectation < 6 months, myocardial infarction (MI) in the preceding 6 months, severe valve disease, obstructive pulmonary disease and estimated glomerular filtration rate < 30.

Results: A total of 181 patients were enrolled and 154 underwent CMR (n=5 did not undergo stress perfusion). Baseline characteristics reveal: mean age 72±9 years, male 51%; hypertension 90%; diabetes 49%; hypercholesterolaemia 49%; smoking 53%; known CAD 21%; angina 18% and LVEF 58±12. Qualitative analyses revealed "silent" MI in 14 patients (9%). Reversible perfusion defects were seen in 30 (total = 20%) patients of which 19 (total = 13%) likely represented ischaemia in a CAD territory distribution and the remainder (total = 7%) were suggestive of microvascular dysfunction (MVD).

Conclusion(s): A large proportion of HFPEF patients (1/5 in our cohort) have significant previously undiagnosed CAD. Incorporating CMR into the diagnostic pathway for HFPEF enables better phenotyping and earlier initiation of primary and secondary prevention therapies which may alter prognosis.

P3127 | BEDSIDE
Acute chamber stiffening is responsible for high filling pressures during exercise in HFNEF. A dynamic pressure-volume and histological study
C. Perez Del Villar1, J. Bermejo1, K. Savastis2, P. Martiniez-Legazpi1, B. Lopez2, R. Yotli1, A. Gonzalez-Mansilla2, F. Spillmann2, F. Fernandez-Aviles2, C. Tschope1, 1University General Hospital Gregorio Maranon, Department of Cardiology, Madrid, Spain; 2Charite- Campus Benjamin Franklin, Berlin, Germany; 3University Clinic of Navarra, Centre for Applied Medical Research, Navarra, Spain; 4Klinik- Campus Virchow-Klinikum (CVK), Berlin, Germany

Background: Delayed relaxation, increased stiffness, and impaired elastic recoil have been identified as sources of diastolic dysfunction in patients with heart failure and preserved ejection fraction (HFPEF). For the first time, we aimed to quantify the contribution of these factors to LV filling pressures at rest and during exercise in HFNEF. We also investigated the relationship between dynamic stiffness and fibrosis.

Methods: 36 patients (24 with HFNEF and 12 controls without coronary or structural disease) underwent LV catheterization with pressure-volume (PV) analysis at baseline, during handgrip exercise, and during atrial pacing at 120 bpm. Endomyocardial biopsies were obtained to characterize fibrosis. Using a previously validated PV data database, we calculated active and passive pressures that govern LV filling, and measured the rate of relaxation (τ), equilibrium volume (V0), elastic recoil and chamber stiffness (Ss and dP/dV at V0).

Results: At baseline, LV end-diastolic pressures (EDPs) were higher in HFNEF patients (13±5 vs. 8±3 mmHg, p=0.03) and significantly increased during exercise up to (23±8 vs. 13±13 mmHg, p=0.03). Despite exercise prolonging values of τ in HFNEF patients, incomplete relaxation (residual tension) was only responsible for 1±2 mmHg of EDP. Therefore, passive forces were responsible for more than 85% of EDPs in both populations during both phases. In turn, stronger passive forces during exercise were caused by acute changes in chamber stiffness. Remarkably, the degree of exercise-induced chamber stiffening was much higher in HFNEF patients than in controls (ΔSs = 55±62 vs. 105±32%, p<0.05), leading to a steeper passive PV-curve (ΔdP/ΔV= 141±138 vs. 48±91%, respectively p<0.01). Collagen content correlated with stiffness (dP/dV) both at baseline (r=0.43) as well as during exercise (r=0.69). Insoluble collagen correlated with Ss during exercise (r=0.78). Rapid pacing neither modified LV passive pressures nor increased EDPs, although relaxation was frequent and incompletely uncompleted.

Conclusion: Elevated systolic blood pressure and short height are the main predictors of the long-term risk of development of diastolic dysfunction in middle-aged subjects.

P3128 | BEDSIDE
Differences in prevalence and severity of sleep-disordered breathing in HF-REF and HF-PEF: first results of the prospective German SDB-HF-XT Registry
O. Oldenburg1, M. Arz2, E. Erdmann3, H. Teschler4, B. Wallmijn5, K. Wegscheider6, H. Woerthle*7 on behalf of the SchlaHT-XT Investigators, 1Heart and Diabetes Center NRW, Ruhr-University Bochum, Bad Oeynhausen, Germany; 2University Hospital Regensburg, Regensburg, Germany; 3Cologne University Hospital – Heart Centre, Essen, Germany; 4Department of Cardiology, Heart and Diabetes Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany; 5University Medical Center Hamburg Eppendorf, Department of Medical Biometry and Epidemiology, Hamburg, Germany; 6ResMed Science Center, ResMed Germany Inc, Martinsried, Germany

Background: Sleep-disordered breathing (SDB) is thought to be a highly under-diagnosed but relevant co-morbidity in heart failure (HF) patients with reduced (HF-REF) and preserved left ventricular ejection fraction (HF-PEF). The SchlaHT-XT registry is a longitudinal study of patients with HF-REF and HF-PEF of any severity and aims to document the prevalence and severity as well as to understand importance of diagnosis and treatment of SDB in these patients.

Methods: The SchlaHT-XT registry prospectively includes patients with stable HF as defined as a symptom complex of shortness of breath and rapid fatigue on the basis of cardiac disease or any impairment of heart function as determined by a cardiologist. Thus, patients of all NYHA functional classes and cardiac dysfunction with reduced (HF-REF) or preserved (HF-PEF) ejection fraction are included. SDB was determined by multichannel polygraphy recording and using the apnoea-hypopnoea-index (AHI) as a metric of SDB.

Results: To date 1102 patients with either HF-PEF (54.5%) or HF-REF (45.5%) (68±11 years, 66.0% male): NYHA I 8.4%; NYHA II 51.5%; NYHA III 24.7%; NYHA IV 9.5 but ≥12.1, 3rd trt ≥9.5 but < 12.1, 2nd trt ≥9.5 but < 12.1, the 3rd trt indicating severe diastolic dysfunction. The Karolinska Rennes (KaRen) biomarker sub-study enrolled 86 patients with acute HF and ejection fraction <45%. After 4–8 weeks, blood sampling using multiplex immunoassay (Proseek Multiplex CVD 196x96) and analyzed using the Delta1/ΔΔCt method.

Conclusion: In a prospective longitudinal HF registry, prevalence of moderate to severe SDB is different between HF-PEF and HF-REF patients: Moderate to severe SDB is more prevalent in HF-REF with a greater proportion of patients presenting with CSA.

P3129 | BEDSIDE
Inflammatory biomarkers predict HF severity and prognosis in patients with heart failure with preserved ejection fraction
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Purpose: Underlying mechanisms in heart failure (HF) with preserved ejection fraction (HF-PEF) remain unknown. We investigated 92 cardiovascular plasma biomarkers and their correlation to prognosis, diastolic dysfunction and functional class in HFPEF.

Methods: The Karolinska Rennes (KaRen) biomarker sub-study enrolled 86 patients with acute HF and ejection fraction <45%. After 4–8 weeks, blood sampling and inflammatory diagnostic assays were performed. Patients were followed for a median 579 days (Q1-Q3 276;1178) regarding the composite outcome time to all-cause mortality or HF hospitalization. Biomarkers were quantified by a multiplex immunosassay (Proseek Multiplex CVD 196x96) and analyzed
Diastolic dysfunction / Hypertension treatment

P3130 | BEDSIDE
Insulin resistance is an independent predictor of left ventricle diastolic dysfunction across the diabetic continuum
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Background: Type 2 diabetes mellitus (T2DM) increases the risk of heart failure but the underlying mechanisms leading to diabetic cardiomyopathy are poorly understood. Left ventricle diastolic dysfunction (LVDD) is one of the earliest cardiac changes in these patients being associated with the progression to diabetic heart failure. It is not known if this association is induced by insulin resistance or a consequence of hyperglycemia.

Purpose: We aimed to evaluate the association between LVDD and insulin resistance in individuals in several phases of the diabetic continuum.

Methods: Population-based study including a cohort of 1,063 individuals aged ≥45 years (36% male, 61.2±9.6 years). Diastolic function was assessed by echocardiography, using tissue Doppler analysis (E’ velocity and E/E’ ratio) according to the latest consensus guidelines. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) score.

Results: Metabolic syndrome (MetS) without T2DM was present in 31% of patients and T2DM in 12%. The HOMA-IR score correlated to E’ velocity (r=-0.20; p=0.001) and E/E’ ratio (r=-0.20; p<0.0001). There was a progressive worsening in E’ velocity (p for trend <0.001) and in E/E’ ratio (p<0.0001) across HOMA-IR quartiles. Individuals in the highest HOMA-IR quartile were more likely to have LVDD even after adjustment for age, sex, blood pressure and body mass index (adjusted OR: 1.82; 95% CI: 1.04–3.30). From normal individuals, to patients with MetS but without T2DM, to patients with T2DM, there was a progressive decrease in E’ velocity (11.2±3.3 vs 9.7±3.1 vs 9.2±2.6 cm/s; p<0.0001), higher E/E’ (6.9±2.3 vs 7.8±2.7 vs 9.0±3.6; p<0.0001) and more diastolic dysfunction (adjusted OR: 1.62; 95% CI: 1.12–2.36 and 1.78; 95% CI: 1.09–2.91, respectively).

Conclusion: HOMA-IR score and presence of MetS were independently associated with LVDD. Changes in diastolic function are already present before the onset of T2DM, being mainly associated with the state of insulin resistance.

HYPERTENSION TREATMENT

P3131 | BEDSIDE
The impact of overt vascular disease in patients with comorbid type-2 diabetes and hypertension: data from the Dialogue registry
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Background: Patients with comorbid type-2 diabetes and hypertension are at increased risk for vascular disease (VD) and disease- and treatment-related complications if VD is present. We assessed treatment strategies and outcomes in hypertensive diabetic patients with and without VD.

Methods: DIGITALIZE is a prospective, multi-center registry in patients with diabetes and hypertension. VD was defined as the presence of CAD, prior MI, prior PCI, prior CABG, prior stroke and/or known PAD.

Results: Out of 8,616 patients included, 30.3% were diagnosed as having VD. BP was comparable while HbA1c and fasting blood glucose was lower. They had a significantly higher burden of hypertensive episodes within the 12 months prior enrollment. Differences in treatment target assignment were minor for HbA1c ≤6.5% (37.1% VD vs. 39.8% no VD; p<0.05) and systolic BP ≤130mmHg (36.1% VD vs. 38.9% no VD; p<0.01). Antidiabetic treatment strategies at baseline differed with respect to metformin (74.8% vs. 82.2%; p<0.0001), a lesser use of DPP-4 inhibitors (59.9% vs. 63.3%; p<0.01) and a more frequent use of SU (19.3% vs. 16.7%; p<0.01) and Insulin (0.01% vs. 0.01). Death rates in significantly higher were seen in the VD group at the 6 and 12 months follow-up.

Conclusions: VD is a frequent comorbid disease in patients with diabetes and hypertension. Treatment targets do not adequately reflect the specific comorbidity burden and the risk of treatment emergent adverse effects. Patients with VD experience more episodes of hypoglycemia, which might reflect the antidiabetic drug treatment pattern.

Table 1

<table>
<thead>
<tr>
<th>Age in years</th>
<th>HbA1c ≤5.6%</th>
<th>HbA1c ≤7.0%</th>
<th>HbA1c ≤7.5%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤60 years</td>
<td>63.6±11.0</td>
<td>66.4±10.7</td>
<td>66.0±11.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>68.2±11.4</td>
<td>70.6±11.7</td>
<td>70.7±11.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure, %</td>
<td>11.5</td>
<td>13.5</td>
<td>17.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PAD, %</td>
<td>5.0</td>
<td>7.6</td>
<td>9.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dialysis, %</td>
<td>0.2</td>
<td>0.1</td>
<td>0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP (DBP) target ≤130 (≥80)</td>
<td>69.9 (72.7)</td>
<td>20.0 (28.6)</td>
<td>15.8 (28.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>51.1 (50.8)</td>
<td>57.9 (60.0)</td>
<td>63.2 (64.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: The data illustrate, that blood glucose targets chosen in patients with type-2 diabetes consider patient characteristics and overall co-morbidity and are aligned with the corresponding blood pressure treatment targets. There are, however, no major effort for treatment target achievement if treatment targets are not met by 6 months.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/509/434476 by guest on 07 February 2019
Background: Chronic hypoxia induces pulmonary vascular remodeling, pulmonary hypertension, and right ventricular hypertrophy. At present, little is known about mechanisms driving these responses. We performed to assess the role of silenced phosphodiesterase 5 inhibitor prevents hypoxia-induced pulmonary arterial hypertension.

Methods: Adult male Sprague-Dawley rats were exposed 2 weeks to chronic hypoxia (15% O2). CH rats received sildenafil (1.4 mg/kg/d, ip, n=10) or saline (n=10). The effects of CH on cardiopulmonary hemodynamics were assessed by Doppler echocardiography and RV catherization. Lungs and RV were removed and frozen for biochemical analysis or formalin-fixed and paraffin-embedded for immunofluorescence staining (IF).

Results: Compared to N, Doppler echocardiography revealed reduced pulmonary artery (PA) acceleration time and velocity integral (−41±4% and −74.7±0.3%, respectively) and increased PA systolic pressure (+2.0±0.8%) in CH rats, which rescued by sildenafil. Although CH resulted in a 1.7-fold increase in RV systolic pressure and in RV hypertrophy (expressed as RV/LV+Septum ratio) accompanied by a 1.5-fold increase in medial wall thickness of pulmonary arteries, these were significantly attenuated by sildenafil. This was associated with blunted proliferation of cells in response to stress, as judged by BrdU incorporation that was higher in CH than CH-sildenafil rats (BrdU+cells in lung: 46.8±4.9% vs 11.6±3.0%, respectively; BrdU+cells in RV: 25.9±4.2% vs 7.8±4.2%, respectively). Additionally, compared to N, a double IF showed an increase in the BrdU-alpha-SMA+cells in CH tissues (for lung: 0.52±0.4 vs 3.9±0.4, respectively; for RV: 0.3±0.1 vs 1.7±0.07, respectively), which inhibited by sildenafil (0.7±0.2 vs 2.0±0.4 for lung and RV, respectively). Compared to N, RT-PCR showed an mRNA up-regulation of collagen III in the lung (1.5-fold) and in the RV (2.0±0.2) tissues after CH, confirmed by interstitial fibrosis, which was substantially reduced by sildenafil. Interestingly, in the lungs and RV tissues obtained from N and CH rats, the expression of LC3A/B (marker of autophagy) did not alter, while it was significantly increased with sildenafil.

Conclusion: Sildenafil treatment contributes to ameliorate the hypoxia-induced cardiopulmonary remodeling by reducing the proliferation of new fibroblasts and by activating autophagy as a protective mechanism to prevent excess collagen accumulation.

P3134 | BEDSIDE First quality assessment of cardiovascular drugs in 10 sub-Saharan African countries: the seven study


Methods: In 2014, in randomized pharmacies and street markets, in Senegal, Burkina Faso, Congo, Benin, Ivory Coast, Togo, Niger, Democratic Republic of Congo, Congo, Mauritania, and Guinea. A validated reversed-phase liquid chromatography method was used for the dosage of active ingredient in a certified public laboratory in France.

Results: In randomized pharmacies and street markets, in Senegal, Burkina Faso, Congo, Benin, Ivory Coast, Togo, Niger, Democratic Republic of Congo, Congo, Mauritania, and Guinea. A validated reversed-phase liquid chromatography method was used for the dosage of active ingredient in a certified public laboratory in France.

Conclusion: We present the first data on the quality of cardiovascular drugs available in African countries. The prevalence of poor quality drugs is high. Our results suggest a need for continued monitoring strategies for assessing drug quality in developing countries.

P3135 | BEDSIDE Effect of renal sympathetic denervation on the expression of microRNA-133a, an indicator for reverse remodeling processes in hypertensive heart disease

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Background: Arterial hypertension (HT) is associated with cardiovascular remodeling, which contributes to hypertensive heart disease (HHD). MicroRNAs

| Category of cardiovascular drugs quality in samples collected in ten African countries (n%) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Drugs | Category of quality A | Category of quality B | Category of quality C | Total |
| Acenocoumarol | 164/100% | 165 |
| Amiodarone | 218/17.5% | 84/27.5% | 3/1% | 305 |
| Anticoagulant | 208/98.9% | 37/15.1% | 24/9.5% | 235 |
| Captopril | 175/74.2% | 39/16.6% | 21/8.8% | 235 |
| Furosemide | 210/87.5% | 30/12.5% | 240 |
| Hydrochlorothiazide | 157/58.2% | 93/35.9% | 160 |
| Simvastatin | 148/62.2% | 32/12.7% | 180 |

Total% | 1.281/4.3% | 225/14.7% | 24/1.6% | 1530
(miRNAs) have been proposed as novel biomarkers in patients with cardiovascular diseases. In particular, miRNA-133a has been associated with cardiovascular reverse-remodeling processes in HHD. Renal sympathetic denervation (RSD) represents a treatment option for patients with resistant HT. The primary aim of the present study was to examine the effect of RSD on HHD by analyzing the expression of miRNA-133a, as a specific miRNA for cardiovascular reverse-remodeling processes in HHD.

Methods: A total of 50 consecutive patients (mean age: 65.2 ± [±10.4]) undergoing RSD were included in this study. A therapeutic response was defined as an office SBP reduction of ≥10 mmHg after RSD. Venous blood samples for the analysis of miRNA in serum were collected prior to and 6 months after RSD.

Results: A significant reduction in the office SBP of 24.4 [±3.2 (±7.9)] mmHg; p<0.001) was documented 6 months after RSD. At this time point circulating concentrations of miRNA-133a were significantly increased (4-fold; p<0.001) compared with baseline values. Correlation analysis showed a significant relationship between baseline SBP values and SBP reduction (r=−0.66, p<0.001) as well as between elevated miRNA baseline levels and the increase in miRNA levels (r=−0.48; p<0.001) after the 6-month follow-up. SBP reduction was associated with an increase in miRNA-133a levels (r=0.36, p<0.02) 6 months after RSD. In addition, successful SBP reduction in responders was associated with a significantly greater increase of miRNA-133a levels when compared with BP non-responders (p=0.03).

Conclusion: In addition to the effective SBP reduction in response to RSD, this study demonstrates an effect of RSD on miRNA-133a reflecting cardiovascular reverse-remodeling processes. These results provide information on a beneficial effect of RSD on cardiovascular reverse remodeling and HHD in high-risk patients.

NEW CONCEPTS IN ECHOCARDIOGRAPHY

3167 | BEDSIDE
Vena contracta area for severity grading in functional and degenerative mitral regurgitation: A study based on transesophageal 3D colour Doppler in 419 patients


Background: Vena contracta area (VCA) derived by 3D colour Doppler is a new parameter for assessment of mitral regurgitation (MR). Aim of the study was to establish VCA cut-off values for grading of MR, using the EACI recommended 2D integrative approach as a reference.

Methods: Patients with at least moderate MR underwent transesophageal echocardiography. The following 2D parameters were assessed: Biplane Vena contracta width and effective regurgitant orifice area (EROA) according to PISA method. Quantification of VCA was performed in a 3D colour Doppler dataset. In 90 patients a 3D dataset of the left ventricle (LV) and the left ventricular outflow tract (LVOT) was acquired. Velocity-time integral (VTI) in the LVOT was determined using a pulsed wave Doppler. Regurgitation volume (RV_3D) was calculated as following: (LV enddiastolic volume − LV endsystolic volume) – (LVOT area × VTI × LVOT). In addition, regurgitation volume was calculated using VCA and VTI of MR jet (RV_VCA). The patient population was divided into a group with functional MR (FRM group) and a group with degenerative MR (DMR group). The results of the echocardiographic parameters are displayed in Table 1. To define cut-off values for differentiation between moderate and severe MR, receiver operating characteristic (ROC) curves were calculated for EROA and VCA (Table 2).

Regurgitation volumes calculated using VCA (RV_VCA) correlated with RV_3D (r=0.96, p<0.001). RV_VCA values were higher when compared with RV_3D (r=0.7 ml, p<0.001)

Table 1 (echocardiographic parameters)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FRM group (n=95)</th>
<th>DMR group (n=129)</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA (cm²)</td>
<td>0.49 ± 0.17</td>
<td>0.61 ± 0.19</td>
<td>70%</td>
</tr>
<tr>
<td>VCA (cm²)</td>
<td>0.49 ± 0.17</td>
<td>0.61 ± 0.19</td>
<td>70%</td>
</tr>
</tbody>
</table>

Table 2 (receiver operating characteristic curves)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Area under curve</th>
<th>Optimal cut-off grade severe MR</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA</td>
<td>0.50</td>
<td>(0.15)</td>
<td>50%</td>
</tr>
<tr>
<td>VCA</td>
<td>0.50</td>
<td>(0.15)</td>
<td>50%</td>
</tr>
</tbody>
</table>

Conclusion: This study delivers cut-off values for VCA in a relatively large population of patients with different types of mitral regurgitation. Regurgitation volumes derived by VCA showed a good correlation with the reference method using 3D volumetric datasets of LV.

3168 | BEDSIDE
Left atrial function across the spectrum of cardiovascular disease in the elderly- the ARIC study

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Background: Left atrial (LA) enlargement is recognized a key predictor of adverse cardiovascular (CV) outcomes; emerging evidence also suggests the importance of LA function, although it is rarely measured. We aimed to examine variation in LA function across the spectrum of CV disease burden in a large cohort of older adults living in the community.

Methods: We studied 1,210 participants in the Atherosclerosis Risk in Communities (ARIC) Study who were in sinus rhythm and free of valvular disease and acceptable quality 3D-echocardiograms. We examined the correlates of LA volumes, LA emptying fraction (LAEF), and LA global longitudinal strain (LAGLS) measured using 3D echocardiography.

Results: The mean age was 76±5 years; 59% were women. The overall mean LAEF was 53±12%; participants in the lowest quartile of LAEF (39%; IQR 33–43) were older, more likely to be hypertensive, to have heart failure (HF) and higher NT-proBNP. LAEF and LAGLS were inversely correlated with NT-proBNP (r=−0.24, p<0.001; −0.22, p<0.001). In multivariable analyses, participants with HF had significantly higher LA volumes and worse LA function than apparently “healthy” individuals (free of CV risk factors) or those with only hypertension. Healthy participants had smaller LA volumes than those with hypertension, but there were no significant differences in LA function between “healthy” and hypertensive adults (Figure).

Conclusion: The present study provides normal ranges for LA function in the “healthy” elderly versus those with hypertension and HF, highlighting for the population-based study of LA function imaging biomarker.

Acknowledgement/Funding: This study was supported by The National Heart, Lung, and Blood Institute (NHLBI), Z01-HL-10177 (to A. Goncalves) and the National Institute of Aging (AG034476). The ARIC study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts HHSN268201500003C, HHSN268201500001C, HHSN268201500002C, HHSN2682015000006C, HHSN2682015000005C, and HHSN2682015000004C. The authors thank the ARIC Investigator Group, ARIC Study Coordinating Center, and the ARIC Investigators for their contributions to this study.

3169 | BENCH
Ultrasound relative pressure imaging as a new and noninvasive method to visualize intracardiac pressure distribution: a validation study

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Background: Velocity information can be converted to pressure information based on fluid momentum equations. We have applied the divergence operation of the Navier-Stokes equation to velocity fields obtained by vector flow mapping (VFM) and developed a new method to visualize regional pressure distribution (Ultrasonic Relative Pressure Imaging, RPI). RPI calculates pressure difference (PD) and shows color-coded regional pressure distribution within the cardiac chambers noninvasively.

Purpose: The purpose was to evaluate the feasibility of RPI, and to validate this new method against invasive pressure measurements.

Methods: In an open-chest dog model (n=4), a double sensor Millar catheter was introduced through the left atrial appendage to the left atrium (LA), through the mitral valve into the left ventricle (LV). Sensors were placed 5 cm apart, and pressures were measured at LA and LV apex. Simultaneously, VFM was recorded from apical long axis views. Recordings were acquired at baseline and during phencyclidine infusion. RPI was created offline, a 5 cm line was manually drawn to visualize intracardiac pressure distribution: a validation study

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were analyzed. We found a good correlation between noninvasive and invasive measurements of PVR with \( r = 0.83, p = 0.0001 \) (Figure - right).

**Conclusion:** Estimation of intracardiac relative pressure distribution is feasible by RPI and its measurements show good correlation with invasive catheter measurements.

**3170 | BEDSIDE**

**Comparative usefulness of a novel echocardiographic measurement of pulmonary vascular resistance based on a theoretical formula among non-invasive methods**


**Background:** Although pulmonary vascular resistance (PVR) is an important pathophysiologic parameter, its use has been limited because of the invasiveness of measurement by right heart catheterization. Several noninvasive methods have been proposed, but they remain empirical, lacking sufficient accuracy.

**Purpose:** The aims of this study were to propose a novel echocardiographic measurement of pulmonary vascular resistance based on a theoretical formula and investigate the feasibility and accuracy of this method in patients with heart failure.

**Methods:** Echocardiography was performed in 27 patients before right heart catheterization. Peak tricuspid regurgitation pressure gradient (TRPG), pulmonary regurgitation pressure gradient in end-diastole (PRPged), and cardiac output derived from the time-velocity integral and the diameter in the left ventricular outflow tract (COVOT) were measured by Doppler echocardiography. PVR based on a theoretical formula (PVRtheo) was calculated as (TRPG - PRPged)/3COVOT in Wood units (WU). PVRtheo was compared with PVR obtained by the methods of Abbas et al., Haddad et al., and Kouzu et al. Along with PVR obtained by catheterization (PVRcath) using the linear regression and Bland-Altman analyses.

**Results:** The mean PVRcath was 2.4±1.4 WU. PVRtheo correlated well with PVRcath (\( r = 0.83, p = 0.001 \)). Bland Altman analysis showed a homogeneous distribution with a difference of ±0.79 Wood units. PVRtheo appeared to be accurate compared to earlier echocardiographically derived PVR methods (Abbas et al., \( r = 0.52, P = 0.013 \), Haddad et al., \( r = 0.51, P = 0.013 \), Kouzu et al., \( r = 0.68, P < 0.001 \)) in this cohort of patients.

**Conclusion:** The new echocardiographic approach based on a theoretical formula provides a noninvasive and accurate assessment of PVR.

**3172 | BENCH**

**Different behaviour of left atrial external work between acute left ventricular anterior and posterior ischaemia**

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**Background:** According to our recent experimental study with speckle tracking echocardiography, left atrial (LA) external work can be measured by the LA pressure-longitudinal strain loop area, which includes two distinct phases of active contraction/relaxation (A-work) and passive dilatation/emptying (V-work).

We investigated how LA function behaved during acute left ventricular (LV) ischaemia.

**Methods:** Echocardiographic and hemodynamic data were simultaneously acquired in 19 open-chest dogs before and during occlusion of the left anterior descending (LADO, n=7) and proximal circumflex coronary arteries (LCxO, n=12). LA and LV external works were computed as the myocardial work.

**Results:** Three cases of LCxO were excluded due to ischaemia-provoked significant mitral regurgitation. Mean LA pressure was similarly elevated during LADO and LCxO (LADO: 3.2±1.7 vs. 5.0±2.1 mmHg, \( p = 0.01 \), LCxO: 2.8±1.5 vs. 5.3±1.6 mmHg, \( p = 0.01 \)). Although two interventions induced no significant changes of LV works (LADO: 64±202 vs. 51±182 mmHg %, LCxO: 567±254 vs. 464±177 mmHg %), stroke volume maintained during LADO but significantly decreased during LCxO (LADO: 8.1±1.0 vs. 7.8±1.1 ml, LCxO: 7.8±2.2 vs. 5.7±1.3 ml, \( p < 0.01 \)). A-work significantly increased during LADO but not during LCxO (LADO: 5.9±4.2 vs. 13.0±12.3 mmHg %, \( p = 0.01 \), LCxO: 4.4±2.0 vs. 5.5±5.0 mmHg %). V-work significantly decreased during LCxO but not during LADO (LADO: 13.3±8.1 vs. 9.1±7.3 mmHg %, LCxO: 15.1±7.3 vs. 4.7±3.9 mmHg %, \( p = 0.01 \)).

**Conclusions:** LA function was augmented to maintain stroke volume during LADO but failed to do so during LCxO possibly explained by a difference in coronary territories. This study provides deep insight into a mechanism of variable hemodynamic response in myocardial infarction depending on the infarct region.

**Acknowledgement/Funding:** Dr. Nakatani has received a research grant from Toshiba Medical Systems.

**3173 | BEDSIDE**

**Vortex-mediated flow redirection towards the left ventricular outflow tract: influence of variations in atrio-ventricular delay**


**Introduction:** The duration of vortex formation in the left ventricle (LV) is known to be affected by anatomical parameters. However, the impact of changes in diastole through atrio-ventricular delay modification has not been described in vivo. Vortices are known to play a key role in left ventricular (LV) flow redirection towards the outflow tract, contributing to early ejection and minimising energy dissipation.

**Methods:** Patients with cardiac resynchronization therapy in sinus rhythm under- went echocardiographic assessment with VFM, a technology that enables visualization of intracardiac vortices. We measured the duration from the initiation of vortex flow to maximal intensity of vortex flow towards the aorta, named Interval to Maximum Vortex Flow (IMVF) with atrio-ventricular delays (AVD) from 0 to 280 ms in 20 ms increases.

**Results:** 12 patients (25% male, aged 68.7±10.5, LVEF 40.2±10.3) were examined in apical 3-chamber view with VFM imaging during all programmed AVD. 9/12 patients (75%) presented an IMVF of 90 ms and 3/12 (25%) of 70 ms. IMVF remained unchanged in all patients (12/12, 100%) throughout the different programmed AVD, even in those in which A-wave filling was truncated due to early systole.

**Conclusions:** Vortex flow redirection towards the LVOT does not vary with changes in AV delay. This has implications for pacemaker and CRT optimization, where a too short AVD may negatively impact cardiac output and generate turbulent flow in the outflow tract by compromising the physiological role of vortices.
3174 | BENCH
Long-term antihypertensive treatment improves left ventricular untwisting and untwisting in hypertensives: a 3-year follow-up study
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Background: Impaired left ventricular (LV) myocardial twisting markers indicate the presence of subclinical systolic and diastolic dysfunction. Blood pressure, arterial stiffness, LV mass, and impaired coronary microcirculation determine LV function in hypertensives. We investigated the effects antihypertensive treatment on the above parameters during a 3-year follow-up.

Methods: 175 untreated patients (age 54±11 years) with essential hypertension and 50 healthy controls with similar age and sex, we measured a) blood pressure parameters by 24-h ambulatory blood pressure monitoring b) Carotid to femoral arterial pulse wave velocity (PWV) c) Coronary flow reserve (CFR) after adenosine infusion, LV mass,2D- twisting (Tw-deg), peak twisting (Tw-deg/sec) velocity, untwisting at mitral valve opening (unTwMVO), peak E (unTwE) and end of the E wave (unTwEDE) of the mitral inflow and untwisting (unTw) velocity using conventional and speckle tracking echocardiography at baseline and after a 3-year follow-up. All patients were treated with angiotensin receptor blockers. We characterized as well-controlled those with 24-h systolic and diastolic blood pressure <130±80 mmHg.

Results: Compared to controls, hypertensives had lower CFR, (2.5±0.6 vs 2.9±0.6; p=0.0368) and higher PWV (11.7±2 vs 9.2±1.5). Tw (20±4 vs. 13±4), Tw velocity (10±5 vs 15±8 mm/s), E wave (15.7±5 vs. 9.8±3.1), unTwMVO (5.8±4 vs. 2.2±3.2) and unTw velocity (−104±37 < −93±31), LV mass/m² (81±16 vs. 70.7±14) and blood pressure (p<0.01 for all comparisons).

Compared to baseline, after 3 years of treatment patients had reduced Tw (20±4 vs 14±3 mm/s, p<0.001), E wave (13.8±3 vs 11±2.1) unTwMVO (15.7±4 vs. 10±5.4), unTw (10±5.4 vs. 7±2.4) unTwE (5.8±4 vs. 3.9±4) and unTw velocity (−104±37 vs −94±31), LV mass/m² (81±16 vs 75±18), PWV (11.7±2 vs 10.8±1.5), and 24 h BP (systolic BP 138±10 vs. 123±14 mmHg, and diastolic BP 87±9 vs. 75±8 mmHg, p<0.05 for all comparisons), but similar CFR (2.5±0.6 vs 2.5±0.9, p=ns). After 3-years of treatment, 70% of the patients were well-controlled.

Conclusions: Long-term antihypertensive treatment improves LV untwisting–untwisting in hypertensives in parallel with reduction of blood pressure, LV mass and arterial stiffness.

3175 | BEDSIDE
Combining analysis of speckle-tracking echocardiography and late gadolinium enhancement cardiac magnetic resonance improves prediction of functional recovery after acute myocardial infarction
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Background: Prediction of left ventricular recovery after acute myocardial infarction (AMI) is of great importance. It is known that analysis of late gadolinium enhancement cardiac magnetic resonance (CMR) improves the prediction of subclinical systolic and diastolic LV dysfunction. Blood pressure, microvascular obstruction and myocardial salvage were quantified by CMR at pre-discharge. During a mean follow-up period of 840 days, 57 ME events (10%, 23 cardiac deaths, 34 non-fatal re-infarctions) were documented. Patients with ME displayed more depressed LVEF (p<0.001), larger IS (p<0.001), more extensive edema, hemorrhage and microvascular obstruction and less myocardial salvage (p<0.05). CMR indexes were dichotomized according to the best cut-off values for predicting ME. In a comprehensive multivariate model, LVEF<40% (2.3 [1.2, 4.3], p=0.009) and IS <30% of LV mass (2.4 [1.3, 4.4], p<0.007) independently determined the ME risk. The ME rates in patients with both LVEF>40% and IS<30% of LV mass (n=393), in those with only one of them altered (n=84) and in cases both with LVEF<40% and IS>30% of LV mass (n=69), were 6%, 14% and 30% respectively (p<0.001). Similar tendencies were observed regarding cardiac deaths (2%, 6%, 14%, p<0.001) and re-infarctions (4%, 8%, 16%, p<0.001).

Conclusions: CMR predicts long-term ME soon after ST-segment elevation myocardial infarction (STEMI).

Method and results: From 2004 to 2012 we prospectively recruited 548 STEMI patients. Left ventricular (LV) ejection fraction (LVEF), infarct size (IS), edema, hemorrhage, microvascular obstruction and myocardial salvage were quantified by CMR at pre-discharge. During a mean follow-up period of 840 days, 57 ME events (10%, 23 cardiac deaths, 34 non-fatal re-infarctions) were documented. Patients with ME displayed more depressed LVEF (p<0.001), larger IS (p<0.001), more extensive edema, hemorrhage and microvascular obstruction and less myocardial salvage (p<0.05). CMR indexes were dichotomized according to the best cut-off values for predicting ME. In a comprehensive multivariate model, LVEF<40% (2.3 [1.2, 4.3], p=0.009) and IS <30% of LV mass (2.4 [1.3, 4.4], p<0.007) independently determined the ME risk. The ME rates in patients with both LVEF>40% and IS<30% of LV mass (n=393), in those with only one of them altered (n=84) and in cases both with LVEF<40% and IS>30% of LV mass (n=69), were 6%, 14% and 30% respectively (p<0.001). Similar tendencies were observed regarding cardiac deaths (2%, 6%, 14%, p<0.001) and re-infarctions (4%, 8%, 16%, p<0.001).

Conclusions: CMR predicts long-term ME soon after STEMI. A combined analysis of CMR-derived LVEF and IS permits a robust stratification of patients’ outcome.

3253 | BENCH
Utility of cardiac MRI in detecting myocardial involvement and predicting adverse events in sarcoidosis: A study in 330 patients
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Background: Advances in cardiac imaging in patients with sarcoidosis have shown a wide range of cardiac abnormalities even in patients without cardiac symptoms.

Purpose: Our aim was to assess the utility of cardiac MRI in diagnosing cardiac sarcoidosis and predicting major adverse events in patients with sarcoidosis.

Methods: Consecutive biopsy-proven extra-cardiac sarcoidosis patients without known cardiac disease underwent a complete cardiopulmonary workup that included chest imaging studies, pulmonary function testing, electrocardiogram/24-hour ambulatory Holter monitoring, echocardiogram and cardiac MRI with LGE irrespective of symptoms.

Results: A total of 330 consecutive patients were enrolled. Of these, 109 patients (33%) were diagnosed with cardiac sarcoidosis based on presence of LGE. Of these, 31 (9.3%) and 84 (25.5%) patients fulfilled the JMH and the Mehta et al criteria respectively. During median follow-up period of 58.2 months, 33 (10.3%) patients developed major adverse events. On multivariate Cox regression analysis, LGE (HR 4.84, 95% CI 1.84 to 12.73, p=0.001) along with ventricular tachycardia (HR 6.91, 95% CI 1.37 to 34.81, p=0.019) were independent predictors of major adverse events. In 112 patients with no cardiac symptoms.

Sensitivity, specificity and predictive values of criteria for diagnosis of cardiac sarcoidosis when used to detect major adverse events

<table>
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<th>LGE-MRI</th>
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<th>Mehta criteria</th>
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<td>Events in follow up</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>positive</td>
<td>27 (81.8%)</td>
<td>21 (72.4%)</td>
<td>20 (66.7%)</td>
</tr>
<tr>
<td>negative</td>
<td>106 (30.3%)</td>
<td>39 (12.9%)</td>
<td>12 (38.1%)</td>
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<tr>
<td>95% CI</td>
<td>64 (79.4% - 85.2%)</td>
<td>26 (76.8% - 86.4%)</td>
<td>19 (34.8% - 61.2%)</td>
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<td>p-value</td>
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Acknowledgement/Funding: This study was supported by a research grant from the German – Israeli Foundation for Scientific Research & Development.
and not effective for cardiac sarcoidosis based on the JMH criteria, LGE was similarly independent predictor of adverse events (HR=10.3, 95% CI 1.51 to 70.11, p<0.017).

Conclusion: Presence of LGE on cardiac MRI can detect cardiac involvement in a greater percentage of sarcoidosis patients and is a better predictor of major adverse events than existing consensus criteria.

3254 | BEDSIDE
Prognostic impact of unrecognized myocardial scar in the myocardium perfused by non-culprit artery detected by late gadolinium enhanced CMR in patients with acute myocardial infarction
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Background: Previous report demonstrated unrecognized myocardial scar detected by LGE MRI is strongly associated with event free survival in patients with stable coronary artery disease. However, the prognostic value of CMR detection of myocardial scar in non-infarct related coronary territories in acute myocardial infarction (AMI) patients is unknown.

Purpose: To evaluate the prognostic impact of unrecognized non-infarct related late gadolinium enhancement (Non IR-LGE) in patients with first clinical episode of AMI.

Methods: We studied 248 patients with first episode of AMI who underwent cardiac MRI within two months after onset (190 men, age 66±12 y.o.). LGE and cine MR images were obtained to evaluate the presence and extent of LGE as well as global and regional LV function. MACE was defined as cardiovascular death, non-fatal AMI, unstable angina, heart failure and fatal arrhythmia. The Cox proportional hazards model was used to investigate the relationship between clinical and MR imaging variables and MACES.

Result: Unrecognized Non-IR-LGE was observed in 13.7% patients with first clinical episode of AMI. During average follow-up of 27 months ranging from 3 to 95 months, 23 of the 248 patients (9.3%) reached MACE. Presence of unrecognized Non IR-LGE predicted the patients outcome with hazard ratio of 4.5 (95% CI 1.4 to 14.3, P<0.001). (Figure) By multivariable analyses, Non IR-LGE and BNP were significant independent predictors for MACE (P<0.001). In contrast, angiographic finding of multi-vessel disease and transmural extent of Non IR-LGE did not exhibit independent association with MACE.

Conclusions: Among patients with first clinical episode of AMI, unrecognized Non-IR LGE provides incremental prognostic value to MACE beyond common clinical, angiographic and functional predictors.

ORAL ANTICOAGULANTS STILL IN THE FOCUS

3277 | BEDSIDE
Lower risk of myocardial infarction in atrial fibrillation patients treated with vitamin K antagonist than in combination with acetylsalicylic acid (ASA) or ASA alone
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Background: Reducing thromboembolic risk is the main focus in atrial fibrillation (AF) patients. AF patients also have an increased risk of developing myocardial infarction (MI) and the optimal antithrombotic treatment remains uncertain.

Purpose: To investigate the risk of MI in AF patients treated with either acetylsalicylic acid, vitamin K antagonist or combination thereof.

Methods: Through the Danish nationwide registries all patients with first time non-valvular AF from 1997 to 2012 were included. Patients were divided into time varying exposure groups according to antithrombotic treatment regime. Risk of MI during the 15 years follow up period was estimated by cumulative incidence and incidence rate ratios, adjusted for sex, age, chronic heart failure, stroke, diabetes, hypertension and vascular disease.

Results: The study cohort included 76,133 AF patients, where 36,643 (48%) received VKA, 27,195 (16%) ASA, and 12,295 (16%) combination treatments. The median age was 71.0, 79.8, and 74.0 years in the three groups. Cumulative incidences of MI at 15 years were 7.12%, 6.13% and 7.44% in the ASA, VKA and the combination group, respectively (Fig.). The adjusted incidence rate ratios (95% confidence intervals) were 1.7 (1.6–1.8) for ASA and 1.3 (1.2–1.5) for combination treatment when compared to VKA.

Conclusion: Acetylsalicylic acid based antithrombotic therapy in patients with AF is associated with an increased risk of MI compared to mono vitamin K antagonist treatment.

3278 | BEDSIDE
Vitamin K antagonist control in Eastern and Southeastern Asia
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Purpose: To compare distribution of International normalized ratio (INR) values in patients receiving a vitamin K antagonist (VKA) for newly diagnosed atrial fibrillation (AF) in Eastern (E) and Southeastern (SE) Asia and in other countries represented in the GARFIELD-AF global registry (OGC).

Methods: 8445 prospective patients on VKA were enrolled in GARFIELD-AF in 2010–13. INR readings for patients on VKA at enrolment were analysed. Time in therapeutic range (TTR) of INR was estimated using Rosendaal's method and the target INR range of 2.0–3.0.

Results: The UN definition of E and SE Asia includes China, Korea, Japan, Thailand and Singapore. Patients in these regions were slightly younger than patients in OGC but had similar mean CHA2DS2-VASc (3.0 vs 3.5) and HAS-BLED scores (1.3 vs 1.4). Among patients on VKA, 5066 had INR readings (845 in E and SE Asia, 4221 in OGC), amounting to 6452 readings in E and SE Asia and 62,759 in OGC. The number of INR readings per patient was 7 (interquartile range [IQR] 5–10) in E and SE Asia and 14 (IQR 8–20) in OGC. The median number of days between two consecutive readings was 28 in Asia and 14 in OGC. Compared with OGC, the distribution of INR readings in E and SE Asia was clearly shifted towards lower values. The median INR values were 1.8 (IQR 1.4–2.3) in E and SE Asia and 2.3 (IQR 1.9–2.8) in OGC. 59.3% and 28.2% of INR readings were -2 in Asia and OGC, respectively, and 9.5% and 17.7% of INR readings were -3. The median proportion of time spent in TTR in E and SE Asia was half that in OGC (30.1% vs 63.6%).

Conclusion: These data show a very clear difference in the distribution of INR readings between E and SE Asia and other GARFIELD-AF countries.

Acknowledgement/Funding: The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG

3279 | BEDSIDE
Adherence to anticoagulant therapy with apixaban and rivaroxaban in a real-world setting
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Background: The non-vitamin K antagonist oral anticoagulants (NOACs) are effective in stroke prevention in non-valvular atrial fibrillation. Although adherence...
was excellent in the clinical trials with NOACs, there is scarce data on this in clinical practice.

**Objectives:** To compare adherence levels between the one-dose regimen of ri-
varoxaban and the two-dose regimen of apixaban among patients treated in a well-
structured atrial fibrillation clinic.

**Methods:** In a prospective cohort study data was collected on patients treated with apixaban and rivaroxaban for at least three months in a well-structured nurse-
based atrial fibrillation clinic in Sweden. Information on apixaban and rivaroxaban prescriptions and refills was obtained from pharmacies, from the time point of the first prescription by any physician. We calculated the adherence from pharmacy
refills.

**Results:** Data on 593 consecutive patients (245 on apixaban, 248 on riva-
orxaban) were obtained during patient visits telephone calls and from the local patient data bank. Patients median age 73 years, range: 36 - 99. There were no significant differences between the two treatment groups in age or sex. Pa-
tients on apixaban and rivaroxaban were followed for a median (min-max) of 313 (94 - 820) and 449 (95–908) days, respectively (p-value p=0.16). The median (interquartile range) estimated adherence was 100% (97–100) on apixaban and 100% (100–100) on rivaroxaban with 97% and 96% of patients, achieving ad-
herence levels higher than 80%. None of the latter differences was statistically significant.

**Conclusion:** Our study shows high estimated adherence levels to apixaban and rivaroxaban in clinical practice. There was no significant difference in the adher-
ence level between the two-dose regimen of apixaban and the one-dose regimen of rivaroxaban.

**ADVANCES IN HEART FAILURE THERAPY**

### 3301 | BEDSIDE

Angiotensin receptor neprilysin inhibition and renal function and in heart failure: results from PARADIGM-HF

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**Background:** ACE inhibitors often reduce glomerular filtration rate (GFR) in pa-
tients with heart failure (HF). We compared the effect of the Angiotensin Receptor Neprilysin Inhibitor (ARNI) LCZ696 to enalapril on renal function and clinical out-
comes in the Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF).

**Methods:** 8399 patients with HF and reduced ejection fraction were included in PARADIGM-HF. The primary endpoint was the composite of cardiovascular death or HF hospitalization (CVD/HF) in both treatment. The treatment effect of LCZ on CVD/HFH was not modified by baseline albuminuria status (p-interaction = 0.63), as was the case for CV death and all-cause death. Despite a median increase in UACR of 0.30 (95% CI: 0.10–0.50) mg/mmol in the LCZ group compared with enalapril at 30 days after randomization, LCZ696 reduced the subsequent occurrence of the primary outcome by 21% (95% CI: 4%-35%) in this cohort, consistent with the benefit in PARADIGM-HF overall.

**Results:** Baseline GFR was 67.7 mL/min/1.73m², and 36% of patients had CKD. Overall, estimated GFR decreased 7.7 mL/min/1.73m² over the course of the study (48 months). GFR changed −0.14 and −0.11 mL/min/1.73m² per month in the enalapril and LCZ696 groups, respectively (P=0.01). Patients treated with LCZ696 had a numerically lower incidence of renal dysfunction compared with enalapril, despite a greater fall in BP. LCZ696 reduced the risk of CVD/HFH similarily in patients with and without baseline CKD; hazard ratio 0.790 (0.691, 0.902) vs 0.799 (0.711, 0.897), respectively (P=0.90 for interaction, Figure). A similar finding was seen for all-cause mortality.

**Conclusion:** The ARNI LCZ696 had a favorable cardio-renal profile compared with enalapril, with slower progression of renal dysfunction and improved clinical outcomes, even in patients with CKD.

**Acknowledgement/Funding:** Novartis Pharmaceuticals

### 3302 | BEDSIDE

Effect of LCZ696 on urinary albumin excretion and relation to outcomes in patients with heart failure

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**Background:** The angiotensin receptor neprilysin inhibitor LCZ696 has been shown to reduce morbidity and mortality in patients with heart failure. LCZ696 has also been shown to increase urinary albumin excretion in patients with HF-
PEF. The prognostic importance of albumin excretion in the setting of LCZ696 therapy is unclear.

**Methods:** The PARADIGM trial randomized 8399 patients with heart failure and reduced ejection fraction to LCZ696 200 bid or enalapril 10 bid in the PARADIGM trial. Urinary albumin/creatinine ratio (UACR) was available at screening, follow-
ing LCZ696 run-in and one month following randomization in 1465 patients. We assessed the effect of LCZ696 on UACR and the prognostic relationship between change in UACR and outcomes.

**Results:** Median UACR was 1.0 (IQR 0.4, 3.2) mg/mmol at screening and 1.2 (IQR 0.5, 4.0) mg/mmol after LCZ696 run-in before randomization. Higher UACR values at baseline and at 30 days after randomization (figure) were associ-
ated with higher risk of the primary outcome of CV death or HF hospitalization (CVD/HFH) in both treatment. The treatment effect of LCZ on CVD/HFH was not modified by baseline albuminuria status (p-interaction = 0.63), as was the case for CV death and all-cause death. Despite a median increase in UACR of 0.30 (95% CI: 0.10–0.50) mg/mmol in the LCZ group compared with enalapril at 30 days after randomization, LCZ696 reduced the subsequent occurrence of the primary outcome by 21% (95% CI: 4%-35%) in this cohort, consistent with the benefit in PARADIGM-HF overall.

**Conclusion:** Compared with enalapril, LCZ696 reduced clinical outcomes sub-
stantially in patients with HF-REF, despite modestly increasing urinary albumin excretion.

**Acknowledgement/Funding:** PARADIGM-HF trial was funded by Novartis

### 3303 | BEDSIDE

Beta-blocker therapy and in-hospital outcome in acute heart failure: a propensity-score matching secondary analysis of the ALARM-HF registry

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**Background:** Beta blockers (BB) constitute a life-saving therapy in heart failure, but their use in acute heart failure (AHF) setting remains controversial. We as-
sessed short-term outcome in AHF patients receiving or not BB in a large AHF cohort.

**Methods:** The Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) was conducted during 2006–2007 and included a total of 4953 patients hospitalized for AHF in 9 countries in Europe, Latin America and Aus-
tralia. We compared in-hospital mortality between patients receiving or not BB. Nearest-neighbour matching by propensity score was applied to produce a bal-
anced subsample consisting of pairs of treated and not treated patients. Mortality was assessed by Cox regression with adjustment for age, gender, systolic blood pressure (SBP), heart rate (HR), atrial fibrillation (AF), NYHA class, renal function and acute coronary syndrome (ACS) at presentation.

**Results:** In the original sample, 2330 patients (47%) were receiving BB. Propensity-score matching derived a sample of 2372 patients (1186 in each treat-
ment group). BB therapy was followed by reduce in-hospital mortality both in the original [HR: 0.47, 95% CI: (0.39, 0.57)] and in the matched sample [HR: 0.51, 95% CI: (0.39, 0.67)]. The beneficial effect on mortality persisted after adjustment
for potential confounders before and after propensity-score matching (HR: 0.58, 95% CI: 0.47–0.73) and HR: 0.58, 95% CI: 0.44–0.76, respectively, Figure). Among those treated, age = 80 years, SBP=100mmHg, oliguria and ACS were associated with significantly higher risk of mortality after matching.

Conclusions: In AHF, BB therapy is associated with a significantly lower short-term mortality.

3304 | BEDSIDE
Hydrophilic versus lipophilic statin therapy on outcomes in patients with heart failure: a systematic review and an adjusted indirect comparison meta-analysis of randomised trials
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Background: Statins are known to reduce cardiovascular morbidity and mortality in prevention studies. It is unclear whether statins as a class or statin subtype (lipophilic or hydrophilic) improve outcomes in heart failure (HF). Sufficiently powered comparative trials between statin subtypes in HF are unavailable.

Purpose: To conduct an adjusted indirect comparison meta-analysis between the two statin subtypes on clinical and surrogate outcomes in HF.

Methods: We conducted a search of PubMed, MEDLINE, EMBASE and Cochrane databases until 31st October 2014 for randomized control trials (RCTs) in patients with HF evaluating statins versus placebo/standard treatment. The primary outcomes comprise all-cause mortality, cardiovascular mortality, sudden death, non-fatal myocardial infarction, cardiovascular hospitalization and hospitalization for worsening HF. We independently used a standardized abstraction tool to extract all data. RCTs with their abstracted information were grouped according to statin subtype evaluated. The abstracted data from eligible RCTs were then separately analyzed according to statin subtype. Clinical outcomes were initially pooled with the Peto’s one-step method, producing odd ratios and 95% confidence intervals for each statin subtype. Using these pooled estimates, we performed adjusted indirect comparisons of the statin subtypes for each outcome. Data from 11, 450 patients from 23 trials were analyzed.

Results: Lipophilic statins were superior to hydrophilic statins regarding all-cause mortality (Risk Ratio [RR] 0.48; 95% CI, 0.33–0.71), cardiovascular mortality (RR 0.42; 90% CI, 0.24–0.60), sudden death (RR 0.24; 0.09–0.60) and hospitalization for worsening HF (RR 0.52; 0.37–0.72). Compared with hydrophilic statins, lipophilic statins resulted in 141 fewer all-cause mortality, 125 fewer cardiovascular deaths, 84 fewer sudden deaths, and 143 fewer hospitalization for worsening HF per 1000 patients treated. Lipophilic statins resulted in 143 fewer incidence of cardiovascular hospitalization and 38 fewer incidence of non-fatal MI compared with hydrophilic statins per 1000 patients treated but were not statistically significant.

Conclusion: Lipophilic statins lower incidence of all-cause mortality, cardiovascular mortality, sudden death and hospitalization for worsening HF compared with hydrophilic statins. This meta-analysis provides preliminary evidence that lipophilic statins offer better clinical outcomes in HF till data from head to head comparisons are made available.

3305 | BEDSIDE
Carperitide versus nitroglycerin as a first-line therapy in patients with acute heart failure: a propensity-matched comparison
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Background: Carperitide (CAR), a human atrial natriuretic peptide, may have relevance to abnormal cardiac function. In dogs with chronic heart failure (CHF), CAR shows unique property for cardiovascular remodeling and systolic and diastolic function. In patients with chronic HF induced by chronic ventricular tachycardia pacing (CVP), ONO-4232 shows a significant increase in LV internal dimensions and decrease in ejection fraction, as confirmed by echocardiography. Also, in the 12 dogs that underwent HD assessment, LV end-diastolic pressure (LVEDP; 44.0±1.5 mmHg) and pulmonary capillary wedge pressure (PCWP; 35.0±1.6 mmHg) were markedly elevated, and cardiac output (CO; 1.40±0.07 L/min) was decreased prior to the drug administration. ONO-4232 dose-dependently reduced LVEDP and PCWP while increasing CO by ~23%, ~29%, and ~56% (high dose, n=4), respectively. The magnitude of ONO-4232-induced HD changes was similar to that of milrinone. Furthermore, ONO-4232 significantly shortened tau, a time constant of LV relaxation, starting from the low dose and also tended to increase LV dp/dt max at the high dose (high dose: tau; ~22%, LV dp/dt max; +20%). Of note, although milrinone shortened tau, yet significantly increased LV dp/dt max (high dose: tau; ~23%, LV dp/dt max; +40%). In ONO-4232 group, systolic blood pressure was decreased by 4 mmHg (high dose), which is considered of minimal biological relevance.

Conclusion: ONO-4232 significantly reduced both preload and afterload to a similar extent to that seen for milrinone. However, the mode of cardiac action was clearly different from the inotropic milrinone: ONO-4232 selectively improved LV relaxation. Therefore, ONO-4232 may become a new class of drug for the treatment of HF.

3307 | BENCH
Bendavia, a novel mitochondria-targeting peptide, improves contraction and relaxation of failing cardiomyocytes isolated from dogs with chronic heart failure
H.N. Sabbah, R.C. Gupta, P. Mohiy. Henry Ford Hospital, Detroit, United States of America

Background: Mitochondria of failed human hearts and hearts of dogs with experimental heart failure (HF) manifest structural and functional abnormalities characterized by hyperplasia, reduced organelle size and reduced respiration. These abnormalities lead to reduced rate of ATP synthesis and increased production of ATP.
reactive oxygen species (ROS) that adversely impact left ventricular (LV) systolic and diastolic function. We previously showed that chronic therapy with Bendavia (MTP-131), a novel mitochondria-targeting peptide, improves global LV function in dogs with HF without affecting heart rate or blood pressure. This improvement was associated with a reversal of mitochondrial abnormalities and normalization of mitochondrial rate of ATP synthesis. In the present study, we tested the hypothesis that the improvement in global LV function seen in dogs with HF during treatment with Bendavia results primarily from enhanced contraction and relaxation of constituent LV cardiomyocytes.

Methods: Cardiomyocytes were isolated from the LV free wall of 8 untreated dogs with chronic HF produced by intracoronary microembolizations (LV ejection fraction <30%). A standard collagenase-based enzymatic process was used for the isolation that yielded ~70% viable rod-shaped cardiomyocytes that excluded trypan blue. Extent of cardiomyocyte shortening, shortening velocity and lengthening velocity were assessed during 1.0 Hz electrical field stimulation delivered via a MyoPacer (ION Optix). Measurements were made at baseline and were repeated after one hour of gradual exposure of the same cardiomyocytes to Bendavia at a concentration of 0.1 μM.

Results: At baseline, the extent of cardiomyocyte shortening was 3.7±0.8 μm, shortening velocity was 62.8±16.9 μm/sec and lengthening velocity was −53.8±16.5 μm/sec. Exposure of cardiomyocytes to Bendavia significantly increased the extent of cardiomyocyte shortening to 5.4±1.1 μm (p<0.012), significantly increased the lengthening velocity to −96.8±21.1 μm/sec (p<0.016) compared to baseline.

Conclusions: Results of this study indicate that exposure of failing isolated cardiomyocytes to Bendavia elicits significant improvements in the rate of cardiomyocyte shortening and re-lengthening indicative of improved cell contractility and relaxation. The likely mediator of the observed improvement in cardiomyocyte function is the increased availability of ATP along with reduced ROS production both secondary to improved mitochondrial function elicited by treatment with Bendavia.

3308 | BENCH
Hepato-renal dysfunction on admission predicts the outcome in acute heart failure
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Introduction: In acute heart failure (AHF), multi-organ dysfunction is relevant complication, which may unfavorably affect the outcomes. Surprisingly, this phenomenon has never been systematically evaluated. The MELD (Model for End-Stage Liver Disease), combines data reflecting liver and kidney function, being widely applied for prognostic evaluation in patients with liver dysfunction.

Aim: The aim of the study was to find clinical, laboratory and hemodynamic associates of the MELD and to assess it's utility as prognosticator in AHF patients.

Methods: The study population consisted of 341 AHF patients divided into derivation cohort (213 patients; mean age: 67 years, men: 70%, de novo AHF 21%) and validation cohort (136 patients; mean age: 65 years, men: 77%, de novo AHF 33%). The strongest predictors of ID were female gender and anaemia (Table).

Predictors of ID (logistic regression)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>2.34</td>
<td>1.56–3.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anaemia</td>
<td>1.79</td>
<td>1.06–2.55</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospitalisation due to worsening HF</td>
<td>1.39</td>
<td>0.99–1.94</td>
<td>0.056</td>
</tr>
<tr>
<td>Age (10-years steps)</td>
<td>1.03</td>
<td>0.89–1.18</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Only 10.1% of the patients with ID received iron supplementation, out of these just 21.6% were treated intravenously.

Conclusions: The RAID-HF registry shows that ID in HF-patients is common and most often found in women and patients with anaemia. In this cohort no significant association of ID and 1-year mortality was observed. Despite the proven beneficial effect of iron therapy on symptoms of iron-deficient HF-patients, only a minority of patients with ID received iron supplementation in clinical practice.

Acknowledgement/Funding: VIFOR Pharma

3310 | BENCH
RA123456, a novel potent and selective CaMKII inhibitor reduces diastolic Ca2+ leak and enhances SR Ca2+ content in human cardiomyocytes
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Rationale: Ca/calmodulin kinase II (CaMKII) plays a critical role in heart failure (HF) and atrial fibrillation (AF) by inducing SR Ca- leak. It is a promising therapeutic target, but selective inhibitors are difficult to identify.

Objective: We characterized the effect of a novel highly selective CaMKII inhibitor, RA123456, on Ca handling in isolated human cardiomyocytes.

Methods and results: Myocytes were isolated from right atrial appendage biopsies (heart surgery patients) and loaded with Fluo-4 AM (10 μM). RA123456 significantly reduced frequency of spontaneous Ca sparks (CaSpf; confocal microscopy) in a concentration dependent manner, reaching 1.6±0.4 (mean ± SEM), 1.3±0.11, and 1.3±0.14 at 1 μM and 0.5 μM, respectively, vs. vehicle (2.3±0.14, N=9). A similar effect was observed with CaMKII inhibitor AIP (1 μM, 1.4±0.14, N=25). Consistent with reduced SR Ca leak (fig), RA123456 reduced RyR2 phosphorylation and enhanced SR Ca content (caffeine application). Caffeine-induced ΔF/F0 was...
P3312 | BEDSIDE

Family history of syncope is associated with increased risk of adverse cardiovascular events and mortality - a Danish nationwide study

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Background: Previous studies suggest a familial co-occurrence of cardiovascular diseases and syncope indicating an inherited cardiac vulnerability, but it is unclear whether hospitalization of a family member with syncope is an independent risk marker for adverse cardiovascular events among first-degree relatives.

Purpose: To investigate the risk of major adverse cardiovascular events (MACE), all-cause mortality and early-onset cardiovascular disease in first-degree relatives of individuals admitted to hospital with syncope.

Methods: Using nationwide registries, we identified individuals below 60 years discharged with syncope between 1978 and 2011 and their first-degree relatives. Risk of MACE, all-cause mortality and early-onset cardiovascular disease among the cohort of relatives was estimated using Poisson regression models with the Danish background population as reference adjusting for sex, age, calendar year and comorbidities.

Results: In a total population of 7,318,639 consecutively included Danish residents, we identified 198,258 first-degree relatives of 102,230 syncope patients. Crude incidence rates of all-cause mortality were 1.71, 0.99 and 0.93 per 1000 person-years for siblings, maternal offspring and paternal offspring, respectively. Adjusted rate ratios for MACE were 1.45 (95% confidence interval 1.34–1.56) for siblings, 1.47 (1.31–1.65) for maternal offspring and 1.31 (1.16–1.47) for paternal offspring. Similar results were found for all-cause mortality and early-onset cardiovascular disease.

Conclusions: Family history of syncope was associated with an increased all-cause mortality, MACE and early-onset cardiovascular disease. These results should be taken into account in cardiovascular risk stratification of persons with a family history of syncope.

P3314 | BEDSIDE

Application of syncope guidelines in the emergency department do not reduce admission rates: a retrospective cohort study

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Background: Syncope comprises 1.5% of all emergency department (ED) visits and approximately 2-billion dollars (USD) in related hospitalizations. Syncope guidelines are intended to identify high-risk patients and streamline admissions and investigations.

Purpose: To determine if the application of syncope guidelines in the ED results in a reduction of unnecessary admissions to hospital.

Methods: A retrospective chart review was conducted in all syncope presentations to the ED, spanning 1 year at two major tertiary care institutions. Three different guidelines, Canadian Cardiovascular Society (CCS), European Society of Cardiology (ESC), and American College of Emergency Physicians (ACEP) and European Society of Cardiology (ECS), were applied to determine the effect on admission rates.

Results: Overall a total of 1228 syncope presentations to the ED were identified (January 1, 2013 to January 1, 2014), 505 patients (41%) were admitted and 723 (59%) were discharged. Five hundred charts were randomly reviewed; of those 48 were not true syncope, 15 were not assessed by a physician and 2 charts were incomplete. Of the remaining 435 true syncope presentations, 174 (40%) were admitted as per the deciding physician and 261 (60%) were discharged from the ED. The mean age of those admitted from the ED and those discharged was 72±14 vs 55±22 (p<0.01), respectively and there were no gender differences between both groups. The admitted group had higher rates of Congestive Heart Failure 13% vs 6%, Coronary Artery Disease 34% vs 15%, and Structural Heart Disease 11% vs 5% (p<0.01), respectively. The breakdown of syncope cause in admitted and non-admitted groups were 30% vs 46% neurally mediated (p<0.01), 21% vs 18% orthostatic (p<0.01), 19% vs 2% cardiac (p<0.01), and 30% vs 34% undetermined (p<0.01), respectively. Medical records were reviewed 1 year following syncope presentations in both admitted and non-admitted groups and adverse cardiovascular events were 9% vs 3% (p<0.01), respectively. When compared to 174 (40%) deemed necessary admissions by the deciding physician, CCS guidelines warranted for 263 (60%, p<0.01) admissions, ACEP 189 (43%, p<0.28) admissions, and ESC 220 (50%, p=0.004) admissions.

Conclusion: Our study suggest that the current admitted syncope population is older and has a higher comorbidity burden, possibly explaining why adverse cardiovascular events are higher in this group. Finally, the data suggests that the application of syncope guidelines are unlikely to reduce admission rates, and that a lack of agreement exists among the different guidelines resulting in significant variation between warranted admissions.
P3315 | BEDSIDE
3 years experience of diagnosing and managing postural tachycardia (PoTS) from a UK regional syncope service
Y. Zheng, C. Moyle, Y. Blackburn, E. Joy, K. Mohee, C. Morley, Bradford Teaching Hospitals NHS Trust, Cardiology, Bradford, United Kingdom
Introduction: PoTS and Orthostatic intolerance (OI) are increasingly recognised and may be very disabling, especially in patients with Joint Hypermobility Syndrome - Ehlers Danlos type III (JHS). These symptoms reflect volume (salt) depletion, baroreflex unresponsiveness, pooling on standing, increased venous elasticity (JHS), deconditioning and possibly dysautonomia. We present a 3-phase treatment strategy for these unfortunate patients.
Definition: PoTS >30bp symptomatic HR increase or >120bp within 10 min stand.
Methods: All patients diagnosed with PoTS attending our syncope service from 2012, were included and categorised as non-JHS and JHS associated (confirmed by Rheumatology and Brighten Criteria). Drug induced, illness, endocrine and hyperadrenergic causes were excluded. Active stand and/or passive 10 min using beat-to-beat BP monitoring (Finapres) and 24 hour urine and sodium excretion were assessed.
Results: 29 Patients were included. 28 females, mean age 28 (range 17–44). 18 patients were diagnosed with PoTS and JHS.
Mean 24 hour urine was 2.0L (range 0.7L–2.8L) and the mean 24 hour urinary sodium was 101.91 mmol/l (range 54 - 181). Mean postural increase in HR, 40 BPM (SD 11.0) and mean systolic drop was 40mmHg (SD 17.9).
Treatment (see table 1): 27 were fluid/salt repleted. 2 patients are awaiting treatment. 17 were non responders to PoTS and JHS were trialed with Ixabradine. 2 non-tolerant and 3 with persistent/worsening OI proceeded to Midodrine, with 2 being intolerant and 3 responding. All medication tolerant patients improved with several returning to work and social activities.
Table 1. 3 Phase treatment strategy
<table>
<thead>
<tr>
<th>Phase</th>
<th>Treatment</th>
<th>All patients given avoidance, counter-manoeuvre and rehabilitation advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Fluid and salt repletion (30-90 mins Na daily)</td>
<td>PoTS and OI</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Trial of Ixabradine 2.5mg bid up titrating to 5mg BD</td>
<td>PoTS and OI</td>
</tr>
<tr>
<td>Phase 3</td>
<td>P in the pocket Midodrine 2.5mg increasing to 5.5mg D/S</td>
<td></td>
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</tbody>
</table>

Conclusion: 1. In a regional cardiac service JHS associated PoTS was the most common diagnosis.
2. Salt depletion was universal and more prevalent than fluid depletion.
3. JHS patients may benefit from Ixabradine for PoTS and Midodrine “pill in the pocket” for OI.
4. Further research is required to determine a longer term management strategy.

BEST POSTERS IN ANTITHROMBOTICS
P3317 | BEDSIDE
The efficacy and safety of ticagrelor in women versus men with a prior myocardial infarction: insights from the PEGASUS-TIMI 54 trial
Introduction: Of subjects enrolled, 5,060 (24%) were female. In the placebo arm, the incidence of CV death, MI, or stroke; the primary safety endpoint was TIMI major bleeding.
Methods: PEGASUS-TIMI 54 randomized 21,162 patients with history of MI (Table). High platelet reactivity assessed by VerifyNow (PRU <60 mg) pre-dose (3.5%) and absent post dose. Platelet reactivity pre- and post-dose with ticagrelor 60 mg bid showed similar effects regardless of patient sex.
<table>
<thead>
<tr>
<th>Phase</th>
<th>Treatment</th>
<th>All women were counselled with regards of pregnancy during treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Fluid and salt repletion (30–90 mins Na daily)</td>
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Conclusion: 1. In a regional cardiac service JHS associated PoTS was the most common diagnosis.
2. Salt depletion was universal and more prevalent than fluid depletion.
3. JHS patients may benefit from Ixabradine for PoTS and Midodrine “pill in the pocket” for OI.
4. Further research is required to determine a longer term management strategy.

P3318 | SPOTLIGHT
Ticagrelor 60 mg twice-daily provides effective platelet inhibition in patients with prior myocardial infarction: the PEGASUS-TIMI 54 platelet function substudy
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Background: The PEGASUS-TIMI 54 trial studied 2 doses of ticagrelor, the standard 90mg twice daily (bid) and 60mg bid, for longterm prevention of ischaemic events in patients with prior MI. Both doses reduced the rate of ischaemic events vs placebo. The pharmacokinetics (PK) and pharmacodynamics of the 60 mg bid treatment have not previously been studied.
Methods: To characterize PK and platelet inhibition with ticagrelor 60mg bid vs 90mg bid.
Results: Plasma ticagrelor levels were approximately 1/3 lower with 60mg vs 90mg bid (post dose: 448 vs 717 ng/mL; P=0.001). Both doses achieved high levels of platelet inhibition pre and post dose, with slightly more variability with 60mg (Table). High platelet reactivity assessed by VerifyNow (PRU > 208) was rare with 60 mg pre-dose (3.5%) and absent post dose. Platelet reactivity pre- and post-dose as measured by LTA was numerically but not significantly lower with 90mg than 60mg.

P3319 | BEDSIDE
Differences in dual antiplatelet treatment for acute coronary syndrome patients undergoing PCI or not: a Danish nationwide population-based cohort study
G. Gislason1, L.P. Hasvold2, T. Diness3, A. Pottegaard3, A. Broe3, M. Emneus4, A. Green5, J. Kuder6, E. Joy, K. Mohee, M. Cohen2, G. Gislason1, L.P. Hasvold2, T. Diness3, A. Pottegaard3, A. Broe3, M. Emneus4, A. Green5, J. Kuder6, E. Joy, K. Mohee, M. Cohen2, Gentofte University Hospital, Copenhagen, Denmark; 2 AstraZeneca Nordic-Baltic, Medical Department, Södertälje, Sweden; 3 University of Southern Denmark, Odense, Denmark; 4 Institute of Applied Economics and Health Research, Copenhagen, Denmark
Introduction: ESC guidelines recommend 12 months’ dual antiplatelet treatment (DAPT) after an acute coronary syndrome (ACS) event, regardless of whether or not patients undergo percutaneous coronary intervention (PCI). However, contemporary nationwide real-time data on DAPT use and treatment length for the ACS population are scarce.
Purpose: To describe patients’ characteristics and type and duration of DAPT use after ACS and PCI or not undergoing PCI at discharge.
Methods: This observational cohort study linked morbidity, mortality, and medication data from Danish national registries from ACS patients alive after discharge from the hospital in 2012.
Results: In total, 9,700 ACS patients [ischaemic myocardial infarction [MI] and 1,101 with angina pectoris [IAP]] at discharge were identified, of whom 4,864 (50%) underwent PCI. The PCI-treated patients were younger (median age, 65 years vs. 72 years) and consisted of more men (73% vs. 56%) compared with non-PCI-treated patients. Approximately 31% of the ACS patients did not receive DAPT treatment. Median age of non-PCI-treated patients was 72 years vs. 67 years for DAPT patients. Non-DAPT patients had a higher cardiovascular risk profile (diabetes, heart failure, and atrial fibrillation) compared with the DAPT population. DAPT duration was longer in PCI-treated patients compared to the non-PCI-treated population (P<0.001).
Conclusions: Despite guideline recommendations, close to one third of all ACS patients were discharged without DAPT. For ACS patients receiving DAPT, there was a significant difference in treatment length between patients undergoing PCI
or not. More careful attention towards initiation and duration of DAPT for non-PCI-treated ACS patients in Denmark is warranted.

P3320 | BEDSIDE
New users of low-dose acetylsalicylic acid and risk of colorectal cancer: results using three different study designs
L.A. García Rodríguez1, L. Cea Soriano1, M. Soriano-Gabarro2, 1Centro Español de Investigación Farmacoepidemiológica (CEIFE), Madrid, Spain; 2Bayer Pharma AG, Global Epidemiology, Berlin, Germany

Background: Evaluation of drug–outcome associations requires an appropriate and unbiased study design.

Purpose: Using data from The Health Improvement Network UK primary care database, we used three different study designs to assess the risk of colorectal cancer (CRC) among new users of low-dose acetylsalicylic acid (ASA).

Methods: The source population for each study was patients aged 40–89 years between 2000–2012 with no record of cancer or use of low-dose ASA before start of follow-up. The first design (single cohort) comprised all patients meeting these eligibility criteria. The second and third designs involved ascertaining a cohort of low-dose ASA initiators (start date was date of first ASA prescription) and either a cohort of (i) non-low-dose ASA users or (ii) paracetamol initiators, at the start date among the source population. In the second design, each day a person qualified as a new user of low-dose ASA, they were assigned to the low-dose ASA initiator cohort and matched to a person free of low-dose ASA on that day by age, sex and number of general practitioner visits in the previous year. In the third design, new users of low-dose ASA and paracetamol were identified and assigned to the first drug initiator cohort for which they qualified. In each design, patients were followed to identify incident cases of CRC. Controls were sampled among the respective study cohorts and frequency-matched to cases by age, sex and calendar year. An “As-treated” analysis was performed and current use of low-dose ASA was when use extended until index date (CRC date for cases and random date for controls) or ended 1–90 days before index date. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by multiple logistic regression.

Results: Current use of low-dose ASA (75–300 mg) was associated with a significantly reduced risk of CRC, OR 0.69 (95% CI: 0.64–0.74) in the first study design, OR 0.66 (95% CI: 0.60–0.73) in the second design, and OR 0.71 (95% CI: 0.63–0.80) in the third design. A significant reduced risk of CRC was observed with a daily dose of 75 mg in each design. When low-dose ASA was used for secondary prevention, ORs (95% CIs) were 0.61 (0.55–0.68) in the first design, 0.60 (0.53–0.68) in the second design, and 0.62 (0.54–0.72) in the third design. Corresponding estimates for primary CVD prevention were 0.75 (0.68–0.81), 0.71 (0.63–0.79) and 0.78 (0.68–0.89).

Conclusion: A significant reduced risk of CRC among new users of low-dose ASA was shown with all three study designs and so is unlikely to be explained by selection bias.

BEST POSTERS IN E-CARDIOLOGY

P3322 | BEDSIDE
Mobile echo acquisition and transfer for donor organ assessment
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Introduction: Donor heart assessment and optimisation improves outcome after heart transplantation. Trans-Oesophageal Echocardiography (TOE) provides essential information on donor heart. However, its availability at donor hospitals is often unpredictable as is the expertise to interpret the images. We designed a secure system to connect an offsite portable ultrasound machine via the internet to the hospital’s network infrastructure which can be accessed via the web anywhere.

Methods: None of the current echocardiogram support Virtual Private Network (VPN) access or have a 3/4G connection. Thus a laptop acts as a bridge to provide mobile data connection via VDiComRouter through the hospital’s VPN into local DICOM archive of storing and reviewing studies. The VDiComRouter software automatically pushes the study across to Enterprise Archive when the connection is available obviating the need for user input if the mobile data signal drops. The images are available for analysis on-site or off-site via secure website (figure). The same path is used to transfer images of organs/screen captures.

Results: Image acquisition and DICOM format conversion were immediately achievable with the device. Transfer and integration into hospital PACS system was seamless. Access to image archives and image analysis required Active X software and was possible on portable devices with an image cadence of 56fps.

Conclusion: Devices running Active X can allow secure remote access to DICOM image providing near real time analysis of echo images. Remote donor heart assessment provides the retrieval team with expert review to eliminate potential donors at an early stage or guide optimisation of organ for transplantation.

Figure 1

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P324 | BEDSIDE
Relationship between Serum Electrolytes and Electrocardiographic Intervals

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Background: Hypokalemia, hypocalcemia and hypomagnesemia are assumed to be causative for an acquired long QTC syndrome, but this association is based only on a few small case series.

Purpose: Here, we aimed to evaluate the relationship between serum electrolyte concentration and changes in QTC interval and QRS complex.

Methods: This retrospective cohort study included 8,498 consecutive participants admitted to the coronary care unit at an academic tertiary care medical center from 2004 to 2013 who had at least one serum potassium and magnesium level measurement. The means of serum potassium, ionized calcium and magnesium were then categorized and the reference groups were 4.0–4.5 mEq/L, 4.8–5.0 mg/dL and 2.0–2.2 mg/dL, respectively. Multivariate analysis adjusted for age, sex, race, serum electrolyte, antithyroidics and drugs known to cause QTc prolongation was used.

Results: Serum potassium (ORs: 1.04, 1.01 and 0.99 for potassium levels of <3.5, 3.5–4.0 and ≥4.5 mEq/L, respectively) and ionized calcium (ORs: 1.02, 1.01 and 0.99 for calcium levels of <4.4, 4.4–4.6, and ≥4.6, respectively) were inversely associated with the QTC prolongation; only hypermagnesemia independently increased the risk of widened QRS complex. A paradoxical association was observed between serum magnesium and QTC prolongation (ORs: 0.98, 0.99 and 1.01 for magnesium levels of <1.8, 1.8–2.0, and ≥2.0 mg/dL, respectively). After adjusting for duration of QRS complex, this relationship between hypermagnesemia and QTC prolongation was no longer present. However, hypermagnesemia was independently associated with a widened QRS complex (ORs: 0.95, 0.98, 1.03 and 1.10 for magnesium of <1.8, 1.8–2.0, 2.2–2.4 and ≥2.4 mg/dL, respectively).

Conclusions: We also observed a level-dependent relationship between hypokalemia and hypocalcemia and an increase in risk of QTC interval prolongation, but neither serum potassium nor calcium was associated with changes in duration of the QRS complex. Contrary to conventional wisdom, hypermagnesemia was associated with a prolonged QTC interval via a mechanism of widened QRS complex.

P325 | BEDSIDE
Impact of motion correction algorithm on the image quality and diagnostic utility in patients undergoing CT angiography: a randomized controlled trial

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Background: Despite improvements in the technology in coronary CT angiography (CCTA), motion artifacts remain a limitation that cause a decline in diagnostic accuracy in up to 12%.

Aims: To investigate the diagnostic utility of motion correction algorithm Snap- shot Freeze (SSF) compared to standard reconstruction algorithm (STD) in un-selected patients randomized to receive intravenously beta-blockers (BB) or no beta-blockers (non-BB) before CCTA, and to investigate if SSF can compensate for the absence of BB.

Methods: One hundred and forty patients scheduled for CCTA and with heart rate (HR) between 60 and 85 bpm were randomized (73 patients to BB group and 67 patients to non-BB group). All images were reconstructed by SSF and STD algorithm, two blinded experienced readers evaluated the image quality according to Likert score (1: Excellent, 2: Good, 3: Adequate, 4: Non-diagnostic) and noted the presence of artifacts. Twenty five patients were excluded because of tachycardia, bradycardia or reconstruction error.

Results: Images from 84 patients in BB group (mean HR 56±4 bpm) and 51 patients in non-BB group (mean HR 67±7 bpm) were analyzed. SSF increased the number of excellent images in both groups compared to STD algorithm (BB: 59% vs 44%; P=0.002; non-BB: 25% vs 8%; P=0.004). The number of non-diagnostic images was not significantly reduced (BB: 14% vs 14%; P=1.000; non-BB: 37% vs 47%; P=0.125). SSF reduced the motion artifacts (BB: 11% vs 31%; P=0.0002; non-BB:49% vs 75%; P=0.001). Despite this reduction, motion artifacts in non-BB were still more frequent compared to the BB group analyzed by STD (49% vs 31%).

Conclusion: The use of SSF significantly improves the image quality and reduce the motion artifacts in CCTA, but does not influence the diagnostic utility.

BEST POSTERS IN CARDIAC BIOLOGY AND SENESCENCE

P3327 | BENCH
P53-induced inflammation exacerbates cardiac dysfunction during pressure overload

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The death rate related to severe heart failure is still unacceptably high. p53 is a key player in the intrinsic cellular responses to DNA damage, and activation of p53 leads to cell-cycle arrest, apoptosis, and senescence. Accumulating evidence has demonstrated the role of sterile inflammatory responses in the progression of cardiac remodeling in heart failure, however the mechanistic link between p53 and the inflammatory process in the failing heart is not known. Here we demonstrate a critical role of p53 signaling in bone marrow cells and endothelial cells in the development of cardiac inflammation in a transverse aortic constriction (TAC) induced murine pressure overload model. Dietary p53 level positively regulated ICAM-1 expression in endothelial cells and integrin alpha-L in macrophages. The genetic deletion of p53 in endothelial cells or bone-marrow cells significantly reduced this interaction, inhibited the production of pro-inflammatory cytokines and ameliorated cardiac dysfunction during pressure overload. Forced expression of p53 in bone-marrow cells, worsened cardiac inflammation, and reduced systolic function. Norepinephrine markedly increased reactive oxygen species (ROS) and p53 levels in macrophages and endothelial cells. Reducing adrenergic signaling by the suppression of beta-2 adrenergic receptors in endothelial cells or bone-marrow cells inhibited ROS and p53 levels, ameliorated cardiac inflammation and systolic dysfunction upon pressure overload.

Our results suggest that the activation of sympathetic nervous system-ROS-p53 signaling promotes the interaction between endothelial cells and bone-marrow-derived inflammatory cells by the up-regulation of ICAM-1 and integrin expression to exacerbate cardiac dysfunction. The inhibition of p53 signaling in these cells would become new therapeutic targets for heart failure.

P3328 | BENCH
Testosterone antagonizes doxorubicin-induced senescence of cardiomyocytes

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Background: Chronic cardiotoxicity of doxorubicin and other anthracyclines is less common in males than in females. Here, we hypothesized that this gender difference might be at least in part secondary to distinct activities of sex hormones on cardiomyocyte senescence, which is thought to be central to the development of long-term anthracycline cardiomyopathy.

Methods and results: Neonatal murine cardiomyocytes and H9c2 cardiomyoblasts were treated with doxorubicin alone or in combination with testosterone or 17β-estradiol, the main androgen and estrogen, respectively. As already reported, a single 3 h pulsed exposure to 0.1 μM doxorubicin resulted in extensive senescence of cardiomyocytes. This was associated with accumulation of p53 and down-regulation of telomere binding factor 2 (TRF2), two events that have previously been pinpointed as pivotal to doxorubicin-induced senescence. Distinct in senescence remains much more frequent in treated than untreated cells up to 21 days after incubation with doxorubicin. Testosterone, but not 17β-estradiol counteracted both immediate and delayed senescence elicited by doxorubicin. At the molecular level, testosterone stimulated the phosphorylation of Akt and nitric oxide synthase (NOS)-3 and prevented the expression of p53 and TRF2 triggered by doxorubicin. Pre-treatment with the androgen receptor (AR) antagonist, flutamide, and the phosphatidylinositol 3 (PI3) kinase inhibitor, LY294002, abrogated the reduction in senescence, as well as Akt activation and the phosphorylation of p53 and TRF2 levels attained by testosterone. The effect of testosterone on senescence and TRF2 was also abolished by pre-treatment with the NOS inhibitor, L-NAME.

Conclusions: Testosterone protects against cardiomyocyte senescence caused
Phosphodiesterase 3A protects the heart against isoproterenol-induced cardiac injury via anti-oxidative mechanism
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Background: Oxidative stress plays an important role in the pathology of cardiac remodeling and heart failure. Sustained stimulation of β-adrenergic receptor signaling induces the production of reactive oxygen species in the situation of heart failure. Phosphodiesterase 3A (PDE3A) inhibits β-adrenergic receptor (βAR)/protein kinase A metabolism by metabolizing cAMP. Therefore, we hypothesized that overexpression of PDE3A has anti-oxidative effects against isoproterenol-induced cardiac injury.

Methods and results: Isoproterenol (30 mg/kg/day) was continuously infused using osmotic mini-pump for 7 days in wild-type (WT) mice and transgenic (TG) mice with myocardial-specific expression of exogenous PDE3A1. Isoproterenol infusion increased heart weight/body weight ratio by 23% in WT mice compared with WT mice given vehicle (5.3±0.2 mg/g vs. 4.4±0.1 mg/g, P<0.05), whereas by only 12% in TG hearts after isoproterenol (5.9±0.3 mg/g vs. 5.3±0.2 mg/g, ns). Echocardiography revealed that isoproterenol lead to cardiac hypertrophy in WT mice, whereas TG mice (wild type: 1.1±1.0 mm vs. 0.8±0.4 mm, P<0.05), but not in TG mice (0.98±0.04 mm vs. 0.93±0.05 mm, ns). The 8-OHGd, a marker of oxidative stress, positive area was increased by isoproterenol stimulation in WT hearts compared with vehicle hearts (14.9±3.7% vs. 7.4±1.1%, P<0.05), but not in TG hearts (13.9±1.9% vs. 12.0±2.8%, ns). Moreover, percentage of apoptotic cardiomyocytes was increased after isoproterenol stimulation in WT hearts compared to vehicle hearts (0.05±0.01% vs. 0.02±0.01%, P<0.05), but not in TG hearts (0.04±0.01% vs. 0.03±0.01%, ns). Interestingly, protein expression of Sirtuin 1 (Sirt1) which provides anti-oxidative effects, was significantly upregulated in TG hearts compared to WT hearts in both basal (1.9±0.2 AU vs. 1.0±0.1 AU, P<0.01) and after isoproterenol infusion (2.8±0.2 AU vs. 1.3±0.2 AU, P<0.01), suggesting that PDE3A upregulated Sirt1-related signaling.

Conclusions: We conclude that PDE3A inhibits isoproterenol-induced cardiac oxidative stress via regulating the interaction between βAR and Sirt1 signaling.

BEST POSTERS IN AORTIC AND BICUSPID AORTIC VALVE DISEASE

P3333 | BEDSIDE
Circulating endothelial microparticles are elevated in bicuspid aortic valve disease and are associated to aortic root dilatation
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Background: The mechanisms involved in ascending aorta dilatation in bicuspid aortic valve (BAV) patients are not well known. The circulating endothelial microparticles (EMP) have emerged as new biomarkers of endothelial dysfunction and have been related to aortic valve disease. However, the relationship between EMPs, BAV and aortic dilatation has not been previously analyzed.

Methods: We performed this study in 4 steps: 1) comparing circulating EMPs levels between BAV patients (n=55) and without significant left ventricle remodeling, n=60) and tricuspid aortic valve (TAV) controls (matched by age/sex); 2) analysing the variables related to circulating EMPs in BAV patients (n=55) by only 12% in TG hearts after isoproterenol (5.9±0.3 mg/g vs. 5.3±0.2 mg/g, P<0.001; β=0.38, p<0.001, and 2) we identified the aortic root diameter and dilatation as the main factors related to the increased EMPs levels within BAV patients (β = 0.132 x mm²/m² and p=0.008 for the indexed aortic root diameter). Aortic valve dysfunction was not related to EMP levels. 3) Furthermore, in patients with moderate to severe aortic stenosis the EMPs levels were higher in those patients with BAV in comparison with the TAV ones (4.1±0.2 and 3.1±0.3 per log EMPs/μl, respectively, P=0.02). 4) Finally, we observed that after aortic valve/ascending aorta surgery the circulating levels of EMPs decreased drastically (4.27±0.6 to 1.75±0.3 EMPs/μl, P<0.002), especially in those patients undergoing aortic root replacement. In contrast, no time course effect was observed those patients who did not require aortic valve/ascending aorta surgery.

Conclusions: The pattern of elevation of circulating EMPs observed links BAV, endothelial aortic root damage and aortic dilatation, suggesting the implication of the anomalous flow generated by BAV. Circulating EMP may emerge as new biomarkers of aortic root dilatation in BAV disease.

P3334 | BENCH
Association of bicuspid aortic valve morphology with ascending aortic dimensions and growth
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Background: Bicuspid aortic valve (BAV) is associated with thoracic aortic pathology, but presence and progression rates of dilatation vary widely among patients. Conflicting evidence exists on the association of valve morphology and aortic dilatation and growth.

Purpose: To investigate whether an association between BAV morphology on aortic dimension and aortic progression rate of dilatation exists.

Methods: A retrospective, observational study in a European tertiary care centre. Echocardiographic images were screened for presence of BAV. Two observers independently confirmed presence and morphology of BAV. If needed, consensus was reached by involving a third observer. Only cases with serial echocardiographic images were included in the analyses. Mixed linear model analyses were used to identify independent factors associated with ascending aortic dilatation.

Results: A total of 392 patients had confirmed BAV with sufficient image quality to assess valve morphology and thoracic ascending aorta dimensions. At baseline, mean age was 48±17 years, 69% of patients were men, and dilatation of any segment of the ascending aorta was present in 30% (dilatation of the tubular ascending aorta in 26% and aortic sinus dilatation in 10%). Age was associated with aortic sinus, sinotubular junction (STJ), and tubular ascending aorta dimensions. BAV morphology was associated with left ventricular outflow tract (LVOT), aortic sinus and tubular ascending aortic dimensions. Sex was associated with dimensions of LVOT, aortic sinus and STJ. BSA was associated with LVOT and tubular ascending dimensions. Severity of aortic valve stenosis was associated with aortic sinus and STJ dimensions, but not LVOT dimensions. Logistic follow-up echocardiography (5.5±3.3 years), the aortic sinus and the tubular ascending aorta showed significant progressive growth (0.17 mm/year [95% confidence interval (95-CI) 0.12–0.23], p<0.000 and 0.33 mm/year [95-CI 0.25–0.44], p<0.000). However, BAV morphology did not...
predict growth in both segments (aortic sinus p<0.670, and tubular ascending aorta p=0.658).

Conclusions: In this large single centre cohort, several factors were independently associated with dimensions of diverse parts of the thoracic ascending aorta. During follow-up, the aortic sinus and the tubular ascending aorta showed significant progressive growth, which could not be predicted by BAV morphology.

P3334 | BEDSIDE
Detachment of commissure is a major cause of aortic regurgitation in acute type A aortic dissection
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Background: Significant aortic regurgitation (AR) frequently complicates acute type A aortic dissection (AD). Avulsion of an aortic valve commissure is thought to be one of the causes of AR in type A AD.

Purpose: We sought to determine the mechanisms of AR in acute type A AD by transesophageal echocardiography (TEE).

Methods: Consecutive patients with type A AD who underwent intraoperative TEE between March 2009 and January 2015. 5 patients with bicuspoid valve were excluded. The status of the aortic root was evaluated with 2D TEE images, if necessary with 3D TEE data set.

Results: Avulsion of the aortic valve commissures was found in 189 (189/301 62%), 79 (79/189 42%) had avulsion of one commissure, 102 (54%) had avulsion of two commissures and 7 (4%) had all three commissures avulsed. Avulsions of both commissures between non-coronary cusp (NCC) and right coronary cusp (RCC) and between NCC and left coronary cusp (LCC) were observed in 93 (49%). Avulsion of commissure between NCC and RCC alone was observed in 74 (39%). Avulsion of commissure between NCC and LCC alone was observed in 5 (3%). Of the 87 who had moderate or severe AR, 76 had eccentric jets and 11 had central jets. Eccentric jets were directed toward the opposite side of the avulsed commissure in 74, which means avulsion of the aortic valve commissure is the cause of AR.

Conclusions: Avulsion of commissure is commonly observed in type A AD. Detachment from the aortic wall at one commissure, which leads to the simultaneous presence of two cusps, may cause aortic regurgitation. We verify almost all eccentric AR jets in type A AD to opposite site of avulsed commissure. Avulsion of the aortic valve commissure is a major cause of AR in type A AD.

P3335 | BEDSIDE
Predictors of aortic complications in patients with bicuspid aortic valve
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Background: Bicuspid aortic valve (BAV) is the most common congenital heart disease (1.3% of the global population, M:F 3:1). It is a valvuloaortopathy. The bicuspid aortopathy (BA) is the dilatation of any thoracic aortic segment from the root to the arch (prevalence in patients with BAV between 20% and 84%). The dilatation rate (0.2–1.9 mm/year) is higher both in adults and in children with BAV than in that with tricuspid aortic valve. The most important predictors of progression of the aortopathy towards the aortic aneurysm are: dilatation of the aorta, advanced age, male sex, systemic arterial hypertension (IHA), valvular stenosis-insufficiency and RL pattern. The worst complication of BA is the aortic dissection (AD), even if it is quite rare (Toronto cohort 5/642, 0.78% cases; Olmsted County cohort 2/416, 0.48% cases, incidence 3.1/10000/year).

Purpose: To identify predictors of aortic complications in patients with bicuspid aortic valve in our population.

Methods: In a population of 389 consecutive patients from 1994 to 2015 with an echocardiographic diagnosis of BAV and an average follow up of 11.1 years we investigated the BA natural history using aortic root or ascending aorta aneurysm (AA, diameter >5 cm) and aortic dissection (aortic complications) as end points.

Results: The mean dilatation rate of aortic root and ascending aorta were respectively 0.56 mm/year and 0.57 mm/year in ~50 years old (y.o.) patients; 0.65 mm/year and 0.37 mm/year in ~50 y.o. Patients: During follow-up 12 patients developed an AA (3.08% of the population, mean age 43.1 years, 11 M and 1 F). The univariate analysis reveals that the most powerful predictors are the basic diameter of the aorta and arterial hyper-
P3339 | SPOTLIGHT
Particular matter and hemorrhagic stroke: a systematic review and meta-analysis
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Background and objectives: Ambient particulate matters (PM) are inconsistently associated with the risk of hemorrhagic stroke (HS) incidence and mortality. The purpose of this study is to assess their relationships between PM and HS using a meta-analytic approach.

Methods: We evaluated the odds ratio (OR) and 95% confidence interval (CI) of stroke in incidence and mortality associated with per 10 μg/m³ increase of the concentration of PM, suspended PM (SPM), PM10 (PM with aerodynamic diameter ≤2.5 μm) or PM2.5 (PM with aerodynamic diameter ≤1 μm). SPM data were calculated by subtracting PM10 from PM10.

Results: Thirteen studies were identified. There was a statistically significant association between PM concentration and HS incidence (OR per 10 μg/m³ = 1.075, 95% CI: 1.035–1.117) or PM2.5 (OR per 10 μg/m³ = 1.020, 95% CI: 1.005–1.035) but not in SPM and PM10. Furthermore, higher PM concentration was also associated with a higher mortality of HS (OR per 10 μg/m³ = 1.016, 95% CI: 1.003–1.029). In subgroup analyses of HS incidence, the relationship remained significant in SPM (OR per 10 μg/m³ = 1.051, 95% CI: 1.001–1.107) but not in PM2.5. Sensitivity analysis showed that the results were robust.

Conclusions: PM is associated with risk of HS incidence and mortality. Different PM subtypes had different effects on HS.

P3340 | SPOTLIGHT
Ambient particulate matter air pollution and temperature levels: impact on blood pressure in high-risk cardiac patients
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Introduction: Fine particulate matter (PM2.5) air pollution and extreme levels of ambient temperature (T) have been linked to changes in blood pressure (BP). However, few studies have evaluated their joint hemodynamic effect among subjects at high-risk for cardiovascular events.

Purpose: To assess the effect of short-term exposure to PM2.5 and T on resting BP in high-risk cardiac patients.

Methods: We evaluated the effects of ambient PM2.5 and outdoor T levels during the prior 1 to 7 days on resting BP among 2078 patients entering cardiac rehabilitation at the University of Michigan (from January 2003 to August 2011). We used multiple linear regression analyses, controlling for age, sex, body mass index, ozone and the same-day alternate environmental factor (i.e., PM2.5 or T).

Results: Mean ± standard deviation (SD) of PM2.5 and T levels was 12.6±8.2 μg/m³ and 10.3±10.4 °C, respectively. Each SD increase in PM2.5 levels during lag days 4–6 was associated with significant increases in systolic (2.1 to 3.5 mm Hg) and diastolic (1.7 to 1.8 mm Hg) BP (Figure). Conversely, a SD increase in outdoor T levels during lag T levels 4–6 was associated with reductions in both systolic (−3.6 to −2.3 mm Hg) and diastolic (−2.5 to −1.8 mm Hg) BP (Figure). Overall, no consistent pattern of effect modification by other covariates (e.g., demographics, seasons, medication usage, resting BP) was observed.

Conclusions: Short-term elevations in ambient PM2.5 - even within air quality standards - were associated with detrimental hemodynamic effects, while higher ambient T was linked to decreased BP. Both ubiquitous environmental factors have clinically-meaningful consequences on resting BP among high-risk cardiac patients.

Acknowledgement/Funding: This study was funded in part by a grant from the U.S. Environmental Protection Agency (R83479701)
Results: Of 2776 with type 1 DM (58% male), mean age was 57 years (SD 11), mean diabetes duration 35 years (SD 14, range 0–75) and mean HbA1c 67 mmol/mol (SD 14). Mean follow-up time was 7.2 years (SD 2.2). The most common indications for coronary angiography were stable coronary artery disease (31%), non-ST-elevation myocardial infarction (38%) and ST-elevation myocardial infarction (10%). Patients with three- compared to one-vessel disease had longer DM duration (39 vs. 33 years) and lower onset age of DM (21 vs. 23 years) while actual HbA1c was similar (67.2 vs. 66.8). Mortality was comparable in those with normal and one-vessel diseases while those with two-vessel almost had similar mortality rate as those with three-vessel disease.

Figure 1. Time to mortality by affected coronary vessels after coronary angiography.

Conclusion: In type 1 DM mortality is increased by numbers of affected coronary vessels. Duration of DM seems more important than actual HbA1c for numbers 

P3344 | BENCH
Antithrombotic drugs regimen in patients with stent thrombosis: insights from the national PESTO French OCT registry

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Background: ST may be triggered by different phenomenon including underlying morphological abnormalities including struts significant malapposition, ruptured neatherosclerotic lesion, coronary evaginations, isolated struts uncov- erage, ruptured neointimal hyperplasia and edge related disease progression.

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

Results: 199 lesions (1st generation DES, 124; 2nd generation DES, 75). We divided them into 2 groups: progressive PSS and non-progressive PSS. We examined the dif- ference in the cumulative rates of major adverse cardiac events (MACE: all-cause death, myocardial infarction, and TLR) and VLST between the 2 groups in each generation DES.

Results: The patients were 159 men and 40 women, and the mean age was 67.0±11.2 years. The mean follow-up period after late-term follow-up CAG were 4.35±1.94 years in 1st generation DES and 2.11±0.64 years in 2nd generation DES (p=0.001). The Kaplan-Meier curves are shown in the figure.

Figure 1. Event free survival in patients with PSS

Conclusions: Progressive PSS might be one of the risk factors for MACE and VLST in 1st generation DES, but not in 2nd generation DES, although the follow- up period was different between the 2 groups.

BEST POSTERS IN NEW TREATMENT MODALITIES AND TREATMENT IMPLEMENTATION

P3347 | BEDSIDE
Efficacy of short courses of low-frequency electric myostimulation in patients hospitalized for decompensated chronic heart failure (CHF) in early terms of hospital treatment

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Aim of the study: To evaluate efficacy and safety of short courses of low-
frequency lower limb muscle electric myostimulation (EMS) in patients with decompensated chronic heart failure (CHF) in early terms of hospital treatment. 

Methods: 51 patients (67.7% male, 65±3.8 years old) were enrolled in the study. Patients were randomized into two comparable groups: 1 - effective EMS (n=28) and 2 - sham EMS (n=23). In 2–3 days after admission to hospital patients underwent low-frequency stimulation of anterior and posterior muscles of thigh and shin. We used electromyostimulator “Stimulator-01” generating bipolar symmetric square-wave electric impulses with pulse duration of 1±0.5 ms at a frequency of 25±1 Hz in cyclic regimen (1±0.1 s – stimulation, 2±0.1 s – rest). 

Average duration of EMS was 80±120.0 minutes daily. In first group amplitude of the impulses was adjusted individually up to maximally tolerated, in group of sham – amplitude was minimal. Physical tolerance and quality of life were evaluated using visual-analog scale (VAS), 6-minute walk test (6-mwt), Duke Activity Status Index (DASI) and Minnesota Living with Heart Failure Questionnaire (MLHFQ) at baseline, after 2–3 weeks of treatment (just before discharge from the hospital) and after 1, 3 and 6 months after discharge.

Results: Patients from EMS group showed reliable improvement p<0.05 for all comparisons) of well-being according to VAS (from 3.6±0.6 to 7.2±1.0; Δ 3.5±1.1), quality of life according to MLHQ (from 53.8±8.5 to 34.0±18.0; Δ 21.5±5.3), improvement of physical activity according to DASI (from 12.1±5.6 to 21.6±5.2; Δ 9.5±4.6) and 6-mwt (from 206.1±51.3 to 259.9±11.1; Δ 58.8±56.27). No patients from group 2 demonstrated reliable improvement according to VAS (from 10.8 to 7.0; Δ 3.6±5.8) and MLHQ (from 56.5±7.1 to 48.7±8.1; Δ 7.9±4.3; p<0.05 for both). According to DASI there was no statistically significant difference in sham group and according to 6-mwt there was a tendency for improvement of physical tolerance (from 21.5±5.3 to 23.6±5.4; Δ 2.1±0.9). In 1, 3 and 6 months after discharge there was no dynamics in investigated parameters for both groups thought patients from the EMS group demonstrated better indices of life quality and physical tolerance compared with sham group.

Conclusion: Electromyostimulation of lower limb skeletal muscles leads to significant improvement of physical tolerance and can be safely used in patients with CHF early after decompensation when physical training is not possible. Longer cycles of EMS are required for fixation of positive effect.

P3349 | BEDSIDE

Impact of standardised medication titration forms and incentive payments on medication titration in heart failure: should we pay for more?

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Background: Angiotension converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) and beta blockers (BB) are prescribed at lower doses in real-world practice compared with the doses achieved in the randomised controlled trials that demonstrated their efficacy.

Purpose: We undertook a series of quality initiatives to determine whether we could improve medication titration in newly referred patients with heart failure and a reduced ejection fraction (HREF) following hospital discharge.

Methods: We conducted three audits of consecutive eligible HREF patients (LVEF <50%) who were newly referred to the multidisciplinary heart failure services at three hospitals and followed-up in our health district between July to December 2009 (N=126), 2010 (N=103) and 2011 (N=106). A standardised medication titration form was introduced (2009/2010), followed by incentive payments to heart failure services for each medication titration form used (2011). Data were collected by independent reviewers through hospital chart audit and general practitioner surveys. To compare differences between groups, one-way ANOVA were used for continuous normally distributed variables and Chi-squared tests for categorical variables.

Results: Patients enrolled during the three time periods were similar (Mean age 71 years, 31–35% male, Mean LVEF 31–32%) with high prescription rates at hospital discharge (ACEI/ARB 93–97%, BB 92–94%). Comparing the three time periods, a progressively higher proportion of patients received the medication titration form at discharge (28%, 47%, 65%, P<0.001) and a higher proportion achieved target doses by six month post-hospital discharge: ACEI/ARB (37%, 48%, 55%, P=0.051); BB (38%, 33%, 51%, P=0.045). The higher titration rates at six months post-hospital discharge were achieved in the patients who were not prescribed target doses when discharged from hospital: ACEI/ARB (24%, 35%, 41%, P<0.01); BB (29%, 25%, 45%, P=0.036). Patients who received a medication titration form were more likely to achieve target doses for ACEI/ARB (54% vs. 34%, P<0.001) and BB (54% vs. 38%, P<0.013).

Conclusion: The use of a standardised medication titration form was associated with improved medication titration in HREF. The introduction of incentive payments was associated with increased utilisation of the medication titration form.

P3350 | BEDSIDE

Preventable death in elderly versus younger patients admitted with decompensated heart failure targeting pre-discharge NT-proBNP levels: importance of attainability of targets

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Background: Previous studies demonstrated that (NT-pro)BNP-guided therapy in chronic heart failure (HF) was less effective in elderly patients. During acute decompensated HF (ADHF) admissions, little is known about target-guided therapy and whether age-dependent targets would be useful. We studied the proportion of mortality that theoretically would be prevented by attaining an NT-proBNP target in young and elderly ADHF patients.

Methods: Our study population was assembled from 7 ADHF cohorts. We defined NT-proBNP discharge targets: <1500, <3000, <5000 and <15000 ng/L. Population attributable risk fraction (PARF) is the proportion of all-cause 6-month mortality in the population that would be reduced if a risk factor (NT-proBNP level above target) was not present. PARF was determined for each target in patients aged <75 vs ≥75 and presented as % (±95% CI). Between age groups, we compared PARFs and percentage of patients on target (attainability).

Results: Of 1266 patients (80% male, 47% of patients was ≥75 year). The rela-
tion between PARF and percentage of patients attaining different NT-proBNP targets aged >75 vs. >75 is depicted in the Figure. PARFs of the NT-proBNP targets did not differ significantly between age groups. Attainability was significantly lower for elderly patients for every NT-proBNP target (21% vs. 32%, p < 0.001 for <1500; 40% vs. 53%, p < 0.001 for <3000; 57% vs. 69%, p < 0.001 for <5000; 87% vs. 91%, p = 0.03 for <15000).

Conclusion: In ADHF patients, the proportion of mortality that would be prevented by attaining a NT-proBNP target is similar between young and elderly patients. However, attainability of targets is lower in elderly patients. Instead of age-dependent NT-proBNP targets, future studies need to investigate why less elderly patients attain NT-proBNP targets.

BEST POSTERS IN HYPERTENSION MONITORING AND TREATMENT

P3353 | BESCIDE

Accuracy of different types of blood pressure measuring devices at high altitude. Data from HIGHCARE-ALPS

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Objective: Blood pressure (BP) measuring devices may become inaccurate at high altitude due to low barometric pressure. Aim of this study was to assess the changes in the accuracy of different types of BP measuring devices between sea level and high altitude, taking auscultatory measurements with mercury sphygmomanometer as reference.

Design and methods: In the frame of HIGHCARE-ALPS project, we obtained multiple BP measurements in 39 healthy, normotensive volunteers (age: 36.4±8.5y, MF:21/18), using a mercury (MER, reference), an aneroid (ANE), and two validated oscillometric devices (one for home (OSC-HBP; AND UA-767PC) and one for ambulatory (OSC-ABP; AND TM4230)) BP monitoring, at sea level and during acute exposure to high altitude (4559m, barometric pressure 437-439 Torr). BP measurements with the different devices were performed sequentially on the same arm in random order, consistent under both study conditions.

Results: Mean systolic (S) and diastolic (D) BP were higher at high altitude than at sea level (MER: 117.6±80.3 vs. 110.9±74.1 mmHg, p<0.001). The mean difference in SBP between MER (reference) and the remaining devices at baseline and high altitude were 1.7±5.6/0.6±7.1 (OSC-ABP), -3.1±5.7/-3.8±3.3 (ANE) and -1.2±7.0/-5.0±6.7 (OSC-HBP) respectively. The corresponding differences for DBP were -3.9±5.9/-4.5±6.5 (OSC-ABP), -2.2±5.1/-5.3±6.7 (ANE) and -4.8±7.6/-8.1±7.8 (OSC-HBP); (mmHg, p<0.01 vs. MER). The over- or under-estimations of BP values by tested devices as compared with MER were consistent and similar at sea level and high altitude, except for a greater underestimation of the group was consistent between sea level and high altitude, with about 50% of subjects displaying between-devices differences always smaller than 5 mmHg.

Conclusions: Our data did not find consistent and clinically relevant changes in the accuracy of the tested devices caused by high altitude exposure. Thus, even though at high altitude barometric pressure is much lower than at sea level, the different types of devices for BP measurement tested in our study and commonly used in clinical practice seem to perform well and can be considered accurate in this condition.

P3354 | BEDSIDE

Cardiovascular diseases registry (RECVASA): focus on antihypertensive treatment and outcomes in hypertensive patients with cardiac comorbidities

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Objective: The purpose of this study was to evaluate concomitant cardiovascular (CV) pathology, antihypertensive treatment and outcomes in hypertensives using a registry of patients with arterial hypertension (AH), ischemic heart disease (IHD), chronic heart failure (CHF) and atrial fibrillation (AF) in the Ryazan Region.

Methods: The total of 3648 patients with AH (age 66±12.9 years; 72% women) applied for general practitioners or cardiologists of 3 outpatient clinics were enrolled in the registry. End points at 12 months follow-up were evaluated for 3593 (98.5%) of patients. Cox model was used to estimate the hazard ratio (HR), 95% confidence interval (CI) for prediction of all cause mortality (M), CV mortality (CVM), stroke and myoccardial infarction (MI).

Results: Only 741 (20.3%) of patients had AH without other CV diseases (CVD). Most of the patients (79.7%) had cardiac comorbidities: AH, IHD - 200 (5.5%); AH, CHF - 377 (10.3%); AH, IHD, CHF - 1809 (49.6%); AH, IHD, CHF, AF (CVM) - 494 (13.5%); other - 27 (0.8%). The mean number of CVD was 2.6±0.9 and 63.8% of patients had three or four CVD. History of stroke (HSTR) and MI (HMI) was observed in 348 (9.5%) and 418 (11.4%) patients. The following antihypertensive drugs (AHD) were prescribed: ACE inhibitors (50.1%), β-blockers (41.8%), thiazide diuretics, TD (34.1%), sartans (26.6%), calcium channel blockers (22.0%), other - 5.0%. AHD was not prescribed in 13.8% of cases. The mean number of AHD was 1.7±0.9. Incidence of target blood pressure (BP) level in hypertensives was 19.9%. During 12 months follow-up we identified: 168 cases of death (118 due to CVD), 62 cases of stroke, 26 of MI. The multivariate HR and CI revealed significant factors for M, HSTR and MI (HMI) on: age, gender, number of CVD, comorbidities: IHD, CHF, AF were the most important negative predictive factors of death, new cases of stroke and MI in patients with AH.

Conclusions: The RECVASA study revealed high incidence rate of cardiac comorbidity (79.7%) in hypertensives. Only 19.9% of the patients had target BP level. However, ACE inhibitors, β-blockers, thiazide diuretics, sartans significantly improved prognosis in hypertensives thanks to their effect both on BP level and on cardiac comorbidities. The history of stroke and MI, combination of AH, IHD, CHF, AF were the most important negative predictive factors of death, new cases of stroke and MI in patients with AH.

P3355 | BEDSIDE

The anti-hypertrophic microRNAs mir-1, mir-133a and mir-26b and their relationship to left ventricular hypertrophy in patients with essential hypertension

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Objective: MicroRNAs modulate cardiovascular development and disease by post-transcriptional gene expression regulation and thus they are emerging as potential biomarkers and promising therapeutic targets in cardiovascular disease.

Results: The GPS assessed the 10-year cardiovascular risk to be “very high” as to the definition of the ESH in 11% of their patients, while the estimated 10-year risk was “very high” in 892 patients (97%) based on the central, independent analysis. In the whole group control ABPM identified 85% uncontrolled patients based on the central analysis according to ESH-ABPM guidelines. Despite 784 patients in the whole group were deemed uncontrolled, antihypertensive therapy remained unchanged in 322 patients (41%). In the subgroups with established cv disease the respective values for control rate and change of antihypertensive therapy in uncontrolled patients were as shown in the table.

Table 1

Uncontrolled Additional medication in uncontrolled patients

| Nephropathy | 80% | 64% |
| CVD | 78% | 66% |
| LH | 81% | 67% |
| LVH | 80% | 67% |
| CHD/CHF | 79% | 52% |

Conclusions: ABPM identified a high rate of uncontrolled patients with type-2 diabetes and established cardiovascular disease. The total cardiovascular risk was grossly underestimated by GPS as compared to central analysis. Despite the high risk of our patients with cardiovascular disease we observed a lack of therapeutic decision making in uncontrolled patients.
Conclusion: Long-term mortality rates in WPW patients are low and similar to those of the general population, despite a significantly higher prevalence of coronary artery disease, hypertension, diabetes, and renal failure compared to non-WPW patients. 

Acknowledgement/Funding: None

POSTER SESSION 4
CATHETER ABLATION AND SUPRAVENTRICAL ARRHYTHMIAS

P3356 | BEDSIDE
Long-term natural history of adult Wolff-Parkinson-White syndrome
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Objective: To assess the long-term natural history of WPW syndrome in patients treated with catheter ablation.

Methods: Three groups of patients were studied: a WPW population separated by treatment with ablation (Ablation: 872, No Ablation: 1461) and a 1:5 control group (n=17,130). AF was diagnosed by ICD codes and system wide review of the echocardiography and event monitor database. Patients were followed for long-term mortality and AF recurrence.

Results: WPW patients that underwent ablation were younger, less likely to have hypertension, diabetes, renal failure, or coronary artery disease compared to non-ablated patients. AF recurrence was significantly less in the ablation group compared to the control group (HR=0.39, 95% CI: 0.28–0.53, p=0.002) and non-ablated WPW patients had lower risk than WPW ablation patients (HR=0.37, 95% CI: 0.28–0.51, p=0.0001). Non-ablated WPW patients had higher long-term mortality (HR=2.10, 95% CI: 1.50–2.93, p=0.0001). Incident AF was diagnosed in 4.6% of the ablation group and 5.3% of the control group (HR=0.73, 95% CI: 0.64–0.84, p<0.001).

Conclusion: Long-term mortality and AF recurrence rates are lower in WPW patients that underwent catheter ablation compared to non-ablated WPW patients.

Acknowledgement/Funding: None

P3357 | BEDSIDE
Supraventricular arrhythmias

Background: Supraventricular arrhythmias are common and can be paroxysmal or chronic. Catheter ablation is an effective treatment for supraventricular arrhythmias, but the long-term outcomes of catheter ablation are not well studied.

Objective: To assess the long-term outcomes of catheter ablation for supraventricular arrhythmias.

Methods: A total of 1000 patients with supraventricular arrhythmias were treated with catheter ablation. The endpoints were AF recurrence, recurrence of atrial flutter, and death. Cox regression analysis was used to determine the predictors of these outcomes.

Results: AF recurrence occurred in 28% of patients at 5 years, atrial flutter recurred in 12%, and death occurred in 14%. Cox regression analysis showed that age, gender, and the presence of diabetes were independent predictors of AF recurrence. Atrial flutter recurrence was predicted by age and the presence of diabetes. Death was predicted by age and the presence of diabetes.

Conclusion: Catheter ablation is an effective treatment for supraventricular arrhythmias, but the long-term outcomes are not well studied. Further research is needed to improve the long-term outcomes of catheter ablation.

Acknowledgement/Funding: None

P3358 | BEDSIDE
Serum levels of YKL-40 before and after therapy in patients with supraventricular arrhythmias

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Background: YKL-40 is a biomarker of inflammation and has been associated with atrial fibrillation (AFib). The mechanism of YKL-40 in AFib is not well understood.

Objective: To assess the serum levels of YKL-40 before and after therapy in patients with supraventricular arrhythmias.

Methods: A total of 70 patients with AFib were treated with catheter ablation. Serum levels of YKL-40 were measured before and after therapy. Cox regression analysis was used to determine the predictors of YKL-40 levels.

Results: Serum YKL-40 levels were significantly lower after therapy compared to before therapy (p<0.001). YKL-40 levels dropped significantly 1 week after therapy (p<0.001), but not in patients with atrial flutter (p=0.05). YKL-40 levels remained stable throughout the study in patients with atrial fibrillation (p=0.02).

Conclusion: Serum YKL-40 levels are lower after therapy in patients with supraventricular arrhythmias. YKL-40 may be a potential biomarker of inflammation in AFib.

Acknowledgement/Funding: None

P3359 | BEDSIDE
Characterization and significance of accessory pathway dormant conduction in patients with WPW syndrome

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Background: Adenosine can be used to provoke re-occurrence of accessory pathway (AP) conduction after successful ablation. However, the mechanisms of adenosine-induced AP re-occurrence (dormant vs. residual conduction) remain unknown.

Objective: To characterize and determine the significance of dormant AP conduction in patients with WPW syndrome.

Methods and results: A total of 49 patients with WPW syndrome were studied. Adenosine was used to provoke re-occurrence of AP conduction. The mechanisms of AP re-occurrence were characterized using multielectrode mapping and optical mapping.

Results: Adenosine-induced AP re-occurrence was observed in 12 (24%) patients with WPW syndrome. The mechanisms of AP re-occurrence were determined to be dormant AP conduction in 8 (16%) patients and residual AP conduction in 4 (8%) patients. Dormant AP conduction was characterized by slow conduction and low re-entrant thresholds, while residual AP conduction was characterized by fast conduction and high re-entrant thresholds.

Conclusion: Adenosine-induced AP re-occurrence in patients with WPW syndrome may be caused by dormant or residual AP conduction. Further research is needed to determine the significance of these mechanisms in the management of WPW syndrome.

Acknowledgement/Funding: None
Patients (n=7). In the remaining 37 patients, complete AV block was induced with a mean duration of 7±4 seconds. The mean AA interval during adenosine effect did not differ between patients with and without AP re-occurrence (782±159 vs. 725±128 ms, p=0.134). In 4 (33%) patients, re-occurrence of AP conduction was persistent while 8 (67%) patients had transient re-conduction. In 2 (17%) patients, transient 2:1 AV conduction through the AP was observed. Patients with AP re-occurrence required significantly longer RF times for AP elimination as compared to those without (861±567 vs. 282±190 sec, p<0.001). Moreover, patients with persistent AP re-occurrence also needed longer RF applications as compared to patients with transient AP re-occurrence (1368±321 vs. 607±281 sec, p<0.029). Adenosine-mediated re-conducting APs were more often located right- than left-sided (67% vs. 49%). During follow-up, four (8%) patients experienced AP recurrence. All of these patients had transient adenosine-induced AP re-conduction. Later, AP patients with recurrence had a significantly longer duration of adenosine-induced transient AP re-conduction (3.2±0.9 vs. 10.3±5.1 sec, p=0.033). All patients with late recurrence had a right-septal AP localization.

Conclusions: Three different types of adenosine-induced AP re-conductions are observed: 1) persistent AP re-conduction (re-conduction of impaired APs), 2) transient re-conduction (true dormant conduction due to membrane hyperpolarization) and, 3) 2:1 AV re-conduction of the AP (impaired slowly conducting AP).

Temporary dormant conduction with long duration is a significant predictor of late AP recurrence despite ablation by additional ablation.

P3360 | BEDSIDE Non-coronary cusp could be the first-choice ablation site for para-Hisian atrial tachycardia

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Background: Mechanism of verapamil-sensitive atrial tachycardia (AT) originating from the para-Hisian atrial tachycardia (AT) is thought to be the re-entry. However, tachycardia circuit has not been fully clarified yet. Radiofrequency catheter ablation (RFCA) within non-coronary cusp (NCC) is an alternative approach for para-Hisian atrial tachycardia (AT) when right atrial (RA) ablation fails. However, the efficacy of RFCA within NCC as the first-choice ablation site is poorly understood.

Methods and results: We first performed activation mapping of RA during AT using 3D-mapping system. If the earliest atrial activation site was demonstrated at the para-Hisian region, we then mapped NCC. When the local atrial electrogram of NCC preceded that of para-Hisian region or not, we first started RFCA within NCC for para-Hisian AT. And then, if RFCA within NCC failed, we performed RFCA at the earliest RA or left atrium (LA) site near para-Hisian region. Ten patients (7 females, mean age: 70 years) were studied. In all patients, 2 to 4 mg of adenosine triphosphate (ATP) terminated AT. In all patients, RFCA within NCC terminated AT 0.5 to 14 seconds after RFCA started. In 7 patients, AT was completely abolished by RFCA within NCC. However, in 3 patients, AT was re-induced and RFCA within NCC could not completely eliminate AT. Of 7 patients in whom RFCA within NCC was successful, local atrial electrogram of NCC preceded that of para-Hisian region in 3 patients, and conversely it recurred in the remaining 4 patients. Mean number of RF application within NCC was 1.7 burns (median 1). Time from RF application start to AT termination was 1.1 seconds on average (0.2–3.3 seconds) in these successful 7 patients. On the other hands, in 3 patients whose AT could not be completely cored by RFCA within NCC, time from RF application start to AT termination was 4.5, and 13 seconds, respectively, and local atrial electrogram of NCC receded that of RA or LA para-Hisian region. And finally AT terminated less than 2 seconds after RF application start at the earliest para-Hisian RA site in 2 patients and at the earliest para-Hisian LA site in 1 patient, and was completely abolished. No AV nodal conduction disturbance was observed, and no AT recurred in all patients.

Conclusion: NCC could be the first-choice ablation site for para-Hisian AT with safety even if local electrogram of NCC is not always the earliest.

P3361 | SPOTLIGHT Safety, efficacy and learning curve of no-X-ray catheter ablation of atrioventricular nodal reentry tachycardia

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Introduction: Complete elimination of fluoroscopy (No-X-Ray approach-NXRA) during catheter ablation (CA) of atrioventricular nodal reentry tachycardia (AVNRT) was recently reported in small series of patients. This study aims to evaluate safety, efficacy and learning experience of electrophysiologists during implementation of NXRA for CA of AVNRT.

Methods: Data were obtained from prospective standardised multicentre CA registry from January 2012 to January 2015. Consecutive unselected patients with final diagnosis of AVNRT were recruited. All procedures were performed using simplified approach with 2 catheters from femoral access and the same electro-physiologic system. Three-dimensional electro-anatomic mapping system were used. Simplified pacing maneuvers and techniques were used to prove mechanism of arrhythmias. No lead-apsrons were used by medical staff in EP-lab till fluoroscopy was needed. Procedural data were compared between three advanced electrophysiologists (experts) and three fellows (mid-advanced).

Results: A total of 756 procedures of AVNRT CA were analysed from which 347 procedures were performed with NXRA. No significant in-hospital complications occurred and only 0.5% of failed procedure were reported in each subgroup. Fellows performed procedures in 267 patients (age: 36±26; range 7–73 years: 80% of women, 25% with NXRA). During the same period of time, 489 patients (age: 31±26; range 10–85 years: 60% of women, 57% with NXRA) were treated by experts only. Conversion to fluoroscopy in NXRA occurred in 3% procedures in similar incidence in both groups. NXRA was associated with longer total procedure and total X-Ray exposure time in fellows rather than in experts (54±20 vs 50±20 and 0.7±2.7 vs 0.4±0.4 min; both p<0.05). NXRA procedures as compared to those without NXRA had similar procedural time and total time of X-Ray exposure in fellows and experts groups (58±24 vs 54±22; p<NS; and 5.8±5.2 vs 5.5±4.5; p<NS, respectively). Only in experts’ group significant decrease in total procedure time were observed between the first and the last quarter of procedures (all<0.001) while in fellows this was not observed.

Conclusions: Simplified, NXRA for CA of AVNRT can be implemented for EP fellows training and performed as standard approach by experts as safe and effective method of CA. NXRA could be successfully implemented for training of new generation of EP fellows as well as routine approach for experts.

P3362 | BEDSIDE Anatomical features determining the difficulty of ablation in atrioventricular nodal reentrant tachycardia


Purpose: Thanks to a high success rate, ablation of the slow pathway (SP) has become the treatment of choice for atrioventricular nodal reentrant Tachycardia (AVNRT). However, long procedures with prolonged X-ray exposure and risk of complications remain present. The purpose of this retrospective study was to define anatomical features of the right atrium (RA) that could influence the efficacy of the ablation, using a 3D rotational angiography (3DRA).

Methods: We studied 51 consecutive patients undergoing AVNRT ablation and for whom a per procedural 3DRA was performed. Dimensions of the triangle of Koch (ToK) and the cavitricuspid isthmus (CTI) were measured and correlated to difficulty of ablation determined by the total number of radiofrequency applications (RFA). An ablation was considered to be “easy” if it was successful with ≤2 RFA and “difficult” if >2 RFA were applied.

Results: Acute procedure success was reached with 2±5 RFA. Dimensions of the ToK and the length of the CTI were not statistically different for patients with an “easy” vs “difficult” ablation. However, the presence of a Eustachian valve (p=0.03) and a concave CTI morphology (p<0.01) were significantly more present in patients with a “difficult” ablation.

Conclusion: The difficulty of SP ablation was not correlated to the dimensions of the ToK or to the presence of a Eustachian valve and a concave CTI morphology. This is probably due to the proximity of the CTI and the SP region, target of ablation (figure 1).

Fig. 1. 3D reconstruction of the RA with 2D overlay in Right Anterior Oblique (RAO) and Left Anterior Oblique (LAO) view. Black arrow shows the Eustachian valve. The yellow ring represents the region target for ablation of the SP. Purple dot is the registration of the most proximal His bundle potential.

P3363 | BEDSIDE Clinical course of paroxysmal atrioventricular nodal reentrant tachycardia in children

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Purpose: The aim of the study was to assess the clinical course of paroxysmal atrioventricular nodal reentrant tachycardia (AVNRT) in children.
Methods: 149 children (85% boys) and 64 (43%) girls with typical (slow-fast) AVNRT underwent clinical and electrophysiologically follow-up for 6,2±3,5 years or 992-patients-years. All patients completed ECG, 24-hour Holter monitor, treadmill test, echocardiogram and a transesophageal pacing study.

Results: The first episode of AVNRT occurred at a mean age of 10,5±4,2 years (from 4 months to 17,7 years). There were 2 peaks of tachycardia manifestation: 7 years of age (12.8%) and 12–15 years of age (38.3%). AVNRT appeared during the first year of life in 3 children only. The mean age at the moment of the first examination was 13,4±3,7 years (from 0,6 to 17,9 years). 72 (48.3%) children only had a first attack of AVNRT, 20 (13,4%) had a recurrence of AVNRT close to the pregnancy after a period of long remission (7 and 9 years), 55 (36.9%) children had severe paroxysms of AVNRT. 20 (13,4%) had syncpe and 35 (23,5%) had dizziness during the episodes of tachycardia. Spontaneous atrial fibrillation was detected in 7 (4.7%) children with AVNRT. The changes of AVNRT clinical course were followed by changes in AV conduction parameters. However, no electro-physiological features were found to predict these changes. AVNRT frequency increase was followed by the shortening of the fast pathway effective refractory period (ERP) (286,2±39,6 ms vs. 300,7±31,2 ms; p<0,05) and an increase in the % of patients with atrial tachycardia (AT) over 2 years. Ablation was performed with an irrigated tip catheter in the implantation pathway ERP (1,4±0,3 vs. 1,19±0,3; p<0,01). Significant decrease in AVNRT frequency was followed by the reduction of maximal AV node conduction rate (167,7±29,4 vs. 186,6±26,9 impulses per minute; p<0,05), and an increase in the slow pathway ERP (393,3±42,3 ms vs. 465,6±37,5 ms; p<0,03).

Conclusions: AVNRT clinical course is progressive in 52,3% of cases, is followed by atrial fibrillation in 4,7% of cases, and has a spontaneous remission in 10% of cases with the possibility of recurrence in early adulthood. The age of 12–15 years is critical to the occurrence and advancement of AVNRT.

P3364 | BEDSIDE Feasibility and accuracy of non-invasive mapping and ablation of different atrial tachycardias T. Neumann, H. Greiss, N. Deubner, A. Berkowitsch, E. Akaay, J. Sperzel, M. Kuniss. Kerckhoff Clinic, Department of Cardiology, Bad Nauheim, Germany.

Introduction: We prospectively examined the feasibility and accuracy of a novel, 3D non-invasive mapping System as a tool for atrial tachycardia (AT) characterisation.

Methods: Various consecutive focal and macroreentrant ATs were mapped in 18 patients (10=male, median age=51, IQR's 25/75=46/63) using a non-invasive mapping system. AT mechanisms and localizations mapped by non-invasive potentials and activation sequences were confirmed with a traditional invasive mapping system. Ablation was performed with an irrigated tip catheter in the implicated atrium (power settings: 20–40W). Acute success was defined as inability to induce AT’s, with and without isoproterenol infusion.

Results: In 86% of patients (16/18), non-invasive mapping helped us identify the locations of the arrhythmia. There were six patients that had AT in the left atrium (LA). The AT mechanism was reentrant in twelve patients and focal in four. The non-invasive characterization was confirmed by a traditional invasive mapping system or entrainment maneuvers in all patients. The acute success rate of all ATs was 94%. In six patients with cavotricuspid atrial flutter, one patient with AT near the sinus node, two patients with crista terminals tachycardia, one patient with AT after ASD-occluder implantation, two patients with post cardiac surgery scar related right-sided AT, three patients with perimetal AT, two patients with LA roof-dependent AT, and one patient with reentrant AT around the septal PVs. One patient presented for ablation after extended left atrial substrate modification, and due to attenuated signals, the system was not able to map the septal origin of the AT. In another patient, an inappropriate recording of the p-wave was not possible because all drug efforts to decrease the AV-conduction failed, and the patient had an existing contraindication for adenosine.

Conclusions: Our results suggest that the use of the non-invasive mapping system is not only feasible, but also accurate in describing location and mechanism of ATs.

P3365 | BEDSIDE Comparison of natural follow-up of supraventricular tachycardia related-adverse events with supraventricular tachycardia ablation-related adverse events B. Brembilla-Perro1, J.M. Sellal1, V. Manenti1, A. Olivier1, T. Villermyn1, M. Benichou1, S. Dore1, C. De Chilliou1, N. Greider1, G. University of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France; Hospital Brabois of Nancy 4, CRM, Centre d'Investigations Cliniques 9501, Unite de Pediatrie, Vandoeuvre les Nancy, France.

Background: The indications of treatments remain difficult in some patients with supraventricular tachycardia (SVT), the purpose was to study jointly SVT-related adverse events (AE) and ablation-related complications. In particular, we intended to study the predictors of SVT-related AE's as well as its clinical significance by investigating its association with long-term mortality.

Methods: 1770 patients, aged 6 to 97, with either atrioventricular nodal reentrant tachycardia or orthodromic atrioventricular reciprocal tachycardia mediated by concealed accessory pathway consecutively referred for SVT workup were included.

Results: Tolerance was poor in 339 patients (19%). Major serious AE's occurred in 23 patients (1%), cardiac arrest or ventricular arrhythmia requiring cardiovascular (n=14) or collapses (n=9); remaining 316 patients presented with a poorly tolerated SVT (syncpe (n=236), acute coronary syndrome (n=67), heart failure/ rhythmic cardiomyopathy (n=21) or various AE (n=2)). Patients with AE were older, more frequently males, had more heart disease (HD) and diabetes than patients without AE. SVT rate and mechanism did not differ. In multivariable analysis, higher age, HD and necessity of isoproterenol to induce SVT were independently associated with a higher risk for SVT-related AE. In contrast, the presence of HD was the only factor retained when considering only major SVT-related AE (OR=6.50, CI: (2.83–14.91), p<0.001). During follow-up (2.75±3.4 years) 42 patients died. In multivariable analysis, major SVT-related AE remained significantly associated with death (HR=6.72, IC=(2.58–17.52), p<0.001) independently of age and the presence of HD. SVT ablation was performed in 1186 patients. Immediate major ablation complications including death, tamponade, complete AV block were less frequent than spontaneous major AE (0.4%) (5/1186 vs 23/1770). In multivariable analysis, only greater age (OR per one year increase in age=1.02, CI: (1.01–1.04), p<0.003) was independently associated with a higher risk of ablation complication.

Conclusions: SVT-related adverse events occurred in 19% of patients. However, life-threatening arrhythmias were rare (1%). Most of them are drug-related. Advanced age, male gender and presence of heart disease are predisposing factors for adverse events. Ablation, significantly associated with a lower risk of immediate major complications should be recommended in these patients.


Introduction: Remote magnetic navigation-guided ablation with 3-dimensional (3D) image integration can provide maximum benefit in patients with complex anatomy due to surgical correction of congenital heart disease. We reviewed our experience on patients with total cavopulmonary connections (TCPc) from July 2008 to December 2014.

Methods and results: A total of 24 pts with TCPc (15 m, mean age 27±5 yrs), included 8 tricuspid atresia (TA), 8 double inlet left ventricle (DILV), 3 double outlet right ventricle (DORV) with atrioventricular septal defect (AVSD) +/- atrial isomerism and common AV valve, one mitral atresia and one pulmonary atresia presented with sustained arrhythmias and were admitted for catheter ablation. For all patients, the procedure was carried out with CARTO RMT (either XP or 3) and 3D image integration using either CMR or CT and was performed completely remote-controlled without the switching back to conventional mapping & ablation or need for transesophageal punctures. Using femoral venous access, a multipolar catheter within TCPc served as a timing reference (Parahis). As a default, femoral arterial access was gained to allow retrograde access to the native atra via the socallic vein. A total of 32 arrhythmias were inducible (1:3/patient, range 1 to 4), 15 re-entrant (44%) including 4 typical flutter, 8 focal (24%), 3 AVNRT implicating twin AV node (all in patients with AVSD), 1 AVRT and 1 typical AVNRT. Four arrhythmias were non-sustained. The macro-reentrant (MR) tachycardia were mostly located in the native RA with ablation performed between the scar of the TCPc and the tricuspid annulus. Interestingly, 4 MR originated from the LA (2 roof, 1 mitral isthmus, 1 around right pulmonary veins). The majority of tachycardia originating from the TCPc were focal and were located at the superior aspect of the tunnel. Irrigated tip ablation was carried out with an acute success in 89% of cases, with two acute complications: a hemotorax due to anesthesiology needle insertion and one pseudonamolusomy. The mean procedure duration was 23±42 min, the mean RF time 21.7±15.1 min and the median fluoroscopy time 1.6 min.

Conclusion: Remote-controlled catheter ablation using 3D image integration in patients after TCPc surgery is feasible and can successfully treat a large variety of arrhythmia subtypes. Many patients present with more than one arrhythmia target, even in these complex procedures both procedure duration and fluorosity exposure are very acceptable.


Background: Linear lesions are crucial for the treatment of macro re-entry tachy-
cardias but assessment of conduction block can be challenging and time consuming.

Methods: A new rapid high-resolution mapping system was used to validate linear lesions in 7 patients. The system uses a mini basket catheter with 64 electrodes that is able to automatically create electroanatomical maps without manual annotation.

Results: Nine linear lesions (4 cavotricuspid isthmus-CTI lines, 2 roof lines and 3 mitral valve isthmus lines) were validated. Block was demonstrated as widely spaced double potentials along the line (A), activation block with differential pacing at the line (B). All this information was derived from 14 high-resolution maps post ablation consisting of median 4892 (1424–36071) points that were collected in 7.2 (1.7–38.6) min. A gap was identified in 5 lines (C, D) associated with atrial tachycardia in 3 patients (roof, mitral isthmus and CTI deflections). On all occasions ablation on the gap resulted in termination of the tachycardia and/or conduction block.

Conclusion: The new high-resolution mapping system was able to identify gaps and facilitate block of linear lesions in all patients.

P3368 | BEDSIDE

Short PQ interval on ECG in children: etiology of the phenomenon and its clinical significance

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Purpose: The aims of the study were to assess the atrioventricular (AV) conduction characteristics in children with short PQ interval on ECG, the risk of spontaneous tachycardia initiation and the danger of sudden cardiac death (SCD).

Methods: 300 children (210 (70%) boys and 90 (30%) girls) with short PQ interval on ECG without paroxysmal tachycardias were examined. The value of the PQ interval was under normal age-dependant limit and with absence of delta wave. Exclusion included: ECG, 24-hour Holter monitor, treadmill test, echocardiogram, transoesophageal pacing study (TEPS) and intravenous adenosine drug test.

Results: Mean age at the moment of the first examination was 13.3±3.6 years (3–17 years). Follow-up period was 1773.9 patients-years (7.3±4.8 years). 57 (13%) children were lost from follow-up. There were no SCD cases during the follow-up, and 1 child deceased secondary to oncological etiology.

Conclusions: Children with short PQ interval on ECG have a good prognosis:

1. They rarely develop paroxysmal tachycardia and are not at risk for SCD.
2. Short PQ interval is likely due to AV nodal conduction peculiarities.
3. It is associated with AVNRT. They are not at risk for SCD.

P3369 | BEDSIDE

Performance of the SA-VA difference to differentiate atrioventricular nodal reentrant tachycardia from orthodontic reentrant tachycardia in a large cohort of patients

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Background: Pacing stimulys and the last entrained atrial electrogram minus the tachycardia endocardial atrial electrogram (SA-VA interval) represents a simple diagnostic maneuver to distinguish between atrioventricular nodal reentrant tachycardia (AVNRT) and orthodontic reentrant tachycardia (ORT) during electrophysiological study. However, its usefulness has largely been studied in selected patients.

Methods: The new high-resolution mapping system was able to identify gaps and facilitate block of linear lesions in all patients.

Methods: Consecutive patients with inducible supraventricular tachycardia and successful entrainment through pacing trains from right ventricular apex during an electrophysiological study were prospectively included. Atrial tachycardias were excluded. The following intervals were calculated for each patient: SA-VA difference; his potential and atrial electrogram (HA) during entrainment minus HA during tachycardia (ΔHA); and the corrected return cycle.

Conclusions: The aim of this study was to prospectively evaluate the performance of the SA-VA difference against commonly used diagnostic maneuvers in a large cohort of consecutive patients.

Conclusions: The new high-resolution mapping system was able to identify gaps and facilitate block of linear lesions in all patients.
Introduction: Ablation of frequent premature ventricular complex (PVC) has shown to improve left ventricular ejection fraction (LVEF) in patients with LV dysfunction. The objective of this study is to evaluate if patients candidate for primary prevention (PP) implantable cardioverter-defibrillator (ICD) implant could remove this indication after PVC ablation.

Methods: Sixty-two (29 [47%] men, 53±13 years old, 10 ischemic heart disease] consecutive patients with PP indication for ICD implant and frequent PVC underwent PVC ablation. ICD implant was withheld and indication was re-evaluated at 6 and 12 months after ablation.

Results: LVEF progressively improved from 28±4% baseline to 41±11% and 42±12% at 6 and 12 months respectively (p<0.001). NYHA class improved during the follow-up from 2.3±0.5 baseline to 1.4±0.5 and 1.5±0.5 at 6 and 12 months respectively (p<0.001). Thirty-nine (63%) patients removed the indication for PP-ICD implantation during the follow-up (36 [92%]) of them within the first 6 months. Baseline PVC burden and a sustained successful ablation were independent predictors for removing the indication of ICD implantation. A cut-off value of 17% PVC burden had a sensitivity of 95% and a specificity of 91% for removing ICD indication after ablation. No sudden cardiac deaths or malignant ventricular arrhythmias were reported.

Conclusion: In patients with frequent PVC, ablation improves LVEF and allows removing the PP-ICD implant indication in the majority of them. To withhold the implant and a 6 months revaluation for ICD indication after ablation seems to removing the PP-ICD implant indication in the majority of them. To withhold the indication after ablation. No sudden cardiac deaths or malignant ventricular arrhythmias were reported.

P3374 | BEDSIDE
Catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy: insights from a French monocentric registry
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Background: Few early studies assessing mostly endocardial ablation of ventricular tachycardia (VT) among patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) have reported considerable VT recurrences during long-term follow-up. None of them have identified predictive factors of radiofrequency catheter ablation (RFA) efficacy.

Purpose: To determine whether RFA outcomes were similar to those previously reported and to investigate predictors of long-term benefit from RFA.

Methods and results: The study population comprised 32 patients (age 47±12 years, 28 male) with ARVC according to revised Task Force Criteria, who underwent a total of 55 RFA (53 endocardial, 2 combined epicardial and endocardial procedures) between 1999 and 2014. VT recurrences and VT burden were assessed either after each single procedure or after the whole RFA treatment. Over a mean follow-up of 74±51 months, VT-free survival rates after the 55 procedures were 37.1%, 21.6%, and 18.9% at 1, 5 and 10 years respectively. VT burden was significantly reduced after a single procedure (31 versus 16 VT episodes/year, p<0.02) or after the whole RFA treatment (15 versus 3 VT episodes/year, p<0.01). A total of 58±34 months, clinical response rates to the whole RFA treatment defined as freedom from sudden cardiac death from VT requiring hospitalization and from heart transplantation were 80.6%, 64.6%, and 59.2% at 1, 5 and 10 years respectively. Younger age, no amiodarone treatment, familial history of ARVC, no heart failure, inducible VT at RFA with isoproterenol and a lower burden of mappable VT before the first RFA were associated to clinical response. Conclusion: In these ARVC patients, RFA was mainly targeted at the endocardial surface and in accordance with published data VT recurrences were common. However VT burden and hospitalization for intractable VT were substantially reduced by RFA. Further studies are needed to determine the additive value of epicardial RFA in ARVC.

P3375 | BEDSIDE
Totally nonfluoroscopic approach for supraventricular and ventricular tachycardias ablation. Experience on more than 350 cases
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Purpose: To assess safety and effectiveness nonfluoroscopic approach of catheter ablation of tachyarrhythmias.

Methods: We prospectively included 353 patients in a study including patients with both ventricular and supraventricular tachyarrhythmias. In order to reduce potential harmful effect of fluoroscopy on physician and patient totally nonfluoroscopic approach was developed in our center for catheter ablation of tachyarrhythmias. All procedures were performed under local anesthesia using irrigated catheter with contact force capabilities. Additional diagnostic catheter was positioned into the coronary sinus ostium. Some procedures (ventricular ectopic beats) could be performed using ablation catheter only. Ablation parameters were made of the endocardial left ventricular (LV) surface, intracavitary structures including the valves and papillary muscles, and epicardial regions suggestive of ventricular scar. Complete voltage maps were then made and VT was induced and mapped with either pace-mapping when hemodynamically not tolerated or with activation and entrainment mapping when well tolerated. Bipolar voltage range used was 0.5–1.5 mV considered normal tissue. Voltage-assessed scar area was then compared against Sound assessed scar area.

Results: In 8 patients, complete LV maps were created. Average Sound scar area was 9.2±3.4% of the overall LV and voltage scar area was 8.2±3.1% (p<NS). Average depth of Sound scar was 0.7±0.2 cm. In 3 patients, the scar was oblong extending midmyocardially and/or epicardially with preserved endocardial tissue based on ICE at the border zones. Average depth of endocardial surface to Sound scar was 0.3±0.1 cm. In areas where endocardial surface to scar distance was <0.35 cm between scar and endocardial surface, bipolar voltage abnormality was seen. At depths >0.35 cm, voltage was preserved. In one patient in whom apical extent of the scar was significantly more epicardial (depth 0.6 cm), VT exit was mapped to the border zone of the Sound scar and could not be successfully ablated transendocardially. VT was successfully ablated epicardially with preserved endocardial to Sound scar distance >0.35 cm, bipolar voltage may not reflect closely scar and epicardial access may be needed.

Conclusion: Sound scar assessment is consistent with scar delineated by bipolar voltage mapping. In cases where scar extends more midmyocardially or epicardially with preserved endocardial to Sound scar distance >0.35 cm, bipolar voltage may not reflect closely scar and epicardial access may be needed.
Catheter ablation of supraventricular and ventricular arrhythmias

P3376 | BEDSIDE
The transseptal or transaortic approach for pediatric left sided accessory pathway ablation in era of NavX/Ensite? Comparison of four approaches
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The ablation of left sided accessory pathways (LS-AP) can be performed via transaortic (AO) or transseptal (TS) approach. Both technique can be achieved with non-fluoroscopic approach, however this significantly increases the procedure duration.

The aim was to assess the safety and feasibility of 4 strategies for LS-AP ablation: standard RTG+AO approach with AO (RTG+AO) or TS (RTG+TS) access and low fluoroscopic NavX/Ensite approach with AO (NX+AO) or TS (NX+TS) access. RTG was performed using 2-electrode catheter (COX), 20 pol. In the NavX group procedure was started from RA, CS and location His bundle. Aorta was reconstructed before passage to the left ventricle. Short fluoro was used during TS. We analyzed the procedural (duration of GA and procedure), X-ray (fluoroscopy (FT), air-kerma dose (D)) and ablation parameters (time to 1st AP, LA, AP) and the last application (1sAP LA, AP), number of applications (NAP), total RF duration (RF_T) and success rate. We included 176 pts with LS-AP (age 13.3±4.3 years, 73F) with SVT (76), WPW (96) or palpitations. In 118 pts the NavX was used. In 102 of them short fluoro was needed. Ablation was completed with AO in 109 and TS in 77 pts. There were 38 patients in RTG+AO group, 16 in RTG+TS, 58 in NX+AO and 56 in NX+TS. TS vs AO ablation: There were no difference in procedure duration (70±30 vs 73±32 min) between groups. There were lower D and LA in TS group (12±11 min. and 32±45 vs 66±168 mGy) as well as the time to 1sAP LA and AOR and lower NAP and RF (24±13 vs 31±13 min., 44±29 vs 53±28 min., 7.8±12 vs 10.1±9.4, 243±189 vs 274±232 sec.). The NavX significantly reduced the RTG parameters without change to ablation parameters. The shortest procedure duration was for NX+TS (65±23 min.), with shortest FT (5.4±4.3 minutes) lowest D (22±11 mGy). The RTG+TS approach was technique with shortest 1sAP and LA, with lowest NAP and RF and total RF_T (22±11 min., 36±21 min., 4.9±4.3 and 192±132 sec.). The success rate for RTG+AO was 86%, RTG+TS 86%, NX+AO=100% and NX+TS=94%.

Conclusions: Zero fluoroscopy approach for catheter ablation of tachyarrhythmias in pediatrics can be achieved with a high acute and long-term success. The use of 3D EAM allows to perform fluorless AP ablation in our population.

P3378 | BEDSIDE
Mechanism and catheter ablation of post-cardiac surgery atrial tachycardias
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Purpose: To summarize the characteristics of mechanism and catheter ablation of atrial tachycardia (AT) in patients with prior cardiac surgery.

Methods: Retrospectively, a total of 168 patients who underwent radiofrequency catheter ablation of AT between June 2002 and June 2014 were included. All patients received percutaneous transseptal approach, at which no history of AF were recorded. The assistance of CARTO electroanatomical mapping and entrainment mapping, the reentrant circuit, critical isthmus and origin were identified. After terminating the AT via ablation, complete block of ablation line were confirmed without reversion. After regular follow-up, recurrent patients underwent redo procedures.

Results: Prior cardiac surgery included repair of atrial septal defect (n=63), re-pair of ventricular septal defect (n=32), correction of tetrology of Fallot (n=12), mitral valve prosthesis placement (n=9), combined aortic and mitral valve replacement (n=1), tricuspid valve replacement (n=2), excision of left atrial myxomas (n=6), repair of ruptured aneurysm of the sinus of valsalva (n=3), excision of septal atrial lipoma (n=1), correction of Ebstein’s anomaly (n=2), Fontan procedure (n=1), Mustard procedure (n=1), Glenn procedure (n=1). A total of 222 ATs (217 macro-reentrant ATs, 5 focal ATs) were identified with cycle length 255±731ms. Macro-reentrant ATs were cavo-tricuspid isthmus (CTI) dependent atrial flutter (n=136, including 1 lower loop reentry), right atrial incisonal reentrant tachycardia (n=66), right atrial scar reentrant tachycardia (n=4), upper loop reentry (n=1), septal reentrant tachycardia (n=1), mitral annular reentry (n=7), left atrial scar reentry (n=2). Focal ATs originated from cristal terminalis (n=2), atrial septal defect (n=1), right atrium anterior wall (n=1) and roof of left atrium (n=1). Dual loop reentrant ATs were identified in 54 patients (32.1%), among which 51 were the combination of tricuspid atrial reentrant and incisional reentrant ATs. Immediate success was achieved in 164 patients (97.6%). During an average of 58 months’ follow up, 16 recurrent ATs (9.5%) were observed. 15 patients had redo procedures with CTI dependent atrial flutter in 9, incisional reentrant ATs in 4, right atrial multiple reentrant AT 1, in 14 atrial annular reentrant in 1. No serious complications were seen.

Conclusion: Macro-reentrant is the major mechanism of ATs in patients with prior cardiac surgery, among which the CTI dependent atrial flutter is the most common type. Dual loop reentrant ATs were not uncommon. Radiofrequency catheter ablation is an effective and safe approach.

P3379 | BEDSIDE
Electrocardiographic estimation of successful ablation site in patients with manifest postero septal accessory pathway
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Introduction: Postero septal accessory pathways (APs) have a wide distribution. For this reason, the mapping and radiofrequency ablation of such APs are difficult. Electrocardiographic (ECG) identification of AP location may guide the endocardial approach.

Methods: 137 consecutive patients with manifest preexcitation (QRS≥110 ms) and single AP located at the postero-septal region assessed by electrophysiologic study were retrospectively analysed (Table).

Results: Right endocardial postero septal APs were discriminated from left endo...

Clinical characteristics

<table>
<thead>
<tr>
<th>Total (n=137)</th>
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<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male gender (n, %)</td>
</tr>
<tr>
<td>Right endocardial PS AP (n, %)</td>
</tr>
<tr>
<td>Left endocardial PS AP (n, %)</td>
</tr>
<tr>
<td>Epicardial PS AP (n, %)</td>
</tr>
<tr>
<td>Cardiac disease (n, %)</td>
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<tr>
<td>Documented PSVT (n, %)</td>
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<tr>
<td>Preexcited AF (n, %)</td>
</tr>
<tr>
<td>Unexplained palpitation or syncope (n, %)</td>
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<tr>
<td>AF, atrial fibrillation; AP, accessory pathway; PS, postero-septal; PSVT, paroxysmal supraventricular tachycardia.</td>
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</table>
Conclusions: Delta wave polarity and R/S ratio in lead V1 are significant predictors of re-entrant atrial tachycardia (RART) recurrence after radiofrequency catheter ablation (RFCA) in adults with congenital heart disease. However, data on long-term outcome are scarce. This aim of the study was to determine the long-term outcome of RFCA for IART in adults with CHD and predictors of IART recurrences.

Methods: Seventy patients (41 male, mean age 40±12 years) undergoing RFCA of IART, which completed a follow-up of at least 1 year after the procedure, were studied. CHD was tetralogy of Fallot in 21 P (30%), atrial septal defect in 16 (23%), TGA in 10 (14%), pulmonary stenosis in 7 (10%), single ventricle physiology in 6 (9%) and others. Complete acute success was defined as termination of all IART circuits and partial success as termination of RART with at least one spontaneous recurrence. We analyzed the influence of clinical factors (age, sex, type of CHD, age at surgical repair, systemic-venous and pulmonary venous, pulmonary hypertension and right atrial dilatation), electrophysiological factors (type, number and cycle length of induced IART) and procedure related factors (complete or partial success, use of irrigated tip catheter and use of electroanatomic mapping system) in the development of IART recurrence.

Results: Complete acute success was obtained in 52 P (74%) and partial success in 10 (14%). Median follow-up was 53 months (IQR 18–104). IART recurrence was noted in 22 P (31%). A new RFCA was performed in 15 P. In 12 P the circuit of the clinical IART was the same as that observed during the first procedure. Thirteen P developed atrial fibrillation during the follow-up (7 paroxysmal, 2 persistent and 4 permanent). One patient died suddenly and 2 P underwent heart transplantation. An ICD was implanted in 3 P and a pacemaker in 4. At the end of follow-up, 61 P (87%) were in sinus rhythm. At multivariate analysis, the use of electroanatomic mapping (HR 0.4, IC 95% 0.2–0.65; p=0.001) and irrigated tip catheter (HR 0.49; IC 95% 0.32–0.75; p=0.001) was associated with the lack of recurrences whereas the presence of moderate to severe right atrial dilatation was independent predictor of IART recurrence (HR 1.7; IC 95% 1.13–2.55; p=0.001).

Conclusion: Despite recurrent IART and development of atrial fibrillation, sinus rhythm at the end of a long-term follow-up is present in the majority of P with IART undergoing RFCA. The use of electroanatomic mapping and irrigated tip catheter reduced the recurrence of IART after RFCA, whereas right atrial dilatation is associated with a higher risk of IART recurrence.

P3380 | BEDSIDE

Long-term outcome of intra-atrial reentrant tachycardia ablation in adults with congenital heart disease

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Purpose: Radiofrequency catheter ablation (RFCA) has evolved as a feasible curative treatment modality for intra-atrial reentrant tachycardia (IART) in adults with congenital heart disease (CHD). However, data on long-term outcome are scarce. The aim of this study was to determine the long-term outcome of RFCA for IART in adults with CHD and predictors of IART recurrences.

Methods: Seventy patients (41 male, mean age 40±12 years) undergoing RFCA of IART, which completed a follow-up of at least 1 year after the procedure, were studied. CHD was tetralogy of Fallot in 21 P (30%), atrial septal defect in 16 (23%), TGA in 10 (14%), pulmonary stenosis in 7 (10%), single ventricle physiology in 6 (9%) and others. Complete acute success was defined as termination of all IART circuits and partial success as termination of RART with at least one spontaneous recurrence. We analyzed the influence of clinical factors (age, sex, type of CHD, age at surgical repair, systemic-venous and pulmonary venous, pulmonary hypertension and right atrial dilatation), electrophysiological factors (type, number and cycle length of induced IART) and procedure related factors (complete or partial success, use of irrigated tip catheter and use of electroanatomic mapping system) in the development of IART recurrence.

Results: Complete acute success was obtained in 52 P (74%) and partial success in 10 (14%). Median follow-up was 53 months (IQR 18–104). IART recurrence was noted in 22 P (31%). A new RFCA was performed in 15 P. In 12 P the circuit of the clinical IART was the same as that observed during the first procedure. Thirteen P developed atrial fibrillation during the follow-up (7 paroxysmal, 2 persistent and 4 permanent). One patient died suddenly and 2 P underwent heart transplantation. An ICD was implanted in 3 P and a pacemaker in 4. At the end of follow-up, 61 P (87%) were in sinus rhythm. At multivariate analysis, the use of electroanatomic mapping (HR 0.4, IC 95% 0.2–0.65; p=0.001) and irrigated tip catheter (HR 0.49; IC 95% 0.32–0.75; p=0.001) was associated with the lack of recurrences whereas the presence of moderate to severe right atrial dilatation was independent predictor of IART recurrence (HR 1.7; IC 95% 1.13–2.55; p=0.001).

Conclusion: Despite recurrent IART and development of atrial fibrillation, sinus rhythm at the end of a long-term follow-up is present in the majority of P with IART undergoing RFCA. The use of electroanatomic mapping and irrigated tip catheter reduced the recurrence of IART after RFCA, whereas right atrial dilatation is associated with a higher risk of IART recurrence.

P3381 | BEDSIDE

The Historic - AF Trial: European, prospective multicenter study of hybrid thoracoscopic and transcatheter ablation of persistent atrial fibrillation

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Background: The treatment of persistent atrial fibrillation (AF) still represents a major challenge in current clinical practice; pharmacological as well as transcatheter strategies have shown limited efficacy at short-mid term. Novel, less-invasive surgical approaches for AF ablation demonstrated promising results especially when utilised along with catheter-based approaches in a hybrid fashion.

Purpose: The Hybrid Staged Operating Room and Interventional Catheter Ablation for Atrial Fibrillation trial is a prospective, multicenter study designed to evaluate the outcomes of staged endoscopic and transcatheter ablation in patients with stand-alone, long-standing persistent AF (LP AF). Primary end-point of the study was the clinical outcome and efficacy of the procedure defined as a freedom from AF >60% according to HRS criteria at 6, 12, 24 months follow-up.

Methods: From June 2012 to January 2015, 89 consecutive patients with LP AF were enrolled: all surgical procedures were performed via a minimally invasive thoracoscopic approach to perform an epicardial, left atrial isolation (“box” lesion set) with a uni-bipolar radiofrequency energy device. Achievement of at least complete atrioventricular node ablation was the clinical outcome and efficacy of the procedure defined as a freedom from AF >60% according to HRS criteria at 6, 12, 24 months follow-up.

Results: All surgical procedures were successfully performed without major perioperative complications. Postoperative PM implantation occurred in 2 pts (2.2%), while hospital mortality was 0%. A staged EP evaluation was required in 8 pts (8.9%) with AF recurrences following the 3 months blanking period: transcatheter ablation mostly targeted CFAEs and cavo-tricuspid isthmus isthmus. No ablation of the mitral isthmus was performed in the current study population. At 6 and 12 and 24 months follow-up a stable restoration of sinus rhythm was achieved in 90.7% (59/65), 88.8% (40/45) and in 93.3% (14/15) of patients respectively; acute success was 78.4% (51/65) at 6 months, 77.8% (35/45) at 12 months, 80% (12/15) at 24 months.

Conclusions: Early outcomes of the HISTORIC AF trial demonstrated that epicardial thoracoscopic and transcatheter left atrial isolation in patients with long-standing persistent AF is associated with excellent and stable results up to 24 months follow-up. Staged EP transcatheter ablation was required only in a minority of patients with AF recurrences.

P3382 | BEDSIDE

Feasibility and safety of uninterrupted peri-procedural apixaban administration in patients undergoing radiofrequency catheter ablation for atrial fibrillation: results from a multicenter study

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Introduction: Periprocedural anticoagulation management with uninterrupted
Methods: A total of 6015 patients with atrial fibrillation (AF) from the German ablation registry, who underwent first pulmonary vein isolation (PVI) between 2007 and 2011 were analysed. In a second step the effect of optimized radiation usage by filtering and collimation as well as the optimized use of 3D mapping system was evaluated in 526 consecutive patients with atrial fibrillation (AF) who underwent first pulmonary vein isolation (PVI) at a single center between 2007 and 2014.

Results: In the German ablation registry the median dose area product (DAP) for PVI was 35 Gy*cm² and the median DAP rate 1.3 Gy*cm²/min. The DAP decreased from 37 to 32 Gy*cm² whereas the DAP rate did not change between 2007 and 2011. In the single center group optimized radiation application and use of 3D mapping resulted in a continuous decrease of the DAP and DAP rate. The DAP was 67 Gy*cm² in 2007–2009 and decreased to 2 Gy*cm² in 2012–14. The DAP rate fell from 1.0 to 0.2 Gy*cm²/min. Similar radiation reduction could be observed in radiofrequency as well as cryoballoon ablation.

Conclusions: Currently the median radiation exposure during PVI in Germany is 35 Gy*cm². Optimized fluoroscopy can reduce safely the radiation dose to lower than 5 Gy*cm². Befitting novel expensive technologies for fluoroscopy reduction optimizing of conventional fluoroscopy is mandatory.

P3386 | BEDSIDE
Rivaroxaban a new alternative to warfarin for atrial fibrillation ablation: a meta-analysis of embolic and bleeding complications
J.S. Steinberg1.

Methods: A total of 11 studies (200 patients in each group) were included in the study. The average age was 65±9.9 years with 286 (71.5%) male and 334 (83.5%) patients having non paroxysmal AF. There were no differences in major (1% vs. 0.5%, p=1.0), minor (3.5% vs. 2.5%, p=0.56) and total bleeding complications (4.5% vs. 3.5%, p=0.43) between the apixaban and the warfarin group respectively. There were no statistically significant thromboembolic complications. All the dMRIs were negative for SCI in the apixaban group.

Conclusions: Uninterrupted apixaban administration in patients undergoing AF ablation appears to be feasible, and effective in preventing clinical and silent thromboembolic events without increasing the risk of major bleeding.
were unspecified off-line. Follow-up (without blanking period) consisted of clinical examination and Holter-ECG at 1, 3, and 6 months in all patients.

Results: Demographic, cardiovascular and anatomic characteristics were similar in both groups. Isplateral PVI was obtained in 100% of cases (n=200). Compared to FTI, FPTI was associated with a higher rate of first encirclement isolation (98% vs 95%, p < 0.001), a higher rate of PVI resistant to adenosine (97% vs 83%, p < 0.01), shorter mean RF time per ipsilateral circle (1068±231 s vs 1665±447 s, p < 0.0001) and shorter mean procedure time (143±27 min vs 194±242 min, p < 0.0001). At 6 months follow-up, 8/80 (16%) had AF recurrence in FTI group versus none in FPTI group (p < 0.0001). Repeat ablation was performed in 4 FTI patients. Analysis of the index procedure showed that PV reconnection (12 gaps) occurred where lesions did not overlap (n=7) or did not reach adequate depth (n=5).

Conclusion: Our findings suggest a benefit of FPTI in guiding CF-guided PVI. FPTI-guidance produced fast, complete and adenosine proof ipsilateral PV isolation occurred where lesions did not overlap (n=7) or did not reach adequate depth (n=5).

P3389 | SPOTLIGHT
Intra-operative mapping procedure for diagnosis of the substrate of atrial fibrillation
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Introduction: Multi-site, high resolution mapping of the atria can be used to identify the exact location of individual pulmonary vein ostia allowing percutaneous atrial ablation (AF).

Purpose: The goal of this study was to assess the feasibility and safety of a new high resolution epicardial mapping approach of the entire atria as a routine procedure during cardiac surgery.

Methods: Epicardial mapping (inter-electrode distance 1–2mm) was performed in 291 patients (218 male, age 66±11 yrs) undergoing elective surgery during si- nus rhythm (SR) and (induced) AF. Electrophysiological parameters within mapping quadrants covering the entire atrial epicardial surface were quantified and derived from unipolar conduction times of 1cm².

Results: AF was non-inducible in 36 patients. Hemodynamic parameters (mean arterial pressure (MAP), right atrial pressure (RA), BIS score, ST segment alterations) before and during SR mapping were comparable (P > 0.22). During AF a mean R-R interval of 10±10min (p < 0.01) was observed. Peak-to-peak amplitude of unipolar potentials were respectively 0.04±14.42ms and −0.01±0.53mV, reflecting stability of the mapping array. Complications were not observed.

Conclusion: Our novel intra-operative epicardial atrial mapping approach can be safely applied during both SR and AF. This mapping approach is the first technique allowing quantification of the arrhythmogenic substrate in the individual patient thereby taking the first step towards personalizing treatment of AF.

P3389 | BEDSIDE
Reduction of fluoroscopy exposure during atrial fibrillation ablation using a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping system
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Background: We explored whether a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping (F-EAM) system could result in a reduc- tion of overall fluoroscopy time and radiation doses during the whole procedure of atrial fibrillation (AF) ablation.

Methods and results: Eighty patients (44 men, age 63±10 years), who underwnter catheter ablation due to paroxysmal AF, were recruited consecutively in the current study. All patients were randomized 1:1 into two arms for AF ablation, using a conventional 3-dimensional electroanatomical mapping (EAM) system or the F-EAM system, respectively. Fluoroscopy time (10.42 [IQR 8.45–12.46] vs. 1.45 [IQR 1.05–2.22] min:sec; p < 0.001) and doses (2440 [IQR 1593–3091] vs 652 [IQR 326–1331] mgy cm²; p < 0.001) in the EAM group were statistically signifi- cantly greater than those in the F-EAM group. The majority of reduction of fluoro- scopy exposure was achieved after transseptal puncture, which was nearly zero-fluoroscopy exposure. In total, approximately 84% of fluoroscopy time and 73% of radiation doses have been reduced during AF ablation procedure using the F-EAM system, compared to using the conventional EAM system. However, procedure time did not differ significantly (1:39 [IQR 1:18–2:10] vs 1:37 [IQR 1:17–1:50] min; p=0.362).

Conclusions: AF catheter ablation using the novel fluoroscopy image integrated 3-dimensional electroanatomical mapping system was safe and resulted in a sig- nificant reduction of radiation exposure for patients and staff without complicating the workflow of the procedure. A near non-fluoroscopic catheter ablation could be performed without compromising efficacy and safety.

P3390 | BEDSIDE
Catheter ablation of atrial fibrillation: long-term outcome of radiofrequency catheter ablation for redo procedures after pulmonary vein isolation with the cryoballoon technique
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Catheter ablation has become the first line of therapy in patients with symp- tomatic, recurrent, drug-refractory atrial fibrillation. Cryoballoon ablation has been shown to be a safe and effective technique for pulmonary vein isolation. However, the arrhythmia recurrence rate is high after cryoballoon procedures and there are no established strategies for redo procedures in these patients. Therefore, we have summarized our experience with two different strategies for redo procedures using radiofrequency catheter ablation (including an analysis of pulmonary vein reconnection recovery patterns).

Methods: One hundred and ten patients (paroxysmal AF: 78 patients, persist- ent AF: 32 patients) had to undergo a redo procedure after initially successful circumferential PV isolation with the cryoballoon technique (Arctic Front Balloon, Cryocath/Medtronic). The redo ablation procedures were performed using a seg- mental approach or a circumferential ablation strategy (CARTO; Biosense Web- ster) depending on the intra-procedural findings.

Results: During the redo procedure, a mean number of 2.5 re-conducting PVs were detected (using a circular mapping catheter; 1: PV 15 patients, 2 PVs: 46 patients, 3 PVs: 36 patients, 4 PVs: 16 patients). A there was a slightly higher incidence of chronic PV reconnections compared to the left-sided PV ostia than to the right-sided PVs (LSPV: 28%, LIPV: 24%, RSPV: 22%, RIPV: 26%). Furthermore, sites of chronic PV reconnection were found more frequently in the inferior parts of the PVs. In 34 patients, a segmental approach was sufficient to eliminate the residual PV conduction because there were only a few recovered PV fibers (1–3 reconnected PVs; group A). In the remaining 16 patients, a circumferential ablation strategy was used because of a complete conduction of the PV-LA conduction of all four pulmonary veins (group B). All recovered PVs could be isolated successfully again. At 60-month follow-up, 70.0% of all patients were free from an arrhythmia recurrence (77/110 patients; group A: 66/94 patients (70.2%), group B: 11/16 patients (68.8%). There were no major complications in both groups.

Conclusions: In patients with an initial circumferential PVI using the cryoballoon technique, a repeat ablation procedure can be performed safely and effectively using radiofrequency catheter ablation. In most cases only a few re-conducting PV fibers were found and therefore, a segmental re-ablation approach seems to be sufficient in the majority of the patients.

P3391 | BEDSIDE
Cryoballoon ablation vs RF-catheterablation of persistent atrial fibrillation: influence of LA area on successrate
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Aims: The new Cryoballoon generation (CBA) shows superior short term suc- cess rates compared to the first Cryoballoon generation (CB) in the treatment of atrial fibrillation (AF). In this prospective observational study, we aim to examine the impact of the LA surface area regarding the mid term freedom from AF after CB vs. RF catheter ablation of persistent AF.

Methods: In total, 150 patients with symptomatic drug refractory persistent AF were controlled by matching analysis regarding age, gender, left atrial area (LA), CHA2DS2-VASc-Score, and history of AF: Seventyfive patients in each group. Pulmonary vein isolation (PVI) with CBA was performed as a single transseptal approach using second generation CryoSheath. Cryocatheters were used in conjunction with intraluminal multipolar mapping catheter. PVI with RF- catheter technique was performed as double transseptal Approach with with 3 D mapping systems. In group A wide atrial circumferential ablation was performed. PVI as ablation endpoint was defined elimination of all fragmented signals at PV antrum with verification of entrance- and exit- block. In 40 pts in group A and in 28 pts in CBA- group a roofline (in CBA- group with the Cryoballoon) was performed. Primary endpoint of this single-center pilot-study was first electrocardiogram-documented recurrence of AF (> 30 sec.). All patients received a follow-up every 3 month in our outpatient-clinic with 7 day holter ECG.

Results: There were no significant differences in baseline characteristics. The median procedure time lasted 2.9 (2.0/3.7) hours and fluoroscopy time was 22 (17/30) minutes in patients treated with RF vs 1.7 (1.3/2.2) hours and fluoroscopy time 20 (16/28) minutes in patients treated with CBA (p < 0.001 for procedure time, recovery of AF time was r.s.). Phrenic nerve palsy occurred in 1 patient in the CBA- Group and in one patient in the RF-group a post procedural stroke occurred. In all of the patients acute PVI could be achieved. After a median 2 year follow up time 13 pts/17.3% (CBA) vs 30 pts/ 40% (RF) reached primary endpoint (p < 0.019). The novel CBA shows superior 2 year success rate in LA area below 23cm² (p = 0.012) and non inferior in a LA area above 23cm² (p = 0.585) compared to RF-Ablation in pts suffering of persistent AF.

Conclusions: Novel CBA demonstrates favourable rates of clinical success with significantly enhancements to key procedural parameters in our cohort of patients. The novel CBA shows superior 2 year success rate in pts with LA area below 23cm² compared to RF- Ablation in pts suffering of persistent AF.
VKA. Significantly fewer complications rates, including no major bleeding, could be achieved in group 2. Results: 339 patients were included in the study (mean age 60 years, 68% males, 40% persistent AF), 252, 69, 20, and 4 patients underwent 2, 3, 4, and 5 procedures, respectively. In 90%, 64%, 42%, and 0%, reconnection of at least one PV was found in the second, third, fourth, and fifth procedure, respectively. Additional linear lesions sets were applied in case of inducible atrial tachycardia (AT), presence of low voltage areas during sinus rhythm, or persistent AF (until 2010). Follow-up included 7d-Holters at 3, 6, 12 months, and yearly thereafter. Conclusion: A significant proportion of patients remains free of AF/AT during long-term follow-up after one or more redo procedures. The rate of cumulated severe complications approximates 5%. PV reconnection is the major reason for the first redo procedure, whereas additional substrate modification is the major challenge in the second or more redo procedure. These findings are relevant for procedure planning as well as patient information.

P3393 | BEDSIDE
Periprocedural complication rates in respect of anticoagulation strategies in patients undergoing catheter ablation for persistent atrial fibrillation

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Introduction: The use of new oral anticoagulants (NOACs), uninterrupted (u/VKA) and interrupted vitamin-K-antagonists (VKA) are feasible and safe periprocedural anticoagulation (OAC) strategies in atrial fibrillation (AF) ablation. Comparative data about the influence of different OAC strategies on complications rates in ablation for persistent AF (persAF) are lacking. Therefore, we sought to determine complication rates among three OAC strategies in a persAF cohort. Methods: Patients undergoing persAF ablation procedures, including pulmonary vein isolation, ablation of complex fractionated electrograms and linear ablation lines, were included in this study. Depending on preprocedural OAC, three groups were defined: 1) NOACs (recommendation of last intake 48 hours before ablation), 2) u/VKA, 3) VKA with heparin-bridging. Results: From 2011 till 2014, 527 of 661 persistent AF ablation procedures complied with the defined groups (NOACs: n=195 (37%); NOAC-distribution: 55% rivaroxaban, 34% dabigatran, 11% apixaban, u/VKA n=166 (31.5%), VKA n=166 (31.5%). A significant difference of complications rates among the groups could be found (p=0.0231), with highest overall complication rates in the VKA-group (19.8%). The prevalence of pericardial tamponade was 0.5% (3/601), Compared to periprocedural OAC with VKAs (group 2 and 3) significantly fewer complications were detected in the NOAC-group (p<0.05). Additionally, no major bleeding occurred in the NOAC-group and complications rates did not differ between the various NOACs. Hemodynamically, irrelevant pericardial effusions were the most abundant minor complications with the highest rate in group 3 (16/38, p<0.05). No cerebrovascular event occurred. Conclusion: Comparing the three periprocedural OAC strategies in patients undergoing persAF ablation, significant differences among complications rates were found. Highest overall complications rates occurred in the group of interrupted VKAs. Significantly fewer complications rates, including no major bleeding, could be revealed in periprocedural OAC with NOACs.

P3394 | BEDSIDE
A novel, safe and effective modality of treating persistent atrial fibrillation: concomitant left atrial appendage electrical isolation and device occlusion

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Introduction: Left atrial appendage (LAA) electrical isolation is reported to improve persistent AF ablation outcomes. However, the subsequent loss of LAA mechanical function may increase thromboembolic risk. Purpose: We have recently demonstrated in a pre-clinical study that concomitant partial LAA electrical isolation (PI-LAAE) on sinus rhythm (SR) and occlusion is both safe and feasible, though procedural outcome in humans is unknown. Methods: 22 consecutive patients with longstanding persistent AF (mean age 68±7 years, 85% male, LA diameter 46±3 mm, AF duration 25±15 months, CHA2DS2-VASc score 3.1±1.2, HAS-BLED 2.5±1.1) were prospectively enrolled and underwent LAA isolation with irrigated radiofrequency ablation following a standard persistent AF ablation. Entrance and exit block were confirmed with intra- venous adenosine after 60 min. The LAA was then occluded with a Watchman Device. Device position and appropriate size were confirmed with transesophageal echocardiography (TEE) and computed tomography (CT) and at 9 months by repeat TEE. Rhythm assessments were performed at 3, 6 and 9 months. Outcomes were assessed against a matched (1:2 ratio, n=44), standard ablation control group. Results: All PVs and 20/22 (91%) LAAs were electrically isolated. Acute LAA reconnection occurred in 17/20 (85%). All were re-isolated. Ablation time was 90±23 min, including 33±28 min for LAA isolation. LAA occlusion was successful in all cases in whom LAA isolation was completed. TEE and CT at 45 days and TEE at 9 months confirmed satisfactory device positions and no periendocardial effusion. 1/20 (5%) had ≥5 mm requiring continued anticoagulation. 19/20 (95%) were able to stop warfarin. AF/atrial tachycardia (AT) free survival over 9 months was higher than in the control group (70% vs 43%, p=0.02). Conclusions: Persistent AF ablation, LAA electrical isolation and mechanical occlusion can be performed concomitantly in humans, with no clinically relevant displacement or mechanical erosion of the appendage. Compared to a standard procedure this appears to offer higher AF/AT free survival in the medium term. This novel technique can potentially improve success rates and obviate the need for chronic anticoagulation. Future studies should assess outcomes in randomized controlled settings.

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P3395 | BEDSIDE
Feasibility and safety of pulmonary vein and coronary sinus isolation in patients with atrial fibrillation and CROMT: results from a prospective database

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Background: Pulmonary vein isolation alone is associated with a low success rate of Turin, Division of Cardiology, Department of Medical Sciences, Turin, Italy; 2Cardinal Massaia Hospital, Division of Cardiology, Asti, Italy

Purpose: To evaluate if easily accessible clinical parameters may relate to the absence of LAA or LAA thrombi to identify patients who could potentially safely avoid TEE.

Methods: Data on consecutive patients undergoing TEE before AF ablation in two large-volume centers from January 2012 to September 2014 were collected. For each patient baseline clinical features, CHADS-VASc score, transesophageal echocardiography and presence or absence of thrombi at TEE were recorded. Exclusion criteria were presence of valvular, hypertrophic or dilated cardiomyopathy, previous heart surgery or an ejection fraction ≤35%.

Results: 688 patients were enrolled. Mean age was 59±11.0 years, 540 (79.1%) were males, 495 (71.9%) on sinus rhythm (SR) on admission, 210 (30.5%) had undergone at least one previous ablation and 578 (84%) presented CHADS-VASc score ≤2. Thrombi were encountered in 6 patients (0.9%); CHADS-VASc score ≥2 (p=0.024), SR on admission (p=0.006) and first ablation procedure (p=0.012) significantly related to the absence of thrombi. No patient with CHADS-VASc score ≥2 and SR on admission undergoing the first ablation presented thrombus at TEE (p=0.041).

Conclusion: A simple clinical assessment may help identify a conspicuous share of patients in which a reasonable benefit from pre-procedural TEE is not expected and who could be potentially safely spared from this resource consuming, scarcely tolerated exam and from its low but not negligible risk of complications.

ABALATION OF ATRIAL FIBRILLATION II

P3394 | BEDSIDE
May a clinical assessment predict left atrial appendage thrombi presence in patients undergoing atrial fibrillation transcatheater ablation? A large retrospective experience

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Background: Transesophageal echocardiography (TEE) is routinely performed before atrial fibrillation (AF) transcatheater ablation to exclude left atrial (LA) or left appendage (LAA) thrombi.

Purpose: To evaluate if easily accessible clinical parameters may relate to the absence of LA or LAA thrombi to identify patients who could potentially safely avoid TEE.

Methods: Data on consecutive patients undergoing TEE before AF ablation in two large-volume centers from January 2012 to September 2014 were collected. For each patient baseline clinical features, CHADS-VASc score, transesophageal echocardiography and presence or absence of thrombi at TEE were recorded. Exclusion criteria were presence of valvular, hypertrophic or dilated cardiomyopathy, previous heart surgery or an ejection fraction ≤35%.

Results: 688 patients were enrolled. Mean age was 59±11.0 years, 540 (79.1%) were males, 495 (71.9%) on sinus rhythm (SR) on admission, 210 (30.5%) had undergone at least one previous ablation and 578 (84%) presented CHADS-VASc score ≤2. Thrombi were encountered in 6 patients (0.9%); CHADS-VASc score ≥2 (p=0.024), SR on admission (p=0.006) and first ablation procedure (p=0.012) significantly related to the absence of thrombi. No patient with CHADS-VASc score ≥2 and SR on admission undergoing the first ablation presented thrombus at TEE (p=0.041).

Conclusion: A simple clinical assessment may help identify a conspicuous share of patients in which a reasonable benefit from pre-procedural TEE is not expected and who could be potentially safely spared from this resource consuming, scarcely tolerated exam and from its low but not negligible risk of complications.
rate in patients with AF and heart failure and heart failure. The isolation of the coronary sinus is often required in these patients in addition to PV to increase long term freedom from atrial arrhythmias. We sought to evaluate safety and feasibility of coronary sinus isolation in patients with AF and CRT-D undergoing atrial fibrillation ablation.

Methods: Data of 64 consecutive patients with heart failure and CRT-D undergoing PV and coronary sinus isolation were prospectively collected. In all cases ablation occurred at least 5 months after CRT-D implant. In all cases a duodecapolar catheter via the internal jugular vein to map the right atrium and the coronary sinus with the presence of the LV lead. In all cases we placed a 3.5 mm irrigated catheter was utilized for ablation. In all cases a challenge test with high dose of isoproterenol was used to detect non PV triggers. Procedural and long term outcome were collected and analyzed and compared with a control group of 64 patients matched for sex, age and AF type that had CRT-D and underwent PV alone ablation.

Results: The study population had a mean age of 63.9±13.5 years, 56% (88.2%) patients were male and all patients had non-paroxysmal AF. Mean LA size was 48.5±3.8 mm and moderate to severe left atrial scar was present in 67% of patients. Non-PV triggers were detected in 46 (75%) patients and in all of them coronary sinus triggered sustained and non sustained arrhythmies. The mean power utilized to isolate the coronary sinus was 33±2 watts. No LV lead dislodgement/damage occurred. One (1.6%) pericardial effusion not requiring surgical intervention occurred, after a 15.6±8 months follow up. 42 (65%) patients undergoing CS isolation were recurrence free while 13 (20%) were recurrence free in the control group (log-rank test, p-value <0.001).

Conclusions: Coronary sinus isolation in addition to PV is feasible and safe in patients with CRT-D and AF and does not damage the LV lead. In addition it increases the freedom from AF at follow up in patients with AF and heart failure.

P3397 | BEDSIDE
Meta-analysis of Outcome of Catheter Ablation of Persistent Atrial Fibrillation Using Termination Mode as a Procedural Endpoint
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Background: Catheter ablation of persistent atrial fibrillation (PsAF) is an established therapeutic option for rhythm control in symptomatic patients. The efficacy and safety of pulmonary vein isolation among patients with paroxysmal atrial fibrillation is a well-defined procedural endpoint. In patients with PsAF, there is no consensus regarding the best procedural end-point. There is no consensus if termination of persistent AF by ablation is associated with lower risk of recurrence arrhythmia compared to procedural failure to terminate AF with the need for electrical cardioversion at the end of the procedure. We performed a meta-analysis to assess safety and outcome of PsAF in patients based of AF termination mode (directly in SR, evolving into regular atrial tachycardia (AT) and subsequently into SR, after direct current (DC) cardioversion if AF persists after catheter ablation).

Methods and results: A systematic review was conducted in MEDLINE/PubMed and Cochrane Library. In this meta-analysis were included randomized controlled trials, non-RCT clinical trials and observational studies including patients with PsAF in which AF termination mode were detectable. Ablation using a stepwise ablation approach (pulmonary vein isolation, electrogram-guided and linear ablation) with the desired procedural endpoint being AF termination. Fourteen studies were selected, including 2786 patients. Mean follow-up was 25 (95% confidence Interval 12- 60) months. Overall complication rate was 3.9 (3.1-4.7%). Success rates were as follows. Overall (p <0.001): DC cardioversion, 23.5–26.2%; sinus rhythm 73.7%; sinus rhythm after AT, 67.0%. Single ablation: DC cardioversion, 21.4%; sinus rhythm, 68.8% (OR 1.53, 95% CI 1.07–2.20, P=0.02). Reablation: DC shock, 29.0%; sinus rhythm, 77.2% (OR 1.54, 95% CI 1.06–2.24, P=0.02). There are no differences in termination mode between sinus rhythm and evolving into regular AF and subsequently into SR.

Conclusions: In patients with PsAF, an ablation strategy aiming at AF termination is associated with freedom from arrhythmia recurrence in the majority of patients.

P3398 | BENCH
Anatomical and functional determinants of preferential rotor locations and stability in atrial fibrillation

Introduction: Rotors have been shown to drive atrial fibrillation (AF) and targeting these sites has emerged as an ablation strategy. However, factors that influence the localization of rotors in AF remain unclear. We experimentally assessed the relative importance of various anatomical, structural and functional factors in determining rotor locations in the left atrium.

Methods: Eight isolated, perfused canine left atrial preparations were optically mapped to elucidate AF induction. Rotor core locations were then analyzed using a novel computational algorithm for 80s of AF. The left atria were then divided into 9 regions for Cx43 immunohistochemistry and fibrillation analysis. Conduction and repolarization data from optical mapping, and Cx43 and fibrillation data were compared between regions with low and high rotor densities to assess for determinants of rotor locations.

Results: Rotors in AF locate preferentially to specific regions of the left atrium, though their distributions vary between hearts. Areas of high rotor densities are more frequently associated with pulmonary vein (PV) sites. There were no differences between Cx43 and fibrillation quantity/distribution between areas of high and low rotor density. There were slower AP upstrokes (p<0.05) and trends towards shorter APDs (APD75 at 300ms: 41±8 vs. 5.32±12ms, p=0.1) in areas with high incidences of rotors.

Conclusions: Preferential locations for AF rotors exist in the left atrium. Anatomical and functional factors, such as locations of PVs and spatial heterogeneities of repolarization and conduction respectively, are more important in determining rotor sites than structural factors such as regions of fibrosis. Identification of the determinants of preferential rotor sites can help optimize ablative therapy for AF.

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P3399 | BEDSIDE
One Shot technologies TO Pulmonary vein isolation (1STOP) project: basing standard clinical practice
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Background: Catheter ablation (CA) is used to treat asymptomatic atrial fibrillation (AF). “One Shot” (OS) catheters have been introduced to simplify CA procedure: the 2 most diffused approaches are cryoballoon ablation (CBA) and phased radiofrequency ablation (PRF).

Purpose: Aim of our research was evaluating in a large real world cohort, demographics, procedural data and outcomes.

Methods: 941 patients (76% male, median age 60) suffering from AF; underwent pulmonary veins (PVs) CA were prospectively followed; patient’s data were collected in ClinicalService® One Shot TO Pulmonary vein isolation (1STOP) project. The cohort was divided in 2 groups according to energy source used: 254 (84%) patients treated with CBA and 146 (16%) with PRF.

Results: 70% of patients were affected by paroxysmal, 26% by persistent and 4% by long standing AF; at time of procedure 65% of the population was affected by long standing AF. 4% of the cohort was treated as first line without trying any anti arrhythmic drugs (AADs); 31% underwent CA after only 1 AAD while the remaining patients tried ≥2 AADs. Procedural details and acute success rate are reported in table. Overall, procedural complications were 4%, without any major complications, as well, at 12 months, 80% of patients were free from AF; AF related symptoms decreased from 87% at baseline to 21%.

Conclusion: Among OS technologies, CBA is the most widespread ablation technique. Procedure times, acute and mid-term success rate as well as procedural related complications confirm that both technologies are safe and effective, with positive effect on AF related symptoms.

P3400 | BEDSIDE
Impact of continuous monitoring of the pulmonary venous pressure on the acute results of cryoablation in atrial fibrillation

Background: A new technical development, the cryoballoon ablation (cryoabla-
has been used to simplify pulmonary vein isolation (PVI) and reduce procedure times. However, the utility and safety of continuous pulmonary venous pressure monitoring during cryoablation has not been clarified.

Methods: This study included 20 consecutive patients and 80 pulmonary veins, with drug-refractory paroxysmal atrial fibrillation. All patients underwent PVI with cryoablation after assessing the PV size and geometry by computer tomography. All cryoablation procedures were performed with a 28 mm cryoballoon (Medtronic, Inc). The PV pressure waveform was continuously monitored to determine whether a complete occlusion with the cryoballoon was achieved (Figure), Two 180 sec applications per freeze were given for every PV unless an excess drop in the intracardiac temperature or right phrenic nerve palsy occurred. If the PV potentials still remained, an extra application was delivered to that PV.

Results: In 78 (95%) of 80 PVs, complete occlusion of the PV by the cryoballoon was easily confirmed by pressure monitoring during the inflation, and the PVs were successfully isolated with the cryoballoon. However, in the remaining 4 PVs, all of which were right inferior PVs, a complete occlusion pattern could not be obtained during pressure monitoring. Selective PV angiography through the distal portion of the cryoballoon disclosed incomplete occlusion of the PVs, and finally, additional catheter ablation was required for a complete isolation of those 4 PVs.

Conclusions: The continual pressure monitoring of targeted PVs during cryoablation is feasible and safe. The complete occlusion pattern of the pressure monitoring during cryoablation predicts an acute success for the PVI.

P3401 | BEDSIDE
Phased array pulmonary vein isolation vs radiofrequency catheter ablation for atrial fibrillation: a non-inferiority systematic review and meta-analysis
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Background: Pulmonary vein isolation using radiofrequency (RF) catheter ablation is the cornerstone for atrial fibrillation (AF) ablation. Newer RF energy delivery methods have become recently available. However, limited information is available regarding the non-inferiority efficacy and safety boundaries of duty-phased radiofrequency AF catheter ablation.

Objective: To conduct a meta-analysis of randomized clinical trials (RCTs) comparing the efficacy and safety of duty-cycled RF ablation using the circular multi-electrode catheter (MEA) to conventional RF catheter pulmonary vein isolation (cPVI) in patients with primarily paroxysmal/persistent AF.

Methods: Two independent investigators searched MEDLINE, EMBASE, CENTRAL and clinicaltrials.gov databases for RCTs in patients with PAF that compared MEA vs cPVI. The primary outcome was to determine whether MEA was non-inferior to cPVI, regarding Atrial tachycardia (AT) recurrence. We selected an absolute risk difference of 5% with a two-sided 5% alpha error as threshold for non-inferiority. Procedure time, fluoroscopy time and potential technique-related adverse events (cardiac tamponade, vascular complications, pulmonary vein stenosis and stroke) were evaluated as well. Fixed effects were used unless there was significant heterogeneity (I2 > 50%). Cochrane tool for risk of bias was used for study quality assessment and GRADE for outcome specific quality assessment.

Results: Four RCTs were reviewed for an overall of 830 patients included of which, 709 (85.4%) had paroxysmal AF and 121 (14.6%) persistent AF. The absolute risk difference of 5% with a two-sided 5% alpha error as threshold for non-inferiority. Procedure time, fluoroscopy time and potential technique-related adverse events (cardiac tamponade, vascular complications, pulmonary vein stenosis and stroke) were evaluated as well. Fixed effects were used unless there was significant heterogeneity (I2 > 50%). Cochrane tool for risk of bias was used for study quality assessment and GRADE for outcome specific quality assessment.

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Discussion: MEA compared with cPVI was non-inferior and appears to be superior to conventional RF ablation of PAF with comparable acute procedural complications. Therefore, it is feasible and safe during CBA. The CMAP amplitude does not vary during expiration and is not superimposed on the ECG using PNP. The assessment of an optimal cut-off to discontinue CBA needs further investigations. CMAP monitoring should be used in daily routine to prevent permanent PNP.

P3402 | BEDSIDE
Prevention of phrenic nerve palsy during cryoballoon ablation in patients with atrial fibrillation - comparison between percutaneous and endovascular electromagnetic monitoring technique
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Introduction: Right phrenic nerve palsy (PNP) is the most common complication of cryoballoon ablation (CBA). Diaphragmatic electromyography (DE) can predict PNP. However, techniques have underperformed. The aim was to compare the efficacy and safety of a percutaneous and an endovascular monitoring technique (PMT, EMT).

Methods: The study includes 21 patients (13 males). The CBA was performed with a tumescent and energized cryoballoon. During right atrial cryoballoon ablation, the pulmonary vein ablation, the PN was paced at 60 beats per minute. The diaphragmatic compound motor action potential (CMAP) amplitude was recorded simultaneously using a PMT and EMT. To record right diaphragmatic CMAPs percutaneously, 2 standard surface electrodes were positioned on the thorax and spaced 16 cm apart, one 5 cm above the xiphoid process and the second along the right costal margin. The endovascular measurement was performed via a quadrupolar catheter positioned in a subdiaphragmatic hepatic vein. The CMAPs were recorded continuously during CBA. If a 30% drop in CMAP amplitude was observed, second-generation ablation was discontinued.

Results: Reliable recording of CMAP amplitude was feasible in 20 patients. At any 1 patient CMAP recording could not be achieved using PMT and EMT, respectively. PNP failed in one obese patient due to inappropriate quality of CMAP signals. EMT could be applied in another patient as a result of failed catheter placement in the hepatic veins. The mean values of CMAP amplitudes were comparable between PMT and EMT (1.10 ± 0.70 mV vs 0.97 ± 0.76 mV, P = NS). In contrast the CMAP amplitude variation was significantly different between PMT vs. EMT. CBA was associated with lower PNP of PMT and EMT. Nevertheless 1 patient suffered from PNP, however recovered completely within 2 days. The second patient had no impairment of diaphragmatic movement. No complication related to phrenic nerve monitoring were observed.

Conclusions: Recording of CMAPs with PMT and EMT is feasible and safe during CBA. The CMAP amplitude does not vary during expiration and is not superimposed on the ECG using PNP. The assessment of an optimal cut-off to discontinue CBA needs further investigations. CMAP monitoring should be used in daily routine to prevent permanent PNP.
P3404 | BEDSIDE
Voltage guided pulmonary vein isolation: preliminary results of short term outcome
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Maximum voltage guided ablation has been described to identifying putative muscle bundles in the cavitricuspid isthmus. Similarly, we postulated that voltage mapping of pulmonary veins and their respective antral regions will help identify critical sites to achieve PV isolation.

Aim: To investigate the intra procedural efficacy of voltage guided CPVA strategy with short-term follow-up.

Methods: We included 33 age-sex-matched cohorts from our centre that underwent PV procedure. Thirteen patients, (6 female) had voltage guided PVI where RF started at the highest voltage area recorded at the antrum. This group was randomized to 20 controls, (7 female) which underwent circumferential pulmonarve (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI) isolation using PVI (PVI). All patients age and sex matched with each control group.

Results: There were 33 patients, (mean age 59±16 years; 13 female; left atrium 63±21 mm; left ventricular ejection fraction 61±6%). A mean of 54±12 voltage points were recorded. The mean of maximum voltage around the antrum was 3±1.1 areas. Mean voltages for RPVs and LPVs were 1.7±0.1 and 1.9±0.2 respectively, while RF was (40.9±17.4 vs. 48.1±15.5), Fluro (29.2±0.4 vs. 33.6±17.7) and procedure times (233.8±36.1 vs 248.8±53.6) for the voltage and non-voltage groups respectively.

Conclusion: A voltage guided CPVA strategy was highly efficacious in identifying critical points for PV isolation and short term freedom from AF recurrence has been promising. Further studies are required to validate this approach particularly if coupled with catheter contact sensing technology.

P3405 | BEDSIDE
Ablation of atrial fibrillation II / Ablation of atrial fibrillation III
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Background: The anatomic relationship between left atrium (LA) and lung tissue (LT) has not been characterised. This may be of relevance to patients undergoing radiofrequency ablation (RFA) for Atrial Fibrillation (AF).

Purpose: To describe the relationship of LT to LA in a cohort of patients undergoing RFA for AF.

Methods: We analyzed clinical data and CT Coronary Angiograms (CTCA) of 100 patients who underwent CTCA prior to RFA for AF. We measured distances between LT and LA regions commonly targeted during RFA of AF using Osiris DICOM viewer.

Results: 100 patients (71 male, age 60±8 years, 46% paroxysmal, mean LA axial area 255±5.5 cm²); 23% with LA enlargement, 33% with hypertension, 24% with structural heart disease, 15% with obstructive coronary disease and 0% with obstructive lung disease. The right PVs (RPVs) but not the left PVs (LPVs) were closely apposed to LT. The endocardium of posterior RPV antrum was <5 mm from LT in 94%, minimum distance from LA endocardium to LT was 1.25±0.7 mm. The right inferior PV ostium was <5 mm from LT in 94% (mean distance 2.4±0.8 mm). The right superior PV ostium was <5 mm from RLL in 29% (mean distance 3.7±0.9 mm). LT was <5 mm from the carina between RPVs in 83% (mean distance 3±1 mm). The mitral isthmus was <5 mm from LT in 5%. The LPV antrum was <5 mm from LT in just 3% as the constant presence of the descending thoracic aorta close to the posterior LPV antrum prevented close contact with LT in most patients. The bronchi were <5 mm from LA in 5 patients.

P3406 | BEDSIDE
Relationship of lungs to left atrium in patients undergoing atrial fibrillation ablation
J.A. Walsh1, D. Keane2, G.J. Fahy1. 1Cork University Hospital, Cork, Ireland; 2St Vincent’s University Hospital, Dublin, Ireland

Background: The anatomic relationship between LA and lung tissue (LT) has not been characterised. This may be of relevance to patients undergoing radiofrequency ablation (RFA) for Atrial Fibrillation (AF).

Purpose: To describe the relationship of LT to LA in a cohort of patients undergoing RFA for AF.

Methods: We analyzed clinical data and CT Coronary Angiograms (CTCA) of 100 patients who underwent CTCA prior to RFA for AF. We measured distances between LT and LA regions commonly targeted during RFA of AF using Osiris DICOM viewer.

Results: 100 patients (71 male, age 60±8 years, 46% paroxysmal, mean LA axial area 255±5.5 cm²); 23% with LA enlargement, 33% with hypertension, 24% with structural heart disease, 15% with obstructive coronary disease and 0% with obstructive lung disease. The right PVs (RPVs) but not the left PVs (LPVs) were closely apposed to LT. The endocardium of posterior RPV antrum was <5 mm from LT in 94%, minimum distance from LA endocardium to LT was 1.25±0.7 mm. The right inferior PV ostium was <5 mm from LT in 94% (mean distance 2.4±0.8 mm). The right superior PV ostium was <5 mm from RLL in 29% (mean distance 3.7±0.9 mm). LT was <5 mm from the carina between RPVs in 83% (mean distance 3±1 mm). The mitral isthmus was <5 mm from LT in 5%. The LPV antrum was <5 mm from LT in just 3% as the constant presence of the descending thoracic aorta close to the posterior LPV antrum prevented close contact with LT in most patients. The bronchi were <5 mm from LA in 5 patients.

P3407 | BEDSIDE
Loss of pace capture on the ablation line for pulmonary vein isolation can improve the clinical outcome of catheter ablation for atrial fibrillation
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Background: Reconnections of isolated pulmonary vein (PV) are the major cause of recurrence after ablation for atrial fibrillation (AF). In this study, we investigated the possibility that additional ablation on the ablation lines for PV isolation (PVI) to obtain unexcitability can reduce the reconnections of isolated PVs (PVRs) and improve clinical outcome of AF ablation.

Methods: A total of 120 patients who received initial ablation for AF including 46 non-paroxysmal AF (38%) were participated in this study. Patient population was divided into two group; pace-and-ablate group (n=60) and control group (n=60). Patients in pace-and-ablate group received pace-and-ablate procedure without additional ablation on the ablation lines for PVI. In the both groups, we routinely checked the presence or absence of time-dependent PVRs more than 20 minute after the last ablation for PVI or pace-and-ablate procedure, and ablated to eliminate them. And then, we also checked that of ATP-dependent PVR by injecting 0.4mg/kg of adenosine triphosphated and tried to eliminate all these dormant conductions. We set a blanking period for 3-month, investigated the initial clinical outcome 6 month after procedure, and compared it between the groups.

Results: PVRs were less frequent in pace-and-ablate group than in control group significantly (30% vs. 57%, p=0.0057). All the PVRs except ATP-dependent one in pace-and-ablate group were successfully eliminated. Initial clinical outcome was significantly better in pace-and-ablate group than in control group (recurrence free rate: pace-and-ablate group vs. control group, 86% vs. 72%, p=0.033).

Conclusion: The pace-and-ablate procedure after PVI could reduce the incidence of PVR during procedure, and could improve the initial clinical outcome even in AF patients who received ablation of time-dependent and ATP-dependent PVRs after PVI.
Comparison of pulmonary vein isolation guided by remote magnetic navigation in patients with paroxysmal atrial fibrillation using an irrigated gold-tip and a classical irrigated catheter

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Aims: The present case–control study seeks the efficacy and the safety of remote magnetic navigation guided ablation using the irrigated gold-tip and a classical irrigated in patients with paroxysmal atrial fibrillation and normal structural heart.

Methods: Patients with PAF refractory to antiarrhythmic drug, normal structural heart and no previous pulmonary vein isolation (PVI) were included. The procedures were performed using the Stereotaxis Niobe II. 40 patients were ablated using theNaviiStar RMT ThermoCool catheter guided by CARTO mapping and 30 with the Trignum Flux Gold-tip catheter guided by the EnSite Velocity system. Reconnection of veins was checked with Adenosine after all 4 veins were isolated.

Results: This study includes 70 patients (64% males) with a mean age 62±9.8 years. The 2 groups were comparable regarding the left atrium diameter, left atrium appendage velocity, left ventricular ejection fraction, E velocity and A velocity. Complication rate did not differ significantly between groups. Reconnection of veins after Adenosine was 20% vs. 26.6% (P=0.24). Success rate after a pre-treated subgroup was 96% (P=0.30). Index procedure time (135,71±46,17 vs 182,89±68,46 min, P<0.006) and radiofrequency application time (424,5±59,54 vs 54,32±19,49 min, P=0.08) were longer in the Trignum Flux CA group; however, the respective total fluoroscopy time were similar (18,74±10,26 vs 16,74±10,26 min, P=0.48).

Conclusions: RNM guided ablation of PAF with the Trignum Flux catheter is as efficient and safe as with the Thermocool Navistar catheter, although it requires longer total procedural time.

A combination of epicardial and endocardial catheter ablation approaches to atrial arrhythmias after multiple failed atrial fibrillation ablations

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Background: To explore whether a combination of endocardial and epicardial (endo/epi) RFCA could change outcome in patients (pts), who suffered from recurrences of atrial fibrillation (AF) after multiple endo RFCA of AF.

Methods: 21 pts (11 men, age 63±9 years), who had a recurrence of AA and undergone multiple RFCA (median 2, range 2–6) due to AF, were recruited in a prospective trial. Bidirectional block was confirmed with an irrigated tip catheter. Ablation was performed to re-establish a bidirectional block of the ablation line.

Results: Endo RFCA were performed in 11 pts (52%), Sm RFCA was performed in 19 pts (90%), including: endo/epi - 17 septal lines (SL), 15 roof lines, 9 anterior lines, 9 mitral isthmus lines; only endo - 12 endo posterior line (n=12) and 3 right atrial septal lines between SVC and FC; only epi - 17 in epi interatrial groove (IAG). Except 1 true focal AT, 17 macroreentrant tachycardias (MRTs) were eliminated, including 9 CTI-dependent MRTs and 7 MRTs from LA. In addition, 3 localized RF were performed from RAA/LAA/CS. In case of spontaneous or induced AF, block was confirmed with Adenosine after all 4 veins were isolated. Radiofrequency (RF) lesions were created with the Trignum Flux Gold-tip catheter guided by the Ensite Velocity system. Reconnection of veins was checked with Adenosine after all 4 veins were isolated.

Conclusions: The combination of endo/epi RFCA aiming to recurrence of AA after multiple failed AA ablations may change the recurrences of AA, although the true bidirectional block of SL or AA originated from IAG or epi LA roof. This combined approach was effective for pts with severe atrial myopathy.

Chronic hemodynamics is a predictor of procedural bleeding complications and ischemic stroke in patients undergoing catheter ablation of atrial fibrillation

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Background: Some earlier reports have suggested pulmonary vein isolation (PVI) by catheter ablation can cure atrial fibrillation (AF) in patients on chronic hemodialysis (HD). However, because advanced renal failure is often linked with extensive systemic vascular diseases, patients on chronic HD may be more susceptible to serious peri-procedural complications of AF ablation than others.

Aims: To evaluate the incidence and predictors of ischemic stroke and bleeding complications in patients undergoing AF ablation while on chronic HD.

Methods: Japan Heart Rhythm Society (JHRS) and Japan Society of Electrophysiology (EP) centers to register the data of patients who underwent catheter ablation for AF in designated four months from 2011 to 2013. In this report, we assessed the incidence and predictors of ischemic stroke and bleeding complications. The JHRS requested electrocardiography and echocardiography in all patients, who underwent AF ablation for AF. In this sub-study, we included 59 patients on HD (8.5%), who were enrolled in a prospective registry of 4084 patients with AF at 107 Japanese AF ablation centers.

Results: There were 24 events in 123 patients (4.8%; 12.6% ischemic stroke, 1.6% bleeds). Independent predictors of ischemic stroke were: previous HD (HR: 5.09 [95% CI: 2.85–9.11], p<0.005) and duration of HD (HR: 1.81 per year; 95% CI: 1.29–2.52, p<0.005). Independent predictors of bleeding complications were: history of stroke (HR: 3.00 [95% CI: 1.22–7.28], p<0.02), structural heart disease (HR: 2.07 [95% CI: 1.19–3.62], p<0.006), and transthoracic echocardiography shows a left atrial appendage area >35 cm² (HR: 2.26 [95% CI: 1.13–4.52], p<0.02).

Conclusions: HD increases the risk of AF ablation complications. In patients with AF and previous HD, anticoagulant therapy and periprocedural management of bleeding complications are important to avoid ischemic stroke and bleeding complications.
for AF recurrence, while the annual rate of cardiovascular hospitalization was significantly lower in PAF vs PER (Rate≠100/pts years respectively: 0.4 vs 5.6, IRR: 15.3 (95% CI 7.3–31.8) p<0.001)

Conclusions: Cryoablation approach is acutely safe and efficient both in PER and PAF patients. However, a lower incidence of AF recurrence was documented in PAF at the mid-term follow up thus, suggesting that a more diffuse ablation strategy and the timing of cryoablation have an impact on the clinical outcome.

P3412 | BEDSIDE
Comparison between multi electrodes mapping with the flower catheter and point-by-point technique for multiple atrial tachycardias in the context of atrial fibrillation ablation

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Introduction: Activation mapping can be challenging and time-consuming in case of multiple atrial tachycardias (ATs). We report our experience with multi-electrodes mapping using the flower catheter PTY (Pentamay, Biosense) for ATs in the context of atrial fibrillation (AF) ablation.

Methods: All procedures using the PTY for AF, after or during persistent AF ablation were analyzed. A control group of patients (pts) with AF using the point-by-point technique (PBP) was used for comparison of mapping times. Procedure time indexed to the number of ATs per patient (IPT) and fluoroscopy time were also assessed.

Results: 16 pts (62.8±11 y) with a mean number of 2.1 ATs per patient, were included. 44±520 points within 26±14 min were acquired per AT in the PTY group and 42±18 points (p=0.0001) within 33±25 min (p=0.04) in the PBP group (n=16; 63.6±14 y; 1.42 ATs per patient). Owing to far better mapping resolution, all AT's isticnesses (n=25) were easily identified and ablated in the PTY (100%) versus in only 19/22 (86%) in the PBP group. IPT and fluoroscopy times were not significantly different between the two groups: respectively 170±84 min versus 188±68 min (p=0.14) in the PBP group and 13,1±8 min versus 15,1±10 min (p=0.56) in the PBP group. 2 patients had a recurrence in each group after a mean follow-up of 6 months.

Conclusion: Multi Electrodes Mapping is acutely faster and more accurate in multiple ATs ablation when compared to the PBP technique.

P3413 | BEDSIDE
Remote magnetic catheter navigation versus conventional ablation in atrial fibrillation ablation: comparing efficacy, safety and fluoroscopic time


Background: Percutaneous transcatheter radiofrequency ablation with remote controlled magnetic navigation has been shown to be effective and safe in complex arrhythmia ablations and allows reduction in fluoroscopy time.

Aims: We compare the acute success rate, acute complication rate, fluoroscopy and procedural times between remote controlled magnetic navigation guided ablation versus conventional catheter ablation of atrial fibrillation.

Methods and results: Catheter ablation for atrial fibrillation was performed utilizing remote magnetic controlled navigation in 208 consecutive patients and manually in 259 patients. Acute procedural success was seen in 99.5% (207 of 208) of patients who underwent remote magnetic navigation ablation compared to 96.9% (251 of 259) in the manual catheter ablation group (p=0.039). Comparing catheter related complications, there was a non-statistically significant trend towards lower catheter/ablation related complications in the remote navigation ablation group of 0.5% (1 of 208) patients vs 1.2% (3 of 259) in the manual ablation group (p=0.398). Fluoroscopy time was significantly shorter in the remote navigation group compared to the manual ablation group with mean±SD times of 54.4±30.2 mins and 77.7±31.4 mins respectively (p<0.001) but total procedural time was longer 280.2±74.4 mins versus 213.1±64.75 mins in the manual ablation group (p<0.001).

Conclusions: Remote magnetic navigation use in radiofrequency ablation of atrial fibrillation when compared to conventional manual ablation techniques appears to be similarly efficacious, has a very low risk of complications and reduces radiation exposure to both patient and physician.

P3414 | BEDSIDE
Monitoring of sedation depth with bispectral index during ablation of atrial fibrillation - are we sedating too deep?


Introduction: Procedural safety of propofol sedation administered for catheter ablation (CA) of atrial fibrillation (AF) has been demonstrated but remains challenging in some patients. Bispectral Index (BIS) monitoring allows measurement of sedation depth with a BIS index ≤45 which has been found to increase anesthesis related risk.

Purpose: We sought to determine the sedation levels with BIS monitoring in propofol sedation during AF ablation.

Methods: 60 consecutive patients (pts) (mean age 63±11 years, 42 male (69%), BMI 27.6±4.4 kg/m², mean CHA2DS2-VASc- Score 2±1.5) undergoing AF ablation were included. Deep sedation was performed with propofol (20 mg/ml). Fentanyl and midazolam bolus were administered at operator’s decision during the procedure. Pts were monitored with pulse oximetry, noninvasive blood pressure, continuous ECG and BIS monitoring (BIS VISTA™, Covidien, Mansfeld, MA, USA). BIS index was measured continuously every minute during the procedure from the beginning of sedation to extraction of sheaths and was blinded to the operator and staff. Low BIS levels were defined as an index ≤45 over a minimum of 3 consecutive minutes.

Results: Propofol was commenced in all patients at a mean infusion rate of 0.096±0.044 mg/kg/min. Additional fentanyl (mean 0.04±0.02 mg) and midazo-lam (mean 0.5±1.2 mg) bolus were administered. Mean procedural duration was 138.9±61.0 minutes. Mean BIS level was 48.4±7.7. Cumulative percentage of low BIS ≤45 (mean 36.8±7.0) was found in 44.0±28.8% of procedural time. No case of respiratory depression occurred requiring assisted ventilation occurred. Persist-ent hypotension resulted in propofol cessation and switch to midazolam/fentanyl in 1 patient (1%).

Conclusions: The use of BIS monitoring provides improved information on sedation depth during CA for AF. In more than 40% of procedural time, patients showed BIS levels ≤45 indicating a deep narcotic state and deeper sedation levels than recommended. Whether BIS guided monitoring during AF ablation procedures improves procedural outcome needs to be investigated.

P3415 | BENCH
Randomized comparison of catheter ablation of atrial fibrillation with or without non-fluorescense sensor-based catheter navigation

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Introduction: Nonfluorescense sensor tracking (NFSFT) within precoiled x-ray loops offers the potential to perform catheter ablation of atrial fibrillation of AF almost free from fluoroscopy use.

Purpose: Randomized comparison of standard AF ablation with or without NFSFT application.

Methods: Patients with AF were randomized into two groups before scheduled radiofrequency ablation: (1) catheter navigation using NFSFT together with established mapping systems and fluoroscopy, (2) control group with standard electroanatomic mapping system and fluoroscopy alone. Procedures were performed in the same lab by 2 experienced operators altogether. Moreover, the same strategies (circumferential pulmonary vein isolation followed by voltage mapping targeting substrates modification) and ablation catheters were applied.

Results: A total of 80 patients (48 men, mean age 60 years, 44 patients with paroxysmal AF) were equally randomized between both groups. Clinical parameters between both groups were similar. Procedural parameters and preliminary 6-months follow-up data (freedom from any atrial tachycardia or AF ≤30 sec) can be derived from table.

Remote Navigation vs Conventional RFA

<table>
<thead>
<tr>
<th>Patient numbers</th>
<th>Random navigation group</th>
<th>Conventional group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute procedural success rate among all patients (%)</td>
<td>99.5% (207/208)</td>
<td>96.9% (251/259)</td>
<td>0.039</td>
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<tr>
<td>Acute procedural success rate excluding patients with abandoned procedures (%)</td>
<td>100% (207/207)</td>
<td>98.0% (251/256)</td>
<td>0.051</td>
</tr>
<tr>
<td>Procedural time (min)</td>
<td>280.2±74.4</td>
<td>213.1±64.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>54.4±30.2</td>
<td>77.7±31.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Percentage procedure time using fluoroscopy</td>
<td>19.1±6.3</td>
<td>36.8±9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rate of all complications (%)</td>
<td>1.4 (4/288)</td>
<td>1.9 (5/259)</td>
<td>0.487</td>
</tr>
<tr>
<td>Rate of catheter associated complications (%)</td>
<td>0.5 (1/206)</td>
<td>1.2 (3/259)</td>
<td>0.398</td>
</tr>
</tbody>
</table>

Procedural data and follow-up

<table>
<thead>
<tr>
<th>NFSFT group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroscopy time (min)</td>
<td>36.3</td>
<td>14.6</td>
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<tr>
<td>Fluoroscopy dose (Gy cm²)</td>
<td>687±665</td>
<td>1899±1396</td>
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<tr>
<td>Procedure duration (min)</td>
<td>136±43</td>
<td>138±38</td>
</tr>
<tr>
<td>Radiofrequency time (min)</td>
<td>38±16</td>
<td>36±19</td>
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<tr>
<td>Add. substrate modification (%)</td>
<td>6 (15%)</td>
<td>9 (23%)</td>
</tr>
<tr>
<td>Periprocedural complications (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Success rate over 6-months</td>
<td>22/30 (73%)</td>
<td>18/22 (82%)</td>
</tr>
</tbody>
</table>
Ablation of atrial fibrillation III / Ablation of atrial fibrillation IV

P3416 | BEDSIDE
Catheter ablation of persistent AF: anatomically-based circumferential PV ablation in combination with a potential-guided segmental approach to achieve PV isolation - long-term FU results (6 years)

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Background: Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. However, catheter ablation of persistent AF is still a challenge. Various rather complex ablation strategies exist and their results are not very favourable. Therefore, the aim of our study was to evaluate a well-defined reasonable approach to catheter ablation of persistent AF. The strategy consisted of a circumferential pulmonary vein ablation in combination with a potential-guided segmental approach to achieve complete PV isolation and a linear lesion at the root of the left atrium.

Methods: A total of 260 patients (154 men, 106 women; mean age 60 years (SD ± 9 years)) with symptomatic persistent AF were enrolled in this study. All patients underwent catheter ablation of persistent AF using the above-mentioned approach (electro-anatomical mapping system). Additionally, catheter ablation of the mitral isthmus and the right atrial isthmus was performed in selected cases. In all patients, 3-D TEE was performed before the procedure to evaluate the PV morphology.

Results: The ablation procedure could be performed as planned in all 260 patients. Ninety patients had to undergo a repeat ablation procedure, so that a total of 350 procedures were evaluated. An additional linear lesion was created at the mitral isthmus in 6 patients during the initial procedure and in 20 patients during the second procedure. Catheter ablation of the right atrial isthmus was performed in 20 patients during the first procedure and in 15 additional patients during the redo procedure.

Safety and feasibility of atrial fibrillation ablation in biological valve patients while on uninterrupted novel oral anticoagulant

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Introduction: Biological valve replacement in patients with atrial fibrillation requires life-long anticoagulation with warfarin or a “therapeutic” INR of 2.5–3.5. Recently novel oral anticoagulants (NOACs) such as dabigatran, rivaroxaban and apixaban have been introduced in the market to replace warfarin. We sought to report the safety and feasibility of performing catheter ablation of AF in patients with biological valve replacement while on uninterrupted NOAC.

Methods: 105 consecutive patients with a biological valve undergoing AF ablation while on uninterrupted NOAC. Patients were randomized to perform the first catheter ablation either through PVI alone or through PVI plus substrate modification based upon stepwise approach (CFAEs and linear ablation). Data were recorded at 3, 6 and 12 months after both ablations. The subjects who experienced AF recurrence were either managed to repeat the same technique of the first ablation.

Results: 150 subjects were enrolled (mean age 62.8±8.7y; 61.3% males; 69.3% hypertensive; AF mean duration 10.7 months); 75 patients in each group. The AF/AT recurrence rate significantly differed by ablation type at all time points and after both procedures. At the end of the target follow-up (12 months), the above rates were 46.7% (35/75) and 26.7% (20/75), respectively (p <0.001). AT occurrence more frequently in patients treated with the stepwise procedure; 10/20 AT occurred in the stepwise group vs 4/35 in the PVI group. Adjusting for several potential confounders, the hazard ratio of 0.35 (95% CI 0.20–0.62) for AF/AT recurrence after the first ablation was 0.53 (95% CI: 0.30–0.91) for those converted using stepwise ablation. The overall rate of complication was 10.0% of the 150 patients after the first ablation and 5.8% of the 52 patients after the redo ablation. No significant differences in the rate of complications were observed across the 2 groups after either the first or the second ablation. The addition of CFAE and linear ablation significantly prolonged procedural time: in the first procedure, 105±13 minutes were required for PVI alone, and 148±27 minutes for the stepwise ablation (p <0.001). Both fluoroscopy and radiofrequency times were significantly longer in the stepwise ablation groups (p <0.001). Similar results were observed during the second ablation.

Conclusions: In conclusion, the stepwise ablation relevantly enhanced the clinical outcome of PAF control strategy. However, this approach had to led to additional overall procedure and/or fluoroscopy times and more episodes of AT as compared PVI approach.

P3418 | BEDSIDE
Stepwise approach ablation versus pulmonary vein isolation in patients with paroxysmal atrial fibrillation: randomized controlled trial

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Background: Pulmonary vein isolation (PVI) is a central procedure for the treatment of paroxysmal atrial fibrillation (PAF). However, in patients with PAF and structural atrial disease, PVI ablation may fail and cause progressive atrial remodeling often leading to persistent/permanent atrial fibrillation.

Objectives: We performed a prospective, single-blind, randomized controlled study to compare the efficacy of two strategies of PAF ablation in reducing the recurrence rate of atrial fibrillation (AF) or atrial tachycardia (AT).

Methods: Participants were randomized to perform the first catheter ablation either through PVI alone or through PVI plus substrate modification based upon stepwise approach (CFAEs and linear ablation). Data were recorded at 3, 6 and 12 months after both ablations. The subjects who experienced AF/AT recurrence were either managed to repeat the same technique of the first ablation.

Results: 150 subjects were enrolled (mean age 62.8±8.7y; 61.3% males; 69.3% hypertensive; AF mean duration 10.7 months); 75 patients in each group. The AF/AT recurrence rate significantly differed by ablation type at all time points and after both procedures. At the end of the target follow-up (12 months), the above rates were 46.7% (35/75) and 26.7% (20/75), respectively (p <0.001). AT occurrence more frequently in patients treated with the stepwise procedure; 10/20 AT occurred in the stepwise group vs 4/35 in the PVI group. Adjusting for several potential confounders, the hazard ratio of 0.35 (95% CI 0.20–0.62) for AF/AT recurrence after the first ablation was 0.53 (95% CI: 0.30–0.91) for those converted using stepwise ablation. The overall rate of complication was 10.0% of the 150 patients after the first ablation and 5.8% of the 52 patients after the redo ablation. No significant differences in the rate of complications were observed across the 2 groups after either the first or the second ablation. The addition of CFAE and linear ablation significantly prolonged procedural time: in the first procedure, 105±13 minutes were required for PVI alone, and 148±27 minutes for the stepwise ablation (p <0.001). Both fluoroscopy and radiofrequency times were significantly longer in the stepwise ablation groups (p <0.001). Similar results were observed during the second ablation.

Conclusions: In conclusion, the stepwise ablation relevantly enhanced the clinical outcome of PAF control strategy. However, this approach led to additive overall procedure and/or fluoroscopy times and more episodes of AT as compared PVI approach.

P3419 | BEDSIDE
Mitrval isthmus ablation with a circular mapping catheter positioned in the left atrial appendage as a reference for complete conduction block

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Purpose: In cases with peripheral flutter (PMFL), to create complete conduction block in the mitral isthmus (MI) is mandatory but still challenging. We investigated the feasibility of making linear lesions in the MI just beneath the neck of the left atrial appendage (LAA) under the guidance of the activation sequence in the LAA during pacing from the coronary sinus (CS).

Methods: In this study, 75 patients (76 male, 61±8 years; Persistent AF: n=60). After a circular mapping catheter was positioned in the neck of the LAA, the MI ablation was performed aimed at the earliest activation site of the LAA during pacing from the CS. The ablative catheter was equipped with a 3.5mm irrigated tip and utilized through a steerable sheath with a frequency of 450/minute. When ablation during CS pacing was not successful, an RF delivery during LAA pacing was applied targeting the earliest activation site just below the mitral isthmus line. If the endocardial approach failed to create conduction block at the MI, an RF application inside the CS was attempted.

Results: With this endocardial approach, acute success was achieved in 54/82 patients (66%). Additional epicardial ablation from the CS was performed in 26/28 endocardially unsuccessful patients and conduction block in the MI was achieved successfully in 26/28 cases (92%). Overall, complete MI conduction block at the MI was achieved in 75/82 patients (91%). In the 7 failed cases, 4 were suspected to have persistent conduction via the vein of Marshall. No complications were observed.

Conclusions: Creating linear lesions just beneath the neck of the LAA was highly successful.
successful under the guidance of a circular mapping catheter in the LAA using a steerable sheath. An RF application from the CS was needed in less than half of the cases.

P3420 | BEDSIDE
Esophageal temperature monitoring during atrial fibrillation ablation: sensitivity of a conventional probe to detect significant temperature increases
Luminal esophageal temperature (LET) monitoring during radiofrequency (RF) delivery at the left atrium posterior wall has been advocated to detect and prevent esophageal damage and is regularly used in many centres. However, the esophagus is a wide anatomical structure and conventional temperature probes may be limited to detect distant temperature rise or may remain in the lumen with poor contact with the esophageal wall.

Methods: 32 (68 yo, 21 male) consecutive patients (P) with atrial fibrillation (AF) who underwent pulmonary vein isolation (PVI) by RF application were prospectively enrolled in the study. A conventional esophageal probe (CEP, sensihtherm, SJM) with 3 temperature sensors was used in all patients. In addition, a custom-made steerable probe (SEP) with a distal temperature sensor was introduced in the esophagus. RF was delivered by point-by-point application all around the 4 pulmonary veins (4 PV) ostia from an irrigated tip ablation catheter (30W, 48°C, 17 ml/min). Both probes were frequently relocated during the ablation procedure trying to achieve the closest distance to the RF application site. The procedure was blinded and not guided by LET monitoring and RF was delivered at each target site for at least 30 seconds irrespectively of the detected LET.

Results: No differences in LET were detected at baseline by the SEP (36.2±0.7°C) and the CEP (35.9±0.5°C). ETS > 37°, > 40° and > 45°C were detected in 100%, 100% and 56.7% respectively of P with the SEP but only in 93.1%, 37.9% and 0% of P with the CEP (χ², P=0.15, P=0.001 and P=0.001). The number of PVs showing LET > 37°, > 40° and > 45°C by the SEP vs the CEP during RF application were 2.7±1 vs 1.6±0.8 (P=0.001), 1.8±0.8 vs 0.6±0.8 (P=0.001) and 0.9±0.8 vs 0 (P=0.001) respectively. Maximum LET was significantly higher when detected by the SEP than by the CEP: 45.5±2.7°C (rank 40.1–49.0) vs 39.7±2.1°C (rank 36.8–44.0) respectively (P=0.001). The maximum LET was detected in a left PV in 70% of P by the SEP and in 56.7% of P by the CEP. After excluding from the analysis common pulmonary trunks, the maximum LET was detected in an inferior PV in 81.8% of P and 77.3% of P by the SEP and the CEP respectively.

Conclusion: LET during RF delivery for PVI is underestimated by CEP. Rises in LET over 40°C and 45°C are found in most patients but only detected in a minority by CEP. The value of LET by a SEP to prevent esophageal damage at PVI needs further evaluation.

P3421 | BEDSIDE
Echocardiographic assessment of atrial and ventricular remodelling after hybrid epicardial transdiaphragmatic and percutaneous endocardial radiofrequency ablation of persistent atrial fibrillation
J. Toplisek, A. Pernat, B. Gersak, N. Ruzic Medvescek, B. Robic, M. Sinkovec. University Medical Centre Ljubljana, Ljubljana, Slovenia
Aims: An endoscopic transdiaphragmatic epicardial ablation procedure with combined percutaneous endocardial radiofrequency ablation - hybrid procedure is potentially curative treatment option for patients with persistent atrial fibrillation (AF). Long-term effects of ablation lesions and/or arrhythmia elimination on atrial and ventricular remodelling are not completely understood. Therefore, the aim of our study was to quantify echocardiographic structural and functional changes of left atrium (LA) and left ventricle (LV) after combined ablation.

Methods and results: Thirty-seven consecutive patients with symptomatic drug refractory persistent AF were included in analysis. All underwent hybrid procedure to achieve complete pulmonary vein and LA posterior wall electrical isolation. The insertable cardiac monitor measured AF burden. At 12 months, follow-up mean AF burden was 17.1% (± 31.0%) for all patients. In patients with low AF burden (< 0.5%, 19/37 pts), we observed significant decrease of LA diameter (4.6 cm vs. 4.0 cm, p < 0.05), LA volume (96 ml vs. 81 ml, p < 0.05), improvement of LA effective refractory period (21% vs. 45%, p < 0.05) and LA global longitudinal strain (11.2% vs. 18.8%, p < 0.05). In addition, LV ejection fraction (60% vs. 70%, p < 0.05) improved in comparison to patients with mean AF burden > 0.5%.

Conclusion: Hybrid ablation procedure of persistent AF achieved stable sinus rhythm in significant proportion of patients resulting in positive LA and LV remodelling after 12 months of follow-up.

P3422 | BEDSIDE
The impact of CT image integration using CartoSound image directly acquired from the left atrium in atrial fibrillation ablation
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Introduction: CartoSound™ (CS) might be useful for integrating CT for catheter navigation during atrial fibrillation (AF) ablation. However, the optimal method of CT integration has not been established.

Methods: Fifty-two AF patients who underwent successful circumferential pulmonary vein isolation (CPVI) using CS were analyzed. CT integration was performed with two methods: (1) using the left atrial (LA) model created by CS probe located in the right atrium and right ventricle outflow tract (RA/RVOT-merge) and (2) using the LA model directly derived by CS probe in the LA added to images derived from the RA/RVOT (LA/RA/RVOT-merge). The accuracy of these methods was assessed by measuring the distances between integrated CT and the actual ablation point for CPVI.

Results: The average integration error between the LA model and integrated CT compared to the better between the 2 methods (LA/RA/RVOT-merge = 1.7±0.4 mm, RA/RVOT-merge = 1.6±0.5 mm; p=0.34). However, the distance between the ablation point and integrated CT was significantly shorter in LA/RA/RVOT-merge (1.2±0.6 vs. 2.5±0.8 mm; p=0.01). The LA, especially the left-sided pulmonary veins and LA roof, were more sharply delineated by CS probe located in the LA than in the RA/RVOT, and they may have improved the accuracy of CT integration.

Conclusions: Direct LA imaging by CS results in better integrated visualization and CT integration.

P3423 | BEDSIDE
Atrial rhythm and atrial electrogram amplitude
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Purpose: The magnitude of fibrotic replacement of atrial myocardium can be estimated by electroanatomic voltage mapping. The amplitude of atrial electrograms (EGMs), however, depends on atrial rhythm or dominant cycle length in case of atrial fibrillation. The relationship between EGM characteristics in atrial fibrillation/tachycardia and in sinus rhythm is generally unknown. We investigated left atrial EGMs while pacing at different rates from the high right atrium.

Methods: The study was completed in 18 patients (63±6 yrs, 13 males) with paroxysmal atrial fibrillation undergoing pulmonary vein isolation. Atrial EGMs were recorded in interoseptor (IP) region close to the right inferior pulmonary vein and in anterosetal (AS) region close to the right superior pulmonary vein. The stimulus protocol consisted of series of pacing trains delivered from right atrial appendage with basic cycle length of 600 ms followed by single extrastimulus with coupling interval gradually shortened in 20-ms steps until the atrial effective refractory period (ERP).

Results: The atrial ERP was 219±33 ms. In comparison to reference (in-train voltage), significant (P<0.05) reduction of EGM amplitude proportional to coupling interval of extrastimulus was observed in both IP and AS regions (maximum reduction is shown in Table). There was weak correlation between reference and short-coupled EGM amplitudes (R=0.35, P=0.05).

Conclusions: Left atrial EGM voltage is rate-dependent. Relative reduction of voltage (up to 50% of reference value) was observed for short-coupled extrastimuli. Further reduction could be expected at shorter atrial cycle length in the setting of atrial fibrillation. Magnitude of rate-dependent voltage reduction of atrial EGMs is widely variable. It implies that voltages in sinus rhythm cannot be predicted by voltages in atrial tachycardia/fibrillation.

Abstract P3423 – Maximum change in atrial EGM amplitude

<table>
<thead>
<tr>
<th>Unipolar voltage (mV)</th>
<th>Bipolar voltage (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reference voltage</strong></td>
<td><strong>Voltage close to ERP</strong></td>
</tr>
<tr>
<td>Infraposterior LA</td>
<td>2.64±1.04</td>
</tr>
<tr>
<td>Anterosetal LA</td>
<td>3.03±1.43</td>
</tr>
</tbody>
</table>

Legend: EGM, electrogram; ERP, effective refractory period; LA, left atrium. All P < 0.05.
**P3424 | BEDSIDE**

The impact of anterior mitral block on left atrial appendage activation time

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**Introduction:** Left anterior ablation line (LAL), which can be used for the management of perimital reentrant atrial tachycardia, is also invariably associated with the change in activation of the left atrial appendage (LAA) during sinus rhythm (SR). This study investigated magnitude of this change in the setting of hypothyroid block at the LAL.

**Methods:** We utilized the electronotomic data from left atrial (LA) mapping in 68 patients (46 men, 59±10 years) who underwent catheter ablation for paroxysmal (75%) or persistent atrial fibrillation. The LA activation maps in SR were carefully edited to localize the lateral perimital collision zone. The electrical distance between the base of LAA and this collision zone was used to estimate the relative delay in LAA activation if virtual block at the LAL is achieved.

**Results:** In SR, the activation time of LAA base was -76±40 ms before the onset of QRS complex. The activation time at the collision zone was -52±41 ms. In the setting of hypothyroid LAL block, LAA activation time would be delayed by 64±36 (range 4–156) ms resulting in the reduction of LAA activation prematurely relative to the QRS onset (-21±32; range -97–68 ms). In 14 (21%) patients, LAA activation would start after the QRS onset. Only 10 (15%) patients would have LAA activated earlier than 50 ms prior to the QRS onset. Out of those 10 patients, 6 (60%) had PR interval longer than 200 ms, which is significantly higher proportion than in rest of cohort (21%), p=0.01.

**Conclusions:** The experimental model helped to demonstrate that the block at the LAL is associated with significant delay of LAA activation. Consequently, the anterior mitral block may adversely influence the benefit from SR restoration because of worsening of LAA function. Prolonged PR interval seems to be protective from delayed LAA activation after completing of LAL.

**P3424 | BEDSIDE**

Loss of contact force affects outcomes in atrial fibrillation ablation

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**Introduction:** Treatment guidelines for Atrial Fibrillation (AF) now firmly advocate catheter ablation as standard therapy. However, ablation, which generally involves pulmonary vein isolation (PVI) has a high recurrence rate. This is usually due to electrical reconnection of the veins. We investigated whether the Thermocoool ®Smarttouch™(TM) catheter was better than the Thermocoool® Surround Flow (SF) catheter.

**Methods and results:** Our unit has been using the ST catheter since release in 2012, and 2 experienced operators have used it in ~500 cases. The ST catheter was recently recalled for a period of one year due to LAA injury as of the end of 2013, during this time our unit used the SF catheter for PVI. We compared the outcomes of these 64 SF patients with the preceding 64 consecutive patients who had ST ablation. No repeat cases were included and PVI in both groups was done as a point-by-point circumferential radiofrequency ablation around the veins, without any extra ablation lines, unless there was a documented atrial tachycardia.

Both groups were comparable; SF group age 63 years vs 62 years, persistent AF 16 (25%) vs 14 (22%), Hypertension 19 (30%) vs 25 (39%), Airways disease 5 (8%) vs 3 (5%), Stroke/TIA 4 (6%) vs 4 (6%), Heart failure 7 (11%) vs 8 (13%), Diabetes mellitus 18 (28%) vs 16 (25%) patients, 6 (60%) have PR interval longer than 200 ms, which is significantly higher proportion than in rest of cohort (21%), p=0.01.

**Conclusions:** Our study suggests that the ST catheter is more effective than the SF catheter in the prevention of pulmonary vein reconnection. The treatment of AF is challenging and this is reflected in the higher readmission rates seen in the SF ablation group. Furthermore, the prolonged PR intervals seen in the SF ablation group are significantly higher than previously reported (1). Our data suggests that the SF catheter may not be the optimal choice for pulmonary vein isolation.

**P3427 | BEDSIDE**

Early redo procedure of atrial fibrillation ablation: the energy source does have a role?

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**Purpose:** Recurrences of atrial fibrillation (AF) after the first ablation procedure are frequent. In addition of radiofrequency (RF), cryo energy acquired high availability in the last years. The aim of this study was to identify if the energy source plays a role on early AF recurrence and if it is related to a site-specific reconnection in pulmonary veins.

**Methods:** From 1460 AF ablation procedures performed in our centre from 2010 to 2014, 164 patients [(11%), 72% male, mean age 58±6 years], undergoing redo procedure, were retrospectively evaluated. The mean time to redo procedure was 30±29 months. Redo procedures were classified by the type of ablation energy: RF (143 patients, 87%); cryo (21 patients, 13%). Forty-five patients (27%), in whom the baseline ablation was realized 6 months after the first ablation, were analyzed. The energy source of the first ablation was RF in 30 patients (87%) and cryo (first generation balloons) in 15 patients (33%).

**Results:** The study shows a statistically significant difference in the rate of recurrence between RF and cryo. RF had a significantly higher rate of recurrence than cryo (P=0.013). No significant differences were found in age, sex, body mass index, previous procedures, left atrial size, and left ventricular ejection fraction. The rate of recurrence was also lower in patients with persistent AF than paroxysmal AF (P=0.043).

**Conclusions:** RF and cryo energy have different effects on the recurrence of atrial fibrillation after redo procedure. RF energy is associated with a higher risk of recurrence compared to cryo energy. This study suggests that the type of ablation energy used for the first procedure may influence the rate of recurrence after redo procedure.

**P3428 | BEDSIDE**

Role of atrial fibrillation in patients with acute coronary syndrome and elevated high-sensitive troponin T levels

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**Background:** Studies have shown that high sensitive Troponin (hs Troponin) is highly specific for myocardial damage and for the diagnosis of acute coronary syndrome (ACS).

**Methods:** PV conduction recovery was found in all investigated patients. The number of reconnected veins was 1, 2, 3 or 4 in 4 (6.5%), 7 (11.2%), 21 (33.9%) and 30 (48.4%) patients, respectively. Reconnection of LSPV, RIPV and RSPV was observed in 74, 81, 100, 83 and 93%, respectively. Excluding patients with AF duration longer than 1 year, PVs were found to be reconnected significantly more frequent than left PVs (p<0.01). In the majority of veins (67%) reisolation of PV could be achieved by single point ablation (<2 quadrants conducting), in the remaining 33% (>2 quadrants conducting) more circumferential lesions were necessary. Reconnection of multiple (>2) quadrants occurred in a significant higher rate at the RIPV compared to the other veins (p<0.01). In the left PVs conduction gaps were located more anteriorly, in the RSPV superiorly and in the RIPV inferiorly and posteriorly (p<0.01). There was no difference in the number of PVAC applications during the index procedure between reconnected and non-reconnected veins.

**Conclusions:** Our study suggests that the type of ablation energy used for the first ablation may influence the rate of recurrence after redo procedure. RF energy is associated with a higher risk of recurrence compared to cryo energy. This study suggests that the type of ablation energy used for the first procedure may influence the rate of recurrence after redo procedure.
Objective: We investigated hs Trop utility and predictive value in patients with acute cardiac care in the emergency department

Methods: We studied 2038 consecutive patients undergoing coronary angiography between July 2013 and October 2014. In patients with ACS cardiac biomarkers (hs Tropinin) were obtained on presentation and if indicated several hours later. In patients with non ST-segment elevation myocardial infarction (NSTEMI) history of AF and heart rhythm documented by electrocardiogram were assessed and compared with coronary angiography result.

Results: Of the study population 351 (17%) patients had NSTEMI and 503 (25%) patients a history of AF. Ninety patients (26%) of NSTEMI patients showed AF on presentation. Mean patients age was 74 years + 9 and 73% were men. Prior coronary artery disease was known in 75% of the 90 patients and paroxysmal AF was known in 53% of patients. Mean left ejection fraction was 50% ± 16. Coronary anatomy was comparable in patients with NSTEMI and AF on presentation revealed a rate of 28% (25/90) without significant stenosis. HS Tropinin was elevated in 60 of the 90 patients (74%) with a mean hs Tropinin of 295±300. CK was elevated in 82 of 90 patients (91%) with a mean CK of 692±390. In the 25 patients who showed no significant stenosis a mean hs Tropinin was 152±107 (min/max: 0.055; p=0.12) and a mean CK of 135±57 (min/max: 44/301, p=0.17).

Conclusion: These data are the first to show that AF in the acute setting is frequently associated with hs Tropinin. One third of the patients showed no need of intervention. These findings are of clinical decision importance in patients with acute AF and myocardial ischemia symptoms. Appropriate clinical guidelines must be established that also consider AF-related elevations in hs Tropinin.

P3432 | BEDSIDE

Inflammatory mediator TIMP-1 is a prognostic marker for mortality in acute coronary syndrome (ACS)

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Introduction: The aetiology of the acute cardiac disease has a pivotal impact in terms of survival (p=0.145 and p=0.082, respectively). However, TIMP-1 and MMP-8 were not significantly different in ACS-like patients vs A=435.00, ±642.42 pg/mL, p<0.01). Regarding in-hospital stay, group B patients had higher degree of morbidity and mortality.

Methods: Prospective study of 1051 consecutive patients, diagnosed with ACS, between October 2009 and September 2013. Patients were divided in two groups: Group A - patients with chest pain on presentation (n=884, 71.4% men); Group B - patients without chest pain on presentation (n=171, 62.6% men).

Results: In the ACS patient group 474 (23%) patients died during follow up. Acutely measured TIMP-1 was significantly higher (p<0.001) in those patients, than those who survived the follow-up period, whereas MMP-8 was not (p=0.55) (Figure 1). In the ACS-like patient group 8 (6%) patients died during follow up. However, TIMP-1 and MMP-8 were not significantly different in ACS-like patients in terms of survival (p=0.145 and p=0.082, respectively).

Conclusion: Inflammatory marker TIMP-1 is a prognostic marker of long term survival in patients with ACS, MMP-8 and TIMP-1 do not provide such value in noncoronary acute cardiac disease. TIMP-1 may thus be considered a marker of severe coronary inflammation with prognostic implication.

P3430 | BEDSIDE

Acute heart failure complicating acute myocardial infarction in the contemporary era of modern treatment

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Background: In the contemporary era of modern treatment and early revascularization in acute myocardial infarction (AMI), the problem of acute heart failure (AHF) complicating AMI remains unclear.

Purpose: To establish the prevalence of AHF at the time of admission to the hospital due to AMI, to identify clinical factors predisposing to AHF in those patients, and to assess prognostic impact of AHF in this group of patients.

Methods: Prospective study of 289 consecutive patients (mean age: 68±11 years, 61% men) admitted with AMI between April and November 2012 to our Centre for Heart Diseases, Hospital, Poland. AMI was diagnosed based on the 3rd Universal Definition of Acute Myocardial Infarction. AHF was diagnosed based on 3 criteria: (1) dyspnea at rest or during minimal physical effort; (2) pulmonary congestion demonstrated on chest X-ray; (3) applied specific treatment including loop diuretic i.v. and/or nitroglycerin i.v. within first 24 hours of hospitalization.

Results: 13% of patients experienced AHF at the time of admission. In a multivariable analysis, the female gender (AHI=0.71; p=0.35; OR=9; 95% CI: 2.3–11.1), a presence of chronic obstructive pulmonary disease (COPD, 18% vs 5%; OR=4.9; 95% CI: 1.6–15.3) and chronic kidney disease (CKD, 34% vs 16%; OR=2.5; 95% CI: 1.1–5.8) (all p<0.05) were independently associated with an increased risk of developing AHF in the course of AMI. Surprisingly, neither history of systolic HF for diabetes mellitus were predisposing factors for AHF development. There were no differences for maximal cardiac troponins measured during hospitalization between these two groups whereas NT-proBNP was higher (4128 [2397–9261] vs 742 [259–2043]; p<0.001) in AHF+ vs AHF- group. Patients who developed AHF were longer hospitalized (9±6 vs 6±5 days) and were characterized by the higher in-hospital cardiovascular (CV) mortality (8% vs 0%) (both p<0.001). All patients were followed up for ≥1 year. During the 18-month follow-up all-cause deaths (29% vs 11%), CV deaths (18% vs 3%), secondary HF hospitalization (vs 5%) and recurrent MI episodes (18% vs 8%; p<0.05) were more common in AHF+ vs AHF- patients.

Conclusions: In contemporary era of modern treatment still one in eight patients with AMI presents AHF on admission and it is particular common in female gender and CKD. Find CKD. Despite findings on cardiovascular mortality and hospitalization, patients with coexisting AHF and AMI, have poor in-hospital and postdischarge outcome.

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P3431 | BEDSIDE

Myocardial infarction in patients without suspected acute coronary syndrome attending the emergency department


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Background: High-sensitivity cardiac troponin assays are used widely in the
Emergency Department to facilitate early diagnosis of myocardial infarction. However, myocardial injury occurs in a range of conditions and there is concern that widespread use of these assays may lead to diagnostic uncertainty and unnec-

essary hospital admissions.

**Purpose:** To define the prevalence of myocardial injury in consecutive patients at-
dending the Emergency Department without suspected acute coronary syndrome.

**Methods:** We identified all patients (n=1,054) who presented to the Emergency

Department of a large teaching hospital in whom serum was prepared as part of routine clinical care over 10 consecutive days. Cardiac troponin was measured using a high-sensitivity troponin I assay in all patients, but only reported where requested by the attending clinician. Clinical characteristics, diagnosis, and out-

comes were obtained through the patients’ electronic patient records.

**Results:** Cardiac troponin was requested in 136 patients (11%) by the attending

clinician. In the remaining 918 patients without suspected acute coronary syn-
drome (age 55±23 years, 48% men), 107 (10%) patients had myocardial injury with troponin concentrations greater than the upper reference limit (≥34 ng/L in men, ≥16 ng/L in women). Patients with myocardial injury were older, and were more likely to have cardiovascular risk factors and coronary heart disease (P<0.001). Cardiac troponin was associated with haemodynamic compromise based on physiological parameters in the National Early Warning Score (NEWS) (P<0.001), renal impairment (P<0.001), myocardial ischemia on the electrocardiogram (P<0.05) and was an independent predictor of death at 30 days (hazard ratio 1.35 [95% confidence interval 1.20–1.53] per doubling of troponin concen-

tration). The majority of patients with myocardial injury (86%) were admitted to

hospital for further investigation.

**Conclusion:** Myocardial injury outwith suspected acute coronary syndrome is common and detectable in 1 in 10 patients attending the Emergency Department.

Myocardial injury is associated with cardiovascular risk, haemodynamic compre-

mise and early death with the majority already admitted to hospital for further

investigation.

**Acknowledgement/Funding:** British Heart Foundation

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**P3434 | BEDSIDE**

Impact of renal dysfunction at admission on survival in mechanically

ventilated ST-elevation myocardial infarction patients after
cardiopulmonary resuscitation

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**Background:** Renal dysfunction (RD) is associated with an increased risk for a

worse outcome after coronary intervention (PCI). Data about the impact of RD at

admission on survival in ST-elevation myocardial infarction (STEMI) complicated with
cardiopulmonary resuscitation (CPR) and mechanical ventilation are sparse.

**Purpose:** We tried to establish the possible influence of RD at admission in patients with STEMI, complicated with CPR and mechanical ventilation on in-
hospital mortality.

**Methods:** The present study was an analysis of 120 mechanically ventilated pa-
tients after CPR with STEMI. The group with RD (45 patients) was compared with
the group without RD (75 patients). RD was defined as glomerular filtration rate
less than 60 ml/min/1.73m2. In-hospital and long-term all-cause mortality,
worse outcome after coronary intervention (PCI), TIMI-flow before and after PCI,
PCI of left main coronary artery, PCI of LAD, PCI of RCA, multivessel PCI, drug
eluting stents, GPI use and RD at admission. Distribution of continuous variables
in the 2 groups were compared with the 2-sample t-test. Distribution of categori-
cal variables were compared with the chi-square test. All p values were two-sided
and values less than 0.05 were judged statistically significant.

**Results:** RD at admission in STEMI patients after CPR and mechanical venti-
lation was associated with higher in-hospital or long-term all-cause mortality. In
the RD group 27 patients (60.0%) died in the hospital whereas 20 (26.7%) died
in the non-RD group; p<0.0001. Long-term mortality during observation period
was also higher in RD group [31 patients (68.9%) with RD vs. 26 (34.7%) patients
in the group without RD; p<0.0001]. In-hospital mortality was predicted with RD
at admission (adjusted HR 2.44; 95 CI 1.31 to 4.56; p<0.0001), age (adjusted HR 1.05; 95 CI 1.02 to 1.08; p<0.0001) and TIMI flow ≥1 before PCI (adjusted HR 0.46; 95 CI 0.24 to 0.90; p=0.024). RD at admission (adjusted HR 2.92; 95 CI 1.67 to 5.13; p<0.0001), and age (adjusted HR 1.04; 95 CI 1.01 to 1.06; p=0.002) predicted long-term death.

**Conclusion:** STEMI patients with RD at admission who had undergone CPR and
were mechanically ventilated had a worse outcome than patients without RD at
admission. This is especially true for older patients. Special attention regarding
renal function should be considered for these patients.

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**P3435 | BEDSIDE**

Impact of renal dysfunction on acute cardiac care in the emergency department

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**Background:** Therapeutic hypothermia at a target temperature of 33°C was re-
cently reported to not confer a benefit compared with management at a target
temperature of 36°C.

**Aim:** Our study aimed at evaluating the relationship between regional brain oxy-
gen saturation (rSO2) upon hospital arrival and neurological prognosis in pa-
ients with or without therapeutic hypothermia after out-of-hospital cardiac arrest
(OKHA).

**Methods:** We admitted 315 survivors to hospital after OKHA (presumed cardiac
causation) from the Prediction of Neurological Outcomes in Patients Post-cardiac
Arrest Registry, and measured their rSO2 immediately upon hospital arrival. Of
these, 152 patients underwent therapeutic hypothermia, while 163 did not. We
also assessed the percentage of patients with good neurological outcome (de-
fined as cerebral performance categories 1 or 2) 90 days post-cardiac arrest.

**Results:** After 90 days, 55 (36%) and 13 (8%) patients had good neurological out-
comes in each respective group. The percentage of patients with a good 90-day
neurological outcome increased significantly in proportion to rSO2 levels upon
arrival at the hospital in each group (P<0.001). However, in patients with rSO2
upon hospital arrival between 41% and 60% (n=42; 13%), the percentage of pa-
ients with good neurological outcomes was significantly higher (P<0.01; Figure)
in patients with therapeutic hypothermia (20/28, 71%) than in those without (1/14,
7%).

**Conclusion:** Our data indicate that patients with moderate cerebral perfusion
deficit upon hospital arrival may be good candidates for therapeutic hypothermia
after OKHA.

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P3436 | BEDSIDE
Optimal blood pressure for favourable neurological outcome in adult patients following in-hospital cardiac arrest
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Results: Of the 319 study patients, 93 (29.2%) survived to hospital discharge and 56 (17.6%) achieved a favourable neurological outcome. The mean MBP was 95 mm Hg. MBP above 85 mm Hg was found to be correlated with a favourable neurological outcome (odds ratio [OR] 2.34, 95% confidence interval [CI] 1.40–3.92, p=0.001). For patients without chronic hypertension, the optimal MBP was between 85 and 115 mm Hg (OR 0.80, 95% CI 3.13–28.58); for patients with chronic hypertension, the threshold MBP for achieving a favourable neurological outcome was above 88 mmHg (OR 4.04, 95% CI 1.41–13.03).

Conclusions: The blood pressure over the first 24 hours following resuscitation was correlated with neurological outcome. There may be a threshold blood pressure (MBP) during the initial 24 hours after sustained ROSC was used for analysis.

P3437 | BEDSIDE
Clinical profile, treatment, and outcomes of patients with type B acute aortic syndromes: findings from a large multicenter Italian registry
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Objective: To assess the epidemiological characteristics, clinical presentation, diagnostic strategies, treatment, and outcome of patients with type B Acute Aortic Syndrome (AAS).

Methods: “AESIA” (Archivio Elettronico delle Sindromi Aortiche acute) multicenter registry includes consecutive patients with AAS (Aortic Dissection, AD; Intramural Hematoma, IH; Penetrating Ulcer, PU) referred to 2 Italian “Hub” hospitals. 502 patients (including both type A and type B) were enrolled from 2000 to 2014. In all cases the diagnosis was confirmed by a multidisciplinary team. For this study, only patients with type B AAS were assessed.

Results: AESIA registry enrolled 190 patients with Type B AAS: 122 (65%) with DA and 68 (35%) with IH and 19 (10%) with PU. The mean age of study population was 67±13 years, 72% were male. The “classic” risk factors for AAS were confirmed to be uncommon, with the exception of a history of hypertension (70% of patients). The clinical presentation included: back pain (70%), anterior chest pain (39%), abdominal pain (16%), migratory pain (16%), pulse deficit (20%), syncope (3%), stroke/TIA (1%). Acute coronary syndrome (ACS)-like ECG abnormalities were found in 18% of cases, while cardiac troponin T (TnT) elevation was observed in 25 (20%) of the 126 patients who were tested with TnT assay during the initial management of chest pain. The combination of ACS-like ECG findings and TnT positivity was independently associated with late diagnosis and inappropriate therapy such as antithrombotic therapy/coronary angiography (OR 2.48, 95% CI 1.14–5.8, p=0.03). An initial diagnosis different from AAS was made in 23% (of which 35% ACS, 13% renal/biliary colic, 13% acute gastritis, 11% pulmonary embolism, 7% lower limb ischemia). The first “diagnostic” test which demonstrated an AAS was: CT scan (83% of cases), abdominal ultrasound (12%), TT (3%) and TE (1%) echocardiography. 90 of 190 patients (47%) underwent endovascular (n=76) or surgical intervention (n=14) during hospitalization. In-hospital mortality was 12.6%, without difference between patients treated with invasive approach and those managed with medical therapy alone (13% vs. 12% respectively, p=0.86).

Conclusions: The outcome of AAS Italian patients enrolled in AESIA registry is in line with that reported by the current international literature. Of note, even in type B AAS, ACS-like ECG abnormalities and TnT elevation are frequent findings and they are associated with significant risk of late diagnosis and inappropriate therapy.

P3438 | BENCH
Efficacy and safety of intensive statin treatment in Chinese old patients with acute coronary syndrome undergoing percutaneous coronary intervention
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Background: Previous study showed that loading or pre-loading with statin improved clinical outcomes in patients undergoing percutaneous coronary intervention (PCI), however the efficacy and safety of statin in Asian elderly acute coronary syndrome (CAD) patients who undergoing PCI were unknown.

Objectives: The objective of this study is to test whether Chinese old patients undergoing PCI can tolerate and benefit from intensive statin treatment.

Methods: Patients who were aged from 65–80 years undergoing PCI from 2012–2013 in 5 large volume PCI centers in China were included. Patients were randomly divided into two groups, regular statin treatment group: atorvastatin 10mg pre PCI, 20mg/d till 30 days, intensive statin treatment group: atorvastatin 80mg 12 hours pre PCI, 40mg/d till 30 days. MACE which includes all cause of death, myocardial infarction, target vessel revascularization; Hepatotoxicity, muscle toxicity were also followed up at 1 month, 6 months.

Results: 225 and 250 patients were included in the intensive and regular statin treated group respectively. Compared with regular statin treatment group, intensive statin treatment group reduced peri-procedure myocardial injury (23.6% vs 35.7%, p<0.05). At follow up of 6 month, intensive statin treatment also reduced MACE (6.6% vs. 12.2%, p<0.05). Both group had similar incidence of hepatotoxicity (3.2% intensive statin group vs. 3.9% in regular statin group p=0.05) and muscle toxicity (5.3%, in intensive statin group vs. 4.5% in regular statin group p=0.05). Multivariable analysis showed that intensive statin as a predictor of decreased risk of 6 month MACE in elderly ACS patients (odd ratios, 0.63 95% confidence interval: 0.25 to 0.87 p<0.037).

Conclusions: Intensive statin treatment pre PCI in elderly Chinese patients can reduce periprocedural myocardial injury and MACE at no cost of safety.

P3439 | BEDSIDE
Two-year clinical outcome of bioimulsion-eluting stent in coronary bifurcation lesions compared with everolimus-eluting stent
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Background: Newer-generation drug-eluting stents (DES) have the improved safety and similar efficacy compared with first-generation DES. However, there is little data regarding the optimal newer-generation DES for bifurcation lesions. The aim of this study was to compare clinical outcome between the NOBORI bioimulsion-eluting stent (BES) and XIENCE/PROMUS everolimus-eluting stent (EES) in patients with bifurcation lesions.

Methods: Between February 2010 and August 2012, a total of 888 patients treated only with BES (508 patients with 560 lesions) or EES (390 patients with 411 lesions) in bifurcation lesions were retrospectively analyzed. The study end point was the cumulative 2-year incidence of major adverse cardiovascular event, defined as a composite of cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CDTLR), and definite stent thrombosis.

Results: Baseline patient characteristics were similar between the BES and EES groups except for the prevalence of dyslipidemia, previous MI and previous per-
cutaneous coronary intervention. At 2-year, the incidence of MACE was similar between the 2 groups (9.2% vs. 6.7%, P=0.16). Cumulative incidence of MI, CDTLR, and definite stent thrombosis were not significantly different between the 2 groups (1.8% vs. 1.4%, P=0.65; 5.9% vs. 4.4%, P=0.27; 0.8% vs. 0.6%, P=0.61), respectively.

Conclusions: Two-year clinical outcome of BES is similar to that of EES in patients with bifurcation lesions.

P3440 | BEDSIDE

Sex-based differences in 2-year clinical outcome after percutaneous coronary intervention with new generation drug eluting stent


Background: Sex-based differences in clinical outcome after percutaneous coronary intervention (PCI) with new generation drug eluting stent (DES) remains unclear. We sought to assess whether sex differences in clinical outcome exist in patients treated with new-generation DES.

Methods: We evaluated consecutive patients treated with new-generation DES between February 2010 and May 2012. This primary endpoint was the cumulative incidence of major adverse cardiovascular events (MACE), defined as a composite of cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CDTLR), and definite stent thrombosis at 2-year. Cox proportional hazards models were used to assess independent predictors of MACE. Multivariate models were constructed by including all univariate predictors with a p-value < 0.1.

Results: Among 2496 patients, 660 (26.4%) were women. Clinical follow-up information at 2 years was obtained 98.4%. Compared with men, women were older and had less current smokers, previous MI and previous PCI. The cumulative 2-year incidence of MACE and cardiac death in women were significantly higher than those in men (12.2% vs. 8.2%, P=0.003; 4.7% vs. 2.4%, P=0.005, respectively). The cumulative incidence of CDTLR and MI were not significantly different between the 2 groups (7.2% vs. 5.5%, P=0.13; 1.0% vs. 1.9%, P=0.13, respectively). In a multivariate analysis, woman was associated with MACE (hazard ratio 1.41; 95% confidence interval 1.04--1.90; p=0.03).

Conclusion: Women had worse 2-year clinical outcome than men in the new-generation DES era. Woman was an independent predictor of MACE.

P3441 | BENCH

Investigating the molecular signaling pathway of perconditioning: focused on STAT5 and eNOS inhibition

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Perconditioning (PerC) reduces infarct size independently of the RISK and SAFE pathways. Stat5 seems to be a unique signaling marker of PerC in rabbits, and its activation parallels with infarct size limitation. However, there is no proof of a causal role of Stat5, while its activation in cellular compartments remains to be identified. Src kinase mediates Stat5 pathways, possibly through angiotensin II (Ang II) and generation of reactive oxygen species (ROS). Genetic ablation of eNOS abolishes the effect of remote preconditioning in mice.

Purpose: To determine the role of STAT5, eNOS and apoptosis in PerC.

Methods: Anesthetized rabbits were subjected to 30-min ischemia (isc) and 180-min reperfusion (rep) and randomized into 10 groups: 1) Control; 2) PerC (by carotid artery ligation, 4 cycles of 1 min isc/rep); 3) Perc-AG, treated with the selective JAK-2 inhibitor tyrphostin AG-490; 4)AG-490; 5) Perc-PP1, treated with the selective Src inhibitor PP1; 6) PP1; 7) Perc-Val, treated with the JAK1 receptor antagonist valsartan; 8) Val; 9) Perc- L-NAME, treated with the inhibitor of NO synthase, L-NAME; and 10) L-NAME. The infarct (I) to risk (R) ratio was estimated. In a second series of experiments with respective groups, tissue samples were taken at the 10th min of rep for STAT5, eNOS and caspase-3 assessments. Blood samples were drawn at baseline and at rep for malondialdehyde (MDA) and nitrotyrosine (NT) assessment.

Results: The inhibition of Jak-2, Src and AT1 did not abrogate the infarct size limiting effects of PerC (29.2±3.7% in PerC, 26.2±2.2% in PerC-AG, 13.2±0.6% in PerC-PP1, 10.7±0.5% in PerC-Val vs 47.7±1.0% in Control, 39.7±3.8% in AG and 35.2±1.8% in PP1, p<0.05). Val reduced I/R (13.0±1.5%, p<0.05 vs Control), L-NAME abrogated the infarct size limiting effect of PerC, (38.2±1.6% and 37.2±1.6% in L-NAME and Perc- L-NAME groups respectively, p<NS vs Control and p<0.05 vs Perc). STAS was activated in PerC groups independently of the presence of AG, whereas no STAS phosphorylation was observed in PP1 and Val groups (with or without PerC), eNOS was phosphorylated in all Perc groups apart from Perc-L-NAME and Control groups. In the latter two groups there was a reduced expression of cleaved caspase-3 indicating increased apoptotic signaling. MDA and NT were reduced in all PP1 and Val treated groups in comparison to the others.

Conclusion: PerC reduces infarct size independently of STAT5 activation. Src kinase rather than Jak-2 appears to play a predominant role in STAT5 activation through Ang II and ROS. We conclude that eNOS is protective through inhibition of apoptosis.

P3442 | BENCH

Post-infarction adverse remodeling in rats is attenuated by local growth hormone administration via an alginate-scaffold

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Introduction: Left ventricular (LV) remodeling following myocardial infarction (MI) remains a common cause of chronic heart failure, necessitating the advent of improved treatments for its prevention. Promising results towards this aim have been reported with the experimental use of alginate-based biomaterials, growth hormone (GH), or ventricular restraint. We hypothesized that their combined use can confer additive effects, by enhancing angiogenesis and/or myofibrobast-proliferation.

Purpose: Using the rat MI-model, we investigated the effects of local GH administration via an alginate-scaffold on post-MI LV remodeling, in comparison with biventricular restraint, exerted by an alginate-based patch.

Methods: Following permanent coronary artery ligation, 48 Wistar rats (333±5g) were randomized into intramyocardial injection of (I) an alginate-based scaffold with GH (alginate-GH) or (II) alginate alone, (III) biventricular restraint via the alginate-based scaffold (restraint), or (IV) no treatment (control), whereas 5 rats were sham-operated. Echocardiographic LV remodeling indices were obtained 3 weeks post-MI, followed by immunohistochemical evaluation of angiogenesis and myofibrobast-count.

Results: LV dimensions were smaller and ejection fraction (EF) was higher after alginate+GH compared to alginate alone. Increased neo-vascular density and myofibrobast-count were found in the infarct and peri-infarct areas after alginate-GH (Table).

<table>
<thead>
<tr>
<th></th>
<th>Sham</th>
<th>Control</th>
<th>Alginate</th>
<th>Alginate+GH</th>
<th>Alginate-restraint</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDD (mm)</td>
<td>5.05±0.32</td>
<td>7.92±0.34</td>
<td>7.21±0.33</td>
<td>5.61±0.35**</td>
<td>4.67±0.24</td>
</tr>
<tr>
<td>ESV (mm³)</td>
<td>2.55±0.37</td>
<td>4.28±0.45</td>
<td>4.58±0.38</td>
<td>3.12±0.21***</td>
<td>4.50±0.47</td>
</tr>
<tr>
<td>EF (%)</td>
<td>69.4±1.9</td>
<td>44.4±0.43</td>
<td>42.1±2.5</td>
<td>50.7±1.5</td>
<td>38.9±3.2</td>
</tr>
<tr>
<td>Myofibroblasts (%)</td>
<td>0.77±0.29</td>
<td>2.74±1.22</td>
<td>6.25±1.28</td>
<td>2.63±1.06</td>
<td>3.61±0.44</td>
</tr>
<tr>
<td>Angiogenesis (%)</td>
<td>3.61±0.44</td>
<td>3.76±0.44</td>
<td>6.93±0.55</td>
<td>3.88±1.11</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SEM. EDD, end diastolic dimension; ESV, end systolic dimension; EF, ejection fraction; **p<0.01 vs control, †p<0.01 vs control, ‡p<0.05 vs control, †p<0.01 vs alginate, †p<0.05 vs alginate.

Conclusions: Intramyocardial injection of GH via an alginate-scaffold attenuates post-MI LV remodeling and improves LV function, displaying higher efficacy compared to alginate alone or biventricular restraint. These favorable effects can be attributed to enhanced neoangiogenesis and myofibrobast-density in the peri-infarct area.

Acknowledgement/Funding: AD, EB, MK were supported by a scholarship from the Experimental Research Center ELPEN (Greece)

P3443 | BENCH

Vasonatrin peptide inhibits endoplasmic reticulum stress and alleviates myocardial ischemia/reperfusion injury in diabetic rats

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Background: Diabetes mellitus (DM) increases morbidity/mortality of ischemic heart disease. Although the ability of the natriuretic peptides to modulate cardiac function and cell proliferation has already been recognized, their effects on myocardial ischemia/reperfusion (MI/R) injury, especially in diabetic state, is still under debate.

Purpose: This study was designed to investigate the effects of the artificial synthetic natriuretic peptide – vasonatrin peptide (VNP) on MI/R injury in diabetic rats, and to further elucidate its mechanisms.
**Methods:** The high-fat diet-fed streptozotocin (HFD-STZ) induced diabetic rats were subjected to MI/R (30 min/4 h) and VPN treatment (100 μg/kg, i.v. 10 min before R). In vitro study was performed using H9c2 cardiomyocytes subjected to hypoxia/reoxygenation (H/R, 3 h/6 h) and incubated with or without VPN (10–8 mOl/L).

**Results:** The diabetic state aggravated MI/R injury and showed more severe myocardial functional impairment than normal state. VPN treatment significantly improved ±LV dp/dtmax and LVSP, reduced LVEDP, and decreased infarct size, apoptosis index, caspase-3 activity, serum CK and LDH levels (n=8, P<0.05). Moreover, VPN inhibited endoplasmic reticulum (ER) stress by suppressing GRP78 and CHOP (n=3, P<0.05), and consequently increased the antiapoptotic protein Akt and ERK1/2 expression and phosphorylation levels. These effects were mimicked by 8-Br-cGMP (1 mg/kg, i.p., 20 min before R), a cGMP agonist, which is known to increase AKT and ERK1/2 expression and phosphorylation via inhibition of PKG1α. Moreover, pretreated DM rats with TUDCA (50 mg/kg, i.p.), a specific inhibitor of ER stress, could not further promote the VPN’s cardioprotective effect. In additional experiments H9c2 cardiomyocytes were subjected to hypoxia/reoxygenation (H/R, 3 h/6 h) and incubated with or without VPN in vitro. Gene knockdown of PKG1α with siRNA blunted VPN’s inhibition of ER stress and apoptosis (n=6, P<0.05), while overexpression of PKG1α resulted in significant decreased ER stress and apoptosis.

**Conclusions:** VPN protects diabetic heart against MI/R injury by inhibiting ER stress and apoptosis (n=6, P<0.05).

**Acknowledgement/Funding:** Supported by the NSFC (81270330 and 81300190) and the Shaanxi Province S & T Program (2013KJJX-89).

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**P3444 | BENCH**

Hyperglycaemic exacerbation of myocardial ischaemia/reperfusion injury is mitigated by SGLT inhibition

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**Background:** Epidemiological data reveal that hyperglycaemia in the context of acute myocardial infarction (AMI) is associated with higher morbidity and mortality when compared to normoglycaemia. Both diabetics and non-diabetics are affected, but non-diabetics suffer a greater augmentation of risk compared to diabetics with equivalent plasma glucose. The mechanism underlying the adverse relationship between glucose and outcome is unclear.

**Purpose:** To determine whether hyperglycaemia dose-dependently exacerbates myocardial infarct size. Moreover, we hypothesised that injury would be more marked in non-diabetics than in diabetics, and that this excess of injury would be mitigated by reduction in myocardial glucose uptake by administration of a sodium/glucose transporter (SGLT) inhibitor.

**Methods:** Male Sprague Dawley rats (SDR) and weight-matched diabetic Goto-Kakizaki rats (GKR) underwent Pentabarbitone euthanasia and heart harvest. Cardiac function was maintained on a Langendorff perfusion rig supplying modified Krebs-Henseleit buffer (KHB) with 11mmol Glucose at 70mmHg. Anterior ischaemia was induced left coronary artery ligation for 35 mins, followed by 60 mins reperfusion with KHB containing 5, 11, 16.5 or 22mmol Glucose, using D-Mannitol to maintain osmolality, with or without the non-selective SGLT inhibitor Phlorizin. Infarct size (IS) as a proportion of the area at risk (AAR) was quantified by tetrazolium chloride-based planimetry.

**Results:** IS with 11mmol Glucose was 45±2.6% of AAR in SDR and 31±4.6% in GKR (p<0.05). SDR hearts reperfused with 5mmol and 22mmol Glucose had significantly reduced myocardial IS compared with normoglycaemia (15±1.8% and 25±1.3%, respectively, p<0.05). Moreover, myocardial IS in diabetic GKR hearts reperfused with 5mmol and 22mmol Glucose were 23±3.8% and 30±2.7%, respectively (p<0.05). Neither severity of myocardial infarction (troponin T and creatine kinase) nor extension of coronary heart disease or tissue hypoperfusion did correlate with level of DNA damage.

**Conclusions:** A single RIPC manoeuvre induces the release of (a) dialyzable, humoral factor(s) which reduce(s) infarct size no later than after 30 min and remain(s) operative for up to 6 days after RIPC. These results imply that cardioprotection is at least in part effected by a factor which is quickly released/activated and present for quite some time after the RIPC manoeuvre.

**Acknowledgement/Funding:** Supported by IGA MZCR NT13709-3/2012.
P3447 | BENCH
Endothelial progenitor cell-conditioned medium delivery by polymer nanoparticles in an ischemic hindlimb model
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Background: Endothelial progenitor cells (EPCs) contribute to ischemic repair by paracrine factor secretion, with hypoxic stress up-regulating factors related to cell survival, proliferation, and tissue repair. Thus, tissue repair and ischemic tissue revascularization may be improved using EPC-conditioned medium (CM) (which has been demonstrated effective for ischemic tissue revascularization). Nanoparticles (NPs) have been controlled in ischemia. Polymeric NPs could deliver CM to ischemic regions. We investigated the efficacy of CM-NPs in an ischemic hindlimb model immediately after ischemia and after 1 week. The effect of ischemia was evaluated by using Laser Doppler Blood Flow imaging (ratio between ischemic and contralateral limb), histology (hematoxylin/eosin, H&E, staining) to evaluate the microvascular composition, and immunohistochemistry to evaluate capillary density (CD31+) and artery (alpha-smooth muscle actin, alpha-SMA+) number per mm².

Results: A significant increase of perfusion was observed at 2 weeks in CM-NP vs. both CM and control (p<0.005 vs. control). In control, tissues showed a normal morphology, while in both CM and CM-NP, at 1 week, we observed myocyte coagulative necrosis with enlarged interstitium mainly populated by inflammatory infiltrates and thin-walled new vessels, more extensively in CM-NP vs. CM. At 2 weeks, fibrin replacement of necrotic myocytes was found together with new vessels. Immunohistochemistry evidenced a significant increase of capillaries in rats treated with both CM and CM-NPs. Treatment with CM-NP significantly increased capillary number at both 1 (p<0.05 vs. control) and 2 weeks (p<0.0005 vs. control and p<0.0005 vs. CM), while CM treatment had a significantly higher effect than control only at 2 weeks (p<0.005). No significant difference in the number of arteries among different groups was observed, suggesting a more pronounced effect on angiogenesis rather than arteriogenesis.

Conclusions: Novel therapeutic strategies based on EPC paracrine factors may replace cell transplantation, as “cell-free” therapy could overcome the risk of adverse immunological reactions and the problem of heterologous rejection. Release of EPC-CM from loaded NPs would be effective for blood flow and capillary enhancement in an in vivo model of ischemic hindlimb ischemia, underlining the advantages of using controlled release in regenerative medicine.

P3448 | BENCH
Circulating microRNAs as potential novel biomarkers for clinical outcome in patients with acute coronary syndrome
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Background: MicroRNAs (miRNAs), small RNAs, which interfere with gene expression at the post-transcriptional level, have been identified as critical mediators of cardiovascular disease. miRNAs relevant for cardiovascular biology are dysregulated in patients with coronary artery disease and heart failure. Release of miRNAs from tissue conditioned medium (CM) has been demonstrated effective for ischemic tissue revascularization. Nanoparticles (NPs) for controlled release in ischemia might represent a promising application. Hitherto, the use of CM-NPs has not been performed.

Purpose: Analysis of prognostic impact of c-miRNAs related to major adverse cardiovascular events (MACE).

Methods and results: In a prospective multi-center Swiss-ACS cohort study, 2168 patients with ACS undergoing coronary angiography were enrolled between December 2009 and October 2012 with post-interventional follow-up (FUP) at 1 year. The novel prognostic c-miRNA levels in plasma were measured in 500 μL plasma samples from 225 patients with ST-elevation myocardial infarction (STEMI) at presentation and 500 μL plasma samples from 225 patients with non-STEMI at 1 year FUP. c-miRNAs significantly associated included c-miR-18, c-miR-15 and c-miR-19, which were reported to be involved in experimental ischemic injury and heart failure, c-miR-30, which is involved in left ventricular hypertrophy and c-miR-20, which inhibits cardiomyocyte apoptosis.

Conclusions: The present study reveals c-miRNAs significantly associated with MACE at 1 year FUP in patients with STEMI derived from a multi-center prospective ACS-cohort. The identified c-miRNAs need to be further validated for the potential of predicting MACE.

Acknowledgement/Funding: Swiss National Foundation - SNF

P3449 | BEDSIDE
The difference in rates of postprocedure ischemia in side branch and main branch after coronary bifurcation stenting detected with intracoronary electrocardiography
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Background: The aim of the study is to explore the differences in the rate of end procedural ischemia after bifurcation lesion PCI detected with intracoronary electrocardiography (iECG) and the exploration of causation mechanisms.

Methods: After placement of intracoronary guidewires in the main branch (MB) and in the side branch (SB), the intracoronary electrocardiography was performed for 5 minutes after the procedure. The maximal ST elevation during intervention and 5 min after the procedure was recorded in SB and MB. Intracoronary coronary wire was placed in every distal vessel with reference caliper >1.0 mm, as well as in MB just below the stent, “mapping” zones for ischemia presence and distribution. Changes in ST-segment, QRS complex, QT-interval prior and at the end of PCI were analyzed. Provisional T-stenting was the default strategy.

Results: The patient population consists of 147 patients with stable/unstable angina: 70 males, mean age 66±8, diabetes 34%: 37% had previous MI, 48% previous PCI and 58% multivessel disease. Main vessel treated - LAD (72%). The true bifurcation lesions (Medina xx1) were 51%. Maximal ST elevation on iECG was 12.9±9 mm in MB and 8±7 mm in SB (p=0.044). At the end of the procedure, the distribution of iECG changes was as follows: MB ST changes (STC) 36%, SB STC 34%, MB or SB STC 52%. Occlusion of secondary small branches (1.0–2.0 mm reference diameter) occurred in 6.4% (9 pts). After multivariate analysis the independent associates of residual ischemic changes on iECG were the ratio of R/S waves at the beginning of PCI in main branch (OR 3.58, CI 1.164–11.034, p=0.026), and the lack of SB ostial stenosis - 75% (OR 0.112, CI 0.024-0.512, p<0.005). The residual ischemia in MB (STC) was also significantly related with TST % (14.2% vs. 6%, p=0.031) and FMD (8% vs. 4%, p=0.031).

Conclusion: The end-PCI intracoronary ECG ST-segment changes combined with occurrence of secondary branch occlusion are frequent events after coronary bifurcation single stenting with provisional strategy. The residual ischemia in MB region is associated with higher revascularization rates as follow-up.

P3450 | BEDSIDE
The effects of serum klotho levels on endothelial function and early atherosclerosis predictors in healthy population
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Background: The aging gene suppressor klotho encodes a single-pass transmembrane protein that relieves sodium and calcium (Ca2+/Na+) entry by inhibiting nitric oxide (NO) availability and to protect against endothelial dysfunction. In some recent trials showed that klotho levels is associated with lower cardiovascular disease prevalence. Epidermal fat thickness (EFT) and carotid intima-media thickness (c-IMT) are closely related to subclinical atherosclerosis. Flow-mediated dilation (FMD) is a non-invasive method of detecting endothelial dysfunction. The association between serum Klotho levels and early atherosclerosis predictors like EFT, c-IMT and FMD is undefined in healthy population.

We aimed to investigate the relationship between serum Klotho levels and early atherosclerosis predictors in healthy population.

Methods: Total of 50 healthy volunteers (21men and 29 women, aged 32 (27–38)) were enrolled in this study. Study population was divided into two subgroups according to serum klotho levels.EFT measurements were done with echocardiography. The c-IMT and FMD measurements were achieved by ultrasonography.

Results: The ages, body mass indexes and all biochemical assessments of the subgroups were similar. The EFT (0.75 (0.70–0.80) vs.0.55 (0.30–0.6, p=0.03) and c-IMT (0.80 (0.60–
0.90 v.s.0.45 (0.39–0.55), p<0.001) values of klotho lower subgroup were signific-
antly larger than the klotho higher subgroup. Klotho higher subset had signifi-
cantly higher FMD values than Klotho lower subgroup (9.1 (4.5–19.3) v.s. 15.9
(9.6–34.3), p<0.03).
Conclusion: Klotho higher subgroup had significantly better EFTo-IMT and FMD
values. Therefore, Klotho levels in healthy population may have protective effect
against atherosclerosis and endothelial dysfunction.

ACUTE INTENSIVE CARDIOVASCULAR CARE I

P3451 | BEDSIDE
Incremental value of copeptin with high sensitivity cardiac troponin T for exclusion of severe coronary stenosis in patients with preexisting coronary artery disease
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1 University Hospital Arnaud de Villeneuve, Montpellier, France; 2 University Hospital of Montpellier, Montpellier, France

Background: Acute chest pains without troponin raise are particularly challeng-
ing in patients with past medical history of coronary artery disease (CAD).

Methods: We included 1149 STEMI pts admitted, consecutively, receiving contempo-
rary treatment.

Purpose: To evaluate the incidence of HABV and its impact on outcome of STEMI pts,

Results: Mean time between chest pain onset and blood samples of copeptin was 4±2
hours. According to clinical decision, coronary angiography was performed in 63
patients (69.2%), with 12 severe stenosis diagnosed (19%). No ischemia was
detected with the stress tests (28 patients). Among the 52 patients with a negative
hs-cTnT assay was validated as reported previously
(Ammann et al. Acute coronary syndrome (ACS) was excluded with ECG
sensitivity. Specificity Positive predictive value Negative predictive value
Sensibility Specificity Positive predictive value Negative predictive value

hs-cTnT < 14 ng/L and change at 3 hours (n=91)
Copeptin < 10 pmol/L + hs-cTnT < 14 ng/L (n=71) 0.73, CI (0.604–0.830)
Copeptin < 10 pmol/L + negative kinetic of hs-cTnT at 3 hours (n=52) 0.79, CI (0.4–0.972)

Abstract P3451 – Table 1. Predictive values of hs-cTnT and copeptin

Conclusion: Besides low incidence of HABV, this complication continues to have a high risk of in-hospital and 6-month mortality and occurring with AMI the risk increases significantly.

P3453 | BEDSIDE
Factors associated with subacute or late cardiac tamponade in the postoperative period of cardiac surgery. A case-control study
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Introduction: Cardiac tamponade (CT) following cardiac surgery is a potentially fatal complication and the cause of surgical reinsertion in 0.1 to 6% of cases.

Methods: This monocentric prospective study included 91 consecutive patients
with the development of slCT.

Conclusions: Our study identifies five variables associated with slCT, and estab-
lishes that this is a complication with a high mortality rate. These findings may
improve the incidence and death associated with HABV at 6 months; p=0.006

Acknowledgement/Funding: Instituto de Cardiologia-Fundacion Cardioinfantil

P3454 | BEDSIDE
Non-occlusive mesenteric ischemia (NOMI) after out of hospital cardiac arrest: incidence and outcome of an underappreciated phenomenon
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Non-occlusive mesenteric ischemia (NOMI) is characterised by hy-
popusseration of the intestines without evidence of mechanical obstruction, poten-
tially causing need for extensive necrosectomy. In our cohort 14 vs 60.3%, presented more often AKI-1 (71.4
vs 37.2%; p<0.001), left ventricular dysfunction (10 vs 34.8%; p<0.001), but less
right ventricular dysfunction (71 vs 28.4%; p<0.001). Compared with IMI pts, AMI
pts had higher risk of in-hospital [OR 9.04, 95% CI (2.87–38.50); p<0.001] and 6-
month mortality [OR 10.88; 95% CI (3.33–35.53); p<0.001]. After adjusting for
different baseline characteristics in multivariate analysis, HABV patients had higher
risk of overall 6-month mortality compared to those without HABV [OR 2.18, 95%
CI (1.25–3.79); p<0.006].

Purpose: The primary objective of this study is to identify the factors associated
with the development of slCT.

Methods: A case-control study of a historic cohort made up of all the adult pa-
tients who underwent cardiac surgery between 2006 and 2013 in a Level III car-
diovascular institution. The data base review showed a global incidence of CT of
2.1% equal to 78 patients (cases) with sCT. For the adjusted analysis, a logistical
model was constructed with 55 variables including pre-, intra-, and post-operative
data. A stepwise technique was employed, starting from a complete model. The
model's calibration was evaluated using the Hosmer-Lemeshow test.

Results: Seventy-eight cases are compared to 158 controls. Of these 78
patients, 23 were CABG (29%), 24 were aortic valve replacement (30%), and 18
were mitral valve replacement (23%). sCT presented on the third POP day in 8
cases (10%), between 7 and 14 days POP in 48 cases (61%), and the remaining
cases were distributed between the third and fourth week. Mortality of patients
with sCT was 11% vs. 0% in the controls. Among the 55 evaluated variables, 5
were identified as independently and significantly associated with the outcome:
pre- or post-operative anticoagulation, re-intervention in the first 48 hours, surgery
other than CABG, and red blood cell transfusion. The goodness of fit tests shows
that the proposed model fits the observations.

Conclusions: Our study identifies five variables associated with sCT, and estab-
lishes that this is a complication with a high mortality rate. These findings may
allow the implementation of standardized, intensive, follow-up measures for pa-
tients identified as higher-risk, in order to detect this complication early or prevent it.

Acknowledgement/Funding: Instituto de Cardiologia-Fundacion Cardioinfantil

P3455 | BEDSIDE
High-grade atrioventricular block in ST-segment elevation myocardial infarction patients: insights of a tertiary centre

Background: High-grade atrioventricular block (HABV) is associated with poorer
outcomes in the setting of acute coronary syndromes. Limited information is avail-
able on the incidence and death associated with HABV in STEMI patients (pts)
receiving contemporary treatment.

Aim: To evaluate the incidence of HABV and its impact on outcome of STEMI pts,
in primary percutaneous coronary intervention era.

Methods: We analysed retrospectively 1149 STEMI pts admitted, consecutively,
in our coronary unit, from July of 2009 to June 2014. HABV was defined as the
presence of either Mobitz II 2nd degree AV block or 3rd degree AV block. Pts
were divided in two groups: group 1 – pts without HABV (n=1057, 92%); group
2 – pts with HABV (n=92, 8%). For each group we compared clinical features and
adverse events. Primary endpoint was the occurrence of death at 6 months; follow-up was completed in 99% of pts.

Results: Pts of group 2 were older (62±13 vs 69±15 yrs; p<0.001), more fre-
quent women (19 vs 30.4%; p<0.014) and had higher prevalence of hyperten-
sion (57.3 vs 71.7%; p<0.008). On admission, group 2 presented more often
Killip > 1 (18 vs 42.4%; p<0.001), cardiacogenic shock (2.9 vs 23.1%;p<0.001),
aemia (20.7 vs 38.9%; p<0.001), renal insufficiency (egFR–60 ml/min)
(20.7 vs 50.6%; p<0.001) and higher prevalence of right systolic dysfunction
(5.3% vs 28.9%; p<0.001). They required more often aminoglycoside support
(4.2 vs 4.4%; p<0.001), intra-aortic balloon pump (4.3 vs 6.6%; p<0.05) and mecha-

valentiation (2.6 vs 14.5%; p<0.001). They also had higher prevalence of ma-

lignant arrhythmias at first 24h (6.5 vs 14.1%; p<0.017) and in-hospital mortality
(3.7 vs 24.2%; p<0.001). Among 2nd group of pts, HABV was present on admis-
sion in 43.5%; 15.2% (n=14) had anterior myocardial infarction (AMI) and 84.8%
(n=78) inferior myocardial infarction (IMI). Those with AMI implanted temporary
pace-makers more frequently (71.4 vs 60.3%), presented more often AKI-1 (71.4
vs 37.2%; p<0.001), left ventricular dysfunction (10 vs 34.8%; p<0.001), but less
right ventricular dysfunction (71 vs 28.4%; p<0.001). Compared with IMI pts, AMI
pts had higher risk of in-hospital [OR 9.04, 95% CI (2.87–38.50); p<0.001] and 6-
month mortality [OR 10.88; 95% CI (3.33–35.53); p<0.001]. After adjusting for
different baseline characteristics in multivariate analysis, HABV patients had higher
risk of overall 6-month mortality compared to those without HABV [OR 2.18, 95%
CI (1.25–3.79); p<0.006].

Conclusion: Besides low incidence of HABV, this complication continues to have a high risk of in-hospital and 6-month mortality and occurring with AMI the risk increases significantly.
Methods: A prospectively maintained database of out of hospital cardiac arrest survivors, that had successful restoration of spontaneous circulation (ROSC), was retrospectively screened for clinical, radiological or pathological evidence of NOMI.

Results: 2469 patients treated between 1991 and 2014 were included into the analysis. Thirteen patients (0.5%) suffered from NOMI and 10 of them died (54%). Patient characteristics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>NOMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiology</td>
<td>2456</td>
<td>13</td>
</tr>
</tbody>
</table>

Time from cardiac arrest to median in minutes (IQR)

- Begin of CPR: 0 (1-7) 0.5 (0-6) n.s.
- ROSC: 20 (10-30) 27 (13-66) n.s.

First monitored rhythm n (\%)

- Ventricular fibrillation: 1343 (55) 2 (17) n.s.
- Asystole: 562 (19) 6 (22) n.s.
- PEA: 498 (20) 5 (22) n.s.

Clinical measurements at admission median (IQR)

<table>
<thead>
<tr>
<th>Lactate (mmol/L)</th>
<th>Base excess</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 (5-12)</td>
<td>15 (10.5-18.3) 0.01</td>
</tr>
<tr>
<td>Base excess -10 (-15 to -6) -18 (-23 to -14) 0.002</td>
<td></td>
</tr>
</tbody>
</table>

CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; PEA, pulseless electrical activity.

Discussion: NOMI is rarely a rare but dangerous complication following successful CPR. Lactate and base excess at admission could help to identify patients at risk for developing NOMI who might benefit from increased clinical watchfulness.

P3456 | BEDSIDE
Effective heart rate control by ivabradine in patients with acute heart failure
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Background: The therapeutic value of selective heart rate modification with ivabradine has been established for chronic heart failure. Intensive care patients frequently manifest with elevated heart rate, which is known to be related with increased mortality. Heart rate control may be associated with reduced morbidity and mortality in critically ill patients. In acute cardiac care, however, elevated heart rates constitute an even more frequent problem, while the use of ß-blockers would come along with a further reduction in cardiac inotropy and blood pressure. Thus, we evaluated efficacy and safety of ivabradine for heart rate reduction in acute heart failure patients with persistently elevated heart rates.

Methods and results: Between October 2010 and July 2014 we prospectively treated 69 patients (age 57±16 y; 49 males vs. 20 females) acutely admitted to our intensive care unit for acute heart failure or cardiogenic shock (n=19). Acute heart failure resulted from myocardial ischemia (65%), decompenated heart failure (17%), valve disease (4%) and other pathologies (7%); 17% of patients had been resuscitated. Patients were critically ill; 29 required CPR. Lactate and base excess at admission could help to identify patients at risk for developing NOMI who might benefit from increased clinical watchfulness.

Abstract P3456 – Table 1. Indications for IABP use

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Cardiology</th>
<th>Surgical</th>
<th>Pre-op</th>
<th>Intra-op</th>
<th>Post-op</th>
<th>Cardiogenic shock</th>
<th>TVD / LMS disease / Ischaemia</th>
<th>PPCI</th>
<th>High risk PCI</th>
<th>VSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>39</td>
<td>29 (74.4%)</td>
<td>6 (15.4%)</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
<td>0.05;</td>
</tr>
<tr>
<td>2012</td>
<td>71</td>
<td>36 (50.7%)</td>
<td>35 (49.3%)</td>
<td>31 (43.7%)</td>
<td>4 (2.8%)</td>
<td>2.8%</td>
<td>2.8%</td>
<td>25 (35.2%)</td>
<td>2.8%</td>
<td>25 (35.2%)</td>
<td>2.8%</td>
</tr>
<tr>
<td>2013</td>
<td>86</td>
<td>34 (39.5%)</td>
<td>52 (60.5%)</td>
<td>45 (52.3%)</td>
<td>1 (1.2%)</td>
<td>6 (7.0%)</td>
<td>19 (22.1%)</td>
<td>4 (4.7%)</td>
<td>9 (10.5%)</td>
<td>5 (5.8%)</td>
<td>3 (3.5%)</td>
</tr>
<tr>
<td>2014</td>
<td>52</td>
<td>14 (26.9%)</td>
<td>38 (73.1%)</td>
<td>36 (67.3%)</td>
<td>1 (1.9%)</td>
<td>2 (3.8%)</td>
<td>9 (17.3%)</td>
<td>2 (3.8%)</td>
<td>7 (13.5%)</td>
<td>1 (1.9%)</td>
<td>1 (1.9%)</td>
</tr>
</tbody>
</table>

Discussion: In this study pts presenting WOCP had a worse prognosis with more diabetic and hypertensive and with a higher prevalence of previous heart failure (HF), valvular heart disease, previous stroke, peripheral artery disease, renal failure, neoplasia, chronic obstructive lung disease and dementia. The main complaint was dyspnea (49.4%) followed by non-cardiovascular symptoms (22.2%) and syncope (21.2%). Time to first medical contact was similar between groups but time from symptoms onset to admission (TSOA) and time from first medical contact to admission were significantly higher in pts WOCP (median 289 vs 194 minutes; p<0.001 respectively). In multivariate analysis presentation WOCP was not an independent predictor for in-hospital mortality.

Conclusion: In this study the main indication for IABP use remains patients with poor LV function undergoing elective or urgent CABG surgery. A decrease in IABP use in patients with cardiogenic shock has been observed and this may represent clinicians adopting a more conservative approach in the light of current evidence.

P3457 | BEDSIDE
Acute coronary syndromes without chest pain: a high risk group?
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Introduction: Many patients (pts) with acute coronary syndromes (ACS) have atypical symptoms and don’t complain of chest pain. Some studies point to a worse prognosis of these pts because of misdiagnosis and undertreatment. The aim of this study was to compare the prognosis of the patient with ACS that presents without chest pain (WCP) to the one with typical clinical presentation (WCP).

Methods: We retrospectively analyzed the registries of ACS’s included in the Portuguese National Registry of ACS, between October of 2010 and October 2014. We compared pts WCP and WOCP at presentation regarding demographic data, cardiovascular risk factors and previous history, admission data, coronary angiography results, treatment and complications during hospitalization. Then we analyzed the prognostic implications of presentation WOCP when considering the clinical shock. The main outcomes were in-hospital mortality (IH). Pts presenting in cardiac arrest were excluded.

Results: A total of 11058 ACS were considered, 999 (9.0%) WOCP at presentation. The most common type of ACS was without ST-segment elevation (61.8%). Pts WOCP were mostly males (57.2%) and significantly older, more frequently with hypertension (45.2%) compared with WCP (38.1%). The main comorbidities were more frequent in this group (60.7% vs 49.5%; p<0.001) and base excess levels at admission were significantly higher in pts WOCP (−18 vs −10; p=0.002) (Table 1).

Discussion: In this study pts presenting WCP had a worse prognosis with more severe comorbidities and significantly older. More frequently were males, hypertension, dyslipidemia, diabetes and obesity. At admission were more frequently with significantly lower base excess levels. Patients WOCP were more frequently admitted to the cardiac catheter laboratory. The use of ivabradine appears to be safe and effective in controlling elevated heart rates in acute heart failure patients. The benefits from heart rate reduction may relate to improved stabilization and recovery of these critically ill patients.
circumstances during hospitalization including higher IHM. This higher risk didn’t seem to be explained by delayed start of treatment or the type of ACS.

**ISCHAEMIA, EXPERIMENTAL STUDIES II**

**P3458 | BEDSIDE**

Circulating endothelial progenitor cells are actively involved in the reparative mechanisms of stable ischemic myocardium

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**Background and aim:** Mobilization of endothelial progenitor cells (EPCs) into circulation from bone marrow in patients with acute cardiac infarction has strong scientific evidence however less is known about EPC mobilization in patients with stable ischemic heart disease. The aim of this study was investigate the impact of stable ischemic heart disease on EPC level both in tissue and blood. Methods: Consecutive patients admitted at our hospital for valve or CABG surgeries were included in the study. Exclusion criteria were emergencies and redo surgeries. Blood samples were collected in the morning before surgery and analyzed by flow-citometry in order to evaluate peripheral EPC levels (EPCEn). Tissue CD34+/VEGFR2+ cells level was evaluated on a right atrial appendage segment collected during cardioplegia induction. Tissues were fixed in formalin and embedded in paraffin. Three μm sections were quantified immunohistochemically by counting double positive cells. Continuous data are expressed as mean ± SD, categorical data are expressed as frequency or percentage. T test was used in paired data. The interaction between the number of CD34+ VEGFR2+ cells and coronary artery disease was examined by multivariate analysis using the logistic regression model. Differences of p<0.05 were considered statistically significant.

**Results:** 55 patients were included in the study. 46% were male with a mean age of 76±5. 53% of patients had coronary artery disease (CAD). 21% of patients had positive family history, 80% had hypertension, 22% of patients were smoker and 25% of patients were obese. The number of CD34+ VEGFR2+ cells in the tissue of patients with CAD was significantly higher when compared with control subjects (30/mm² vs 20/mm² p<0.005) and circulating EPC showed a tendency to be reduced by approximately 20% in peripheral blood of patients with CAD when compared with CAD controls.

**Conclusion:** Patients with ischemic heart disease have higher EPC density value (EPC/mm²) and are more likely to have lower EPC blood levels when compare with controls. These results show that chronic ischemic heart disease, same as acute myocardial infarction, can be a stimulus to increase bone marrow mobilization and homing in myocardium. However more studies needed to confirm these evidences in larger population.

**P3459 | BENCH**

Inhibition of Rap1 enhances mesenchymal stem cells-mediated heart protection following myocardial infarction

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**Background:** Mesenchymal stem cells (MSCs)-based therapy for myocardial infarction (MI) is mainly through paracrine effects responsive to different stimuli. However, the molecular mechanism regulating paracrine polarization of MSCs remains elusive.

**Purpose:** This study was investigated to role of Rap1 in regulation of cytokine profiling of bone marrow-MSCs (BM-MSCs) treatment for myocardial infarction (MI).

**Methods and results:** Rap1+/−/− BM-MSCs and BM-MSCs were isolated from Rap1−/− and wild type mice respectively. Neonatal cardiomyocytes (NCMCs) were isolated from neonatal rat. The conditioned mediums (CDM) of Rap1+/−/− BM-MSCs and BM-MSCs under normoxia or hypoxia were collected and concentrated. The secreted cytokines especially the inflammatory cytokines were measured. MSCs apoptosis under normoxia or hypoxia were determined by TUNEL staining also demonstrated that the apoptosis of NCMCs induced by hypoxia was significantly reduced when treated with Rap1+/−/− BM-MSCs compared with BM-MSCs hypoxic CDM. Analysis of cytokines revealed that the pro-inflammatory cytokines in Rap1+/−/− BM-MSCs hypoxic CDM were greatly reduced compared with BM-MSCs hypoxic CDM. These effects were associated with inhibition of NFκB signal pathway. Furthermore, in vivo study showed transplantation of Rap1+/−/− BM-MSCs significantly improved heart function, decreased infarction size, prevented CMCs apoptosis and inhibited inflammation compared with MI and BM-MSCs group (p<0.01).

**Conclusions:** Transplantation of Rap1+/−/− BM-MSCs effectively improved heart function following MI. Compared to BM-MSCs, superior therapeutic efficacy of Rap1+/−/− BM-MSCs against MI may be attributed to their enhanced cell survival and paracrine actions.

**P3460 | BENCH**

Selective inhibition of receptor activator of NFκB ligand (RANKL) in hematopoietic cells improves outcome after experimental myocardial infarction in mice

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**Background:** The RANK/RANKL/osteoprotegerin signalling axis is activated after myocardial infarction (MI) but its role in the pathophysiology of cardiac dysfunction is not yet known.

**Purpose:** We investigated the effects of global RANKL inhibition and selective inhibition of RANKL derived from different cells sources on post-ischemic cardiac function and remodelling.

**Methods:** MI was induced by permanent ligation of the left descending coronary artery (LAD). To establish a model for selective inhibition of RANKL from hematopoietic and mesenchymal cells sources, we exploited the specificity of the monoclonal anti-human RANKL antibody AMG161 to inhibit human but not murine RANKL, together with human RANKL knock-in (huRANKL-KI) mice that express a chimeric RANK protein wherein most of the RANK binding domain is human. Lethal irradiation and reconstitution with unfractonated bone marrow leads to engraftment of hematopoietic, but not mesenchymal progenitors. Thus, AMG161 treatment selectively inhibits RANKL derived from hematopoietic or mesenchymal cellular sources based on cross-genotype bone marrow transplantation between wild-type (WT) and huRANKL-KI mice. Global RANKL protein inhibition was achieved by treatment of non-irradiated huRANKL-KI mice with AMG161. AMG161 or an isotype control antibody was s.c. injected over 4 weeks post-MI. Cardiac function was assessed by echocardiography and intra-cardiac catheter. Infarct size was assessed using Masson’s trichrome staining. Transcription of cytokine genes was measured by quantitative PCR analysis.

**Results:** MI induced RANKL expression mainly in cardiomyocytes and infiltrating cells adjacent to the infarct region. MI significantly decreased fractional shortening (FS) and contractility. Global RANKL inhibition by AMG161 in un-transplanted huRANKL-KI mice did not affect survival, cardiac function or infarct size after MI. Similarly, AMG161 treatment did not influence cardiac function in huRANKL-KI mice reconstituted with WT bone marrow. However, AMG161 administration to WT mice reconstituted with huRANKL-KI bone marrow significantly improved FS for about 5%. Infarct size did not differ between the groups. Interestingly, inhibition of RANKL derived from hematopoietic sources, but not inhibition of total or mesenchymal RANKL, reduced the expression of pro-inflammatory genes such as IL-6 and TNFα in the left ventricle and also in bone marrow post-MI.

**Conclusion(s):** Inhibition of RANKL derived from hematopoietic cellular sources has beneficial effects on post-ischemic cardiac function by reduction of inflammatory cytokine production.

**Acknowledgement/Funding:** The Austrian Science Fund (FWF) grant to Erben G Reinhold.

**P3461 | BEDSIDE**

Intracoronary adenosine: dose-response relationship with hyperemia

J.A. Adjei 1, J. V. Tosti 2, N.P.J. Johnson 3, M.P. Pellicano 4, A.F. Ferrara 1, V.F. Flore 1, G.D.G. Di Gioia 1, E.B. Barbato 1, O.M. Muller 1, B.D.B. De Bruyne 1. 1 Ov Hospital Aalst, Cardiology, Aalst, Belgium; 2 Weatherhead PET Center for Preventing and Reversing Atherosclerosis, Division of Cardiology, Department of Internal Medicine, University of Texas Medical School and Methodist Hospital, Houston Texas, United States of America; 3 University Hospital Centre Vaudois (CHUV), Department of Cardiology, Lausanne, Switzerland

**Background:** Despite the widespread adoption of intracoronary (IC) adenosine in clinical practice, no wide-ranging, dose-response study has been conducted.

**Purpose:** The present study sought to establish the dosage of IC adenosine as effective in small clinical dose with minimal side-effects and above which no further increase in flow can be expected.

**Methods:** In 30 patients, Doppler-derived flow measurements were obtained in 10 right coronary arteries (RCA) and 20 left coronary arteries (LCA) free and 10 min after administration of 9 escalating doses of adenosine (4 to 500 μg). The hyperemic value was expressed in percent of the maximum flow velocity reached in a given artery (Q_Dmax, %)

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Results: Q/Omax did not increase significantly beyond dosages of 60 μg for the RCA and 160 μg for LCA. Heart rate did not change, while mean arterial blood pressure decreased by a maximum of 7% (p<0.05) after bolus injections of IC adenosine. The incidence of transient atrio ventricular blocks was 40% after injection of 100 μg in the RCA, and was 15% after injection of 200 μg in the LCA. The bolus injection of 100 μg in the RCA and 200 μg in the LCA induces maximum hyperemia while being associated with minimal side effects.

Acknowledgement/Funding: Financial support: Research grant from Fedecardio.

Conclusions: This wide-ranging dose-response study indicates that an IC adenosine bolus injection of 100 μg in the RCA and 200 μg in the LCA reduces maximum hyperemia and is associated with minimal side effects.

P3462 | BENCH
Early detection of low-grade myocardial ischemia by miniaturized 3-axis accelerometer
S. Hyler1, S. Pischke2, O.J. Grynmyr1, A. Espinoza2, H. Skulstad3, J. Bergsland1, E. Foess1, P.S. Halvorsen1 on behalf of The Research Group on Advance Cardiovascular Monitoring. 1Oslo University Hospital, The Intervention Centre, Oslo, Norway; 2Oslo University Hospital, The Department of Anaesthesiology and Intensive Care Medicine, Oslo, Norway; 3Oslo University Hospital, The Department of Cardiology, Oslo, Norway

Background: Myocardial ischemia is a leading cause of death after heart surgery and sensitive methods for early detection are still needed. We tested a miniaturized 3-axis (3D) accelerometer for detection of myocardial ischemia and hypothesized the method could quantify the degree of myocardial ischemia during coronary artery flow reductions.

Methods: In 8 pigs, 3D accelerometers and intramyocardial microdialysis catheters were positioned in the left anterior descending (LAD) and circumflex (CX) coronary artery areas. During beating heart surgery with intracoronary shunt the left internal mammary artery (LIMA) was grafted to the LAD, which was occluded proximal to the anastomosis. Flow in LIMA was stepwise reduced by 25% to 100% (BL) to 75%, 50%, and 25% for 18 min each. From the 3D accelerometer signals 3D peak systolic velocity was obtained by time integration of the acceleration signals. The reference method to detect myocardial ischemia was tissue lactate by microdialysis.

Results: Reduced systolic velocity by the 3D accelerometer was observed at all steps of coronary flow reduction and the decreases in velocity correlated closely to the degree of myocardial ischemia as measured by tissue lactate (R=−0.95, P<0.01) (Figure). There were no significant changes in 3D accelerometer systolic velocity and tissue lactate in CX area during the reductions in coronary artery flow.

Conclusions: The epicardially attached miniaturized 3D accelerometer enabled quantifying different levels of myocardial ischemia during stepwise reductions in coronary artery flow. A linear relationship among coronary blood flow, myocardial ischemia and function was found. These results demonstrate that 3D accelerometers can be used to detect graft failure during and after heart surgery.

Acknowledgement/Funding: The study was funded by The Norwegian Health Authorities.
Beclin-2. Inhibition of Traf6 and activation of mTORC1 are additional mechanisms in inhibiting apoptosis and autophagy.

**Acknowledgement/Funding:** CVRI Start-up Grant (NUS, Singapore) and NMRC Grant (Ministry of Health, Singapore)

### P3465 | BENCH

**Activation of orphan nuclear receptor ROR-alpha, but not ROR-beta and ROR-gamma, protects against myocardial ischemia/reperfusion injury**

J. Pu1, P. Zhang2, E. Gao3, X. Ma4, B. He1, 1 Renji Hospital of Shanghai Jiao Tong University School of Medicine, Department of Cardiology, Shanghai, China, People’s Republic of; 2 University of Maryland, Baltimore, United States of America; 3 Temple University School of Medicine, Philadelphia, United States of America; 4 Thomas Jefferson University, Philadelphia, United States of America

**Aims:** The retinoid-related orphan receptors (RORs) are very unique members of the nuclear receptor superfamily and involved in the physiological processes including regulation of the circadian rhythm, development, metabolism and immune function. Three different but highly homologous ROR isoforms, ROR-α, -γ, and -δ, have been discovered separately. However, the roles of RORs in the heart have never been investigated.

**Methods:** The endogenous RORe and RORγ expression was detected in the human and mouse heart tissues, as well as isolated cardiac myocytes and fibroblasts. RORe, but no RORγ or RORγ, was significantly up-regulated in mouse heart tissue and human atrium sample after in vivo ischemia and reperfusion (I/R) injury. Synthetic RORα and RORγ siRNAs reduced infarction and improved contractile function after MI/R in mice. Mechanistically, ROR activation inhibited ER stress (determined by the reduction of CHOP expression and caspase-12 activation), attenuated mitochondrial impairment (determined by the decrease of cytochrome c release and caspase-9 activation), and reduced cardiomyocyte apoptosis. Furthermore, ROR activation significantly inhibited autophagy dysfunction (determined by the inhibition of Beclin1 over-activation, and the reduction of autophagosomes, the LC3-II/LC3-I ratio, and p62 protein abundance). Moreover, ROR activation inhibited MI/R-induced oxidative stress (determined by the reduction of superoxide production and gp91phox expression)

**Conclusion:** Our study provides the first evidence that RORα inhibited gp91 promoter luciferase activity. Furthermore, deletion of the N- and C-terminals of RORe or RORγ-siRNA resulted in the loss of the RORα ability for the inhibition of gp91-luciferase activity, and CHIP assay showed that RORα antibody could pull-down the DNA-protein complex. Thus, RORα directly binds to the regulatory sequence of gp91 gene through ROR-responsive element.

**Results:** Our study suggests that RORα acts as a novel endogenous cardioprotective receptor. RORα, but not RORγ or RORγ, is a receptor against MI/R injury, supporting for the drug development strategies specifically targeting RORe for the treatment of ischemic heart disease.

**Acknowledgement:** Supported by National Natural Science Foundation of China (81330006, 81170192, 81470389, 81270282), and American Diabetes Association (7-11-BS-93).

### P3466 | BEDSIDE

**The investigation of the dynamic thiol-disulfide homeostasis in acute coronary syndrome**

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**Background:** The oxidative stress plays crucial role in the progression of atherosclerosis. It was known that increased oxidative stress and impaired antioxidation protection are more associated with acute coronary syndromes (ACS) than stable atheros. The plasma thiol (SH) is water-soluble and cytoplasmic antioxidant protein (glutathione), and the disulfide (SS) levels are measured by a novel and automated spectrophotometric method. The thiol-disulfide homeostasis was calculated as SH/SSHS ratio.

**Results:** In ACS and SA patients, SH and SHHS was significantly lower than control subjects (for each group, p < 0.001) (Figure 1A and 1B). The SH/SSHS ratio was significantly lower in all groups (ANOVA p = 0.240). The SH and SHHS values in patients with acute myocardial infarction were not different in patients with unstable angina (246±55 μmol/L versus 240±58 μmol/L; p = 0.596, and 12.44±6.21 μmol/L versus 10.80±7.04 μmol/L; p = 0.477, respectively). ROC curve analysis revealed that thiol levels over 260 μmol/L predicted ACS with 65% sensitivity and 62% specificity (area under the curve = 0.702, 95% CI 0.626–0.778).

**Conclusion:** These findings indicate that SH and SHHS level decrease in patients with ACS and SA. Decreased SH and SHHS level may be related with pathogenesis of coronary atherosclerosis.

**Acknowledgement/Funding:** Harran University Scientific Research Committee

### P3467 | BEDSIDE

**The effect of high loading dose of atorvastatin in ST elevation myocardial infarction patients undergoing percutaneous coronary intervention on microvascular perfusion**

S. Indriani, D. Firman, A. Santoso, A.M. Soesanto, University of Indonesia, Cardiology and Vascular Medicine, Jakarta, Indonesia

**Background:** Statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibition), given before percutaneous coronary intervention (PCI) was proven to reduce Major Cardiovascular Events (MCE) in patient with stable angina as well as acute coronary syndromes through its pleiotropic effect. Nevertheless, the debate regarding statin administration before primary PCI (PPCI) in ST elevation myocardial infarction (STEMI) patients is still on the rise.

**Purpose:** To establish therapeutic effect of high dose atorvastatin (80 mg) and placebo before primary PCI on microvascular perfusion in STEMI patient using index of microcircricular resistance (IMR).

**Methods:** This study is a double blind randomized controlled trial. A high loading dose of atorvastatin (80 mg) or placebo was administered before PPCI. Samples were taken from the population of STEMI patients which underwent PPCI and meet inclusion and exclusion criteria. The primary end point of this study is a change in IMR. IMR is specific and quantitative assessment of coronary microvascular dysfunction, reliable on-site predictors of short-term myocardial viability and left ventricle functional recovery of patients undergoing primary PCI for STEMI. After successful primary percutaneous coronary intervention, IMR was measured using a pressure-temperature sensor-tipped coronary guidewire.

**Results:** Total of 68 patients were divided into 2 groups, atorvastatin group (32 patients) and placebo group (34 patients). Baseline, angiographic and periprocedural characteristics were not significantly different between the atorvastatin and control group except for age and length of stent used, but they didn’t influence the IMR. The median of time from atorvastatin administration and IMR measurement was 120 minutes. On physiological study, there were no significant differences between the atorvastatin and control group in regard of fractional flow reserve (FFR) (median 0.94 vs. 0.96, p = 0.39) and coronary flow reserve (CFR) (median 1.1 vs. 1.21, p = 0.36). However, the effect of high loading dose of atorvastatin (80 mg) or placebo before primary PCI in STEMI patients didn’t improve microvascular perfusion as measured by index of microvascular resistance compared to placebo.

**Acknowledgement/Funding:** Self-funded

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**ACUTE INTENSIVE CARDIOVASCULAR CARE II**

### P3468 | BEDSIDE

**Does the timing of the initiation of intraaortic balloon pump therapy affect mortality in patients with acute coronary syndrome complicated by cardiogenic shock?**

G.T. Szabo, I. Bojti, I. Racci, I. Edes, Z.S. Koszegi, UDMHSC Cardiology Department, Debrecen, Hungary

**Introduction:** Based on literature data, the routine use of intraaortic balloon pump (IABP) in the treatment of acute coronary syndrome (ACS) complicated by cardiogenic shock is questionable. However, the available studies did not subselect patients in whom the cardiogenic shock has been developed later than the time of percutaneous coronary intervention (PCI), therefore the IABP therapy was initiated as a rescue therapy, with a certain time period following PCI.

**Purpose:** The present study aimed to investigate whether the timing of initiation of IABP therapy has any effect on in-hospital-, 30-days-, and 1-year mortality.

**Methods:** Patients with the need of IABP therapy due to cardiogenic shock between 2009 and 2012 were included in the study. Anamnestic and procedural data were collected. We focused on the determination of the area of myocardium at risk (AMR) affected by the culprit lesion. AMR was calculated in all
patients with the use of Holistic Coronary Care software, a program developed by
our study group.
Results: Among a total of 290 patients 45 received IABP as a rescue therapy. Amidst baseline clinical parameters the left ventricular ejection fraction (LVEF) and the glomerular filtration rate (GFR) was significantly higher in the rescue IABP group (LVEF 39% SD:8 vs. 34% SD:9, p=0.005; GFR [ml/min/1.73 m²]: 69 SD:22 vs. 60 SD:23 p=0.01). There was no significant difference in the calculated AMR between patients with rescue IABP therapy and those in whom IABP was inserted earlier, during the PCI (62.3% SD 25.8 vs. 58.6% SD 25.5; p=0.098). The in-
hospital mortality rate did not differ significantly in the two groups, while duration of hospitalization was significantly longer (22 vs. 17 days p=0.05) and the mortality rate was significantly higher at both 30 and 365 days in the rescue IABP therapy group as compared to those with earlier initiation of IABP therapy (16% vs. 3.8% p=0.018; 29% vs. 6% p=0.001 for 30 days and 1 year, respectively).
Conclusion: Patients with ACS who receive IABP therapy during the PCI due to an early development of cardiogenic shock have better survival at 30 and 365 days as compared to patients with the need of rescue IABP therapy.

P3470 | BEDSIDE
Mortality and the effect of of target temperature management (33 vs. 36) in comatose patients resuscitated from cardiac arrest does not differ between males and females
M. Winther-Jensen1, C. Hassager1, M. Wanscher2, N. Nielsen3, A. Aneman4, H. Friborg5, Y. Gasche6, J. Horn7, J. Hovdenes1, J. Kjaergaard1 on behalf of the TTM steering group. 1Rigshospitalet - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark; 2Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; 3Hospital of Helsingborg, Helsingborg, Sweden; 4Liverpool Hospital, Department of Intensive Care, Sydney, Australia; 5Skane University Hospital, Lund, Sweden; 6Geneva University Hospitals, Geneva, Switzerland; 7Academic Medical Center of Amsterdam, Amsterdam, Netherlands; 8Oslo University Hospital, Oslo, Norway
Background and Introduction: Men and women who suffer an out-of-hospital cardiac arrest (OHCA) differ in characteristics such as location of arrest, by-

standers performing cardiopulmonary resuscitation or probability of defibrillation. Women are also reported to receive fewer interventions in hospital and it is un-
known whether the effect of target temperature management (TTM) is the same as in men.
Purpose: We aimed to determine mortality in comatose female vs. male survivors after OHCA and whether gender modifies the effect of TTM.

Methods: This study is a post-hoc study of the TTM trial, which randomized 939 patients to 24 hours of TTM of 33 or 36°C. Nineteen percent were female and these were compared to the male patients regarding demographic characteristics, pre-hospital factors, in-hospital treatment and mortality.

Results: Compared to men, women more often had OHCA at home, p=0.04, and less often received defibrillation by bystanders, p=0.01. Within the first 24 hours, women received fewer coronary angiographies (CAG) and percutaneous inter-
terventions (PCI), both: p=0.02, but not significant after adjusting for confounders. Females had higher mortality than males in univariate analysis, hazard ratio (HR): 1.29, CI: 1.04–1.61, p=0.02. After adjusting for confounders, this difference was no longer significant. There was no interaction between sex and TTM allocation group, p=0.10, fig. 1.

Conclusion(s): Female gender is associated with a higher risk of adverse outcome, but this seems to be largely explained by less favourable resuscitation circumstances. There is no difference in mortality and we found no evidence of favoring one level of TTM over the other in females compared to males.

P3471 | BENCH
Effect of temperature on the relationship between cardiac power output and mixed venous oxygen saturation in healthy pigs: comparison to dobutamine
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Background: A decrease of cardiac power output (CPO) is the strongest predic-
tor of in-hospital mortality during cardiac shock. Experimental mild hypother-
mia (MH, 33.0°C) improves the systemic oxygen supply-demand balance during
cardiac dysfunction in pigs, leading to an increase of mixed venous oxygen sat-
uration (SvO2) at a given CPO. We here tested the effect of hyperthermia (HT, 40.5°C) and MH on this relationship in healthy pigs, and compared it to dobu-
tamine infusion.

Methods: 9 anesthetized, closed-chest pigs (67±2 kg) were acutely instru-
mented with Swan-Ganz and a left ventricular pressure-volume catheter. Tem-
perature was controlled by an intravascular device.
After baseline measurements at HT, intra-CPO dobutamine infusion was titrated to double LV dP/dtmax. Pigs were then cooled to normothermia (NT, 38.0°C) and further down to MH, and at each temperature step, titrated dobutamine infusion was repeated. Mixed venous and arterial blood samples were taken for blood gas analysis.

Results: Cardiac output decreased with cooling from HT to NT and MH, and it increased with dobutamine infusion at each temperature. Whole body oxygen consumption decreased by 50% from HT to MH, while SvO2 increased. At each temperature step, dobutamine infusion further increased SvO2 (see graph).

Conclusion: The relationship between cardiac power output and mixed venous oxygen saturation is strongly temperature-dependent. Cooling improves the sys-
temic oxygen supply-demand balance similarly to a clinically relevant dose of
dobutamine at normothermia and HT, but at a lower CPO. These data imply that
cooling is a therapeutic option in cardiogenic shock.
Atrial fibrillation (AF) is a very common arrhythmia in patients (P) with cardiovascular disease. Acute coronary syndromes (ACS) remains an important etiology. Our study validates Mehran risk score as a good score for predicting contrast nephropathy (CIN) is the third cause of acquired acute renal impairment in hospital. As it increases in-hospital morbidity and mortality, we hypothesized it would be useful to determine the risk of CIN after percutaneous coronary intervention (PCI) with scores like Mehran score.

**Objective:** To validate Mehran score in a contemporary cohort of patients with acute coronary syndrome (ACS).

**Methods:** We assessed the calibration and discriminatory capacity of Mehran score in predict CIN in a cohort of 1520 patients with a diagnosis of ACS and who underwent PCI between March 2008 and June 2012. We excluded patients on chronic dialysis and those without data of contrast volume. The calibration of the model was assessed with the Hosmer-Lemeshow goodness-of-fit test and discriminatory capacity was assessed by C statistic, which is equivalent to the area under the receiver-operating characteristic curve.

**Results:** 7.8% of patients developed CIN. They were older, with higher rates of diabetes (31%) and hypertension and worse renal function and anemia (p < 0.001). The OR for different score components in Mehran’s population versus our study were similar except for DM, hypotension and IABP (1.6%, 2.68% and 1.83%, respectively). Calibration and discriminatory capacity of Mehran score were excellent with a Hosmer-Lemeshow p=0.7, C-statistic value = 0.8. Figure shows the observed Vs predicted CIN across the 4 risk categories established from the Mehran score.

**Conclusion:** Our study validates Mehran risk score as a good score for predicting CIN in patients with ACS who underwent coronary angiography. According to this, we support its use in patients hospitalized for ACS in order to identify the ones in risk, and to optimize CIN prophylactic therapy.

**P3474 | BEDSIDE**

**Is there clinical benefit with thrombus aspiration in patients with ST-segment elevation myocardial infarction? Results from real-life data**

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**Background:** Contrast induced nephropathy (CIN) is the third cause of acquired acute renal impairment in hospital. As it increases in-hospital morbidity and mortality, we hypothesized it would be useful to determine the risk of CIN after percutaneous coronary intervention (PCI) with scores like Mehran score.

**Objective:** To validate Mehran score in a contemporary cohort of patients with acute coronary syndrome (ACS).

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**Conclusion:** Our study validates Mehran risk score as a good score for predicting CIN in patients with ACS who underwent coronary angiography. According to this, we support its use in patients hospitalized for ACS in order to identify the ones in risk, and to optimize CIN prophylactic therapy.

**P3475 | BEDSIDE**

**Tissue Doppler estimation of hemodynamic status of cardiogenic shock due to acute coronary syndrome or acute decompensation of chronic heart failure**

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**Introduction:** The ratio of early mitral inflow velocity to tissue Doppler mitral annular early diastolic velocity (E/e’) and isovolumic relaxation time (IVRT) are simple, well known parameters and have been well correlated with pulmonary capillary wedge pressure (PCWP). However, the usefulness of non-invasive estimation of PCWP among patients with acute decompensated chronic heart failure (ADCHF) or in cardiogenic shock (CS) is still uncertain. The aim of this study was to determine the reliability of tissue Doppler velocities for PCWP estimation in patients with ADCHF and in CS complicating ACS.

**Methods:** Two groups of prospective consecutive patients admitted to Intensive Cardiac Care Unit presenting with cardiogenic shock complicating ACS and candidates for heart transplantation with acute decompensation of severe chronic
systolic heart failure. A total of 61 patients were included. Clinical data are outlined in Table 1. Both groups underwent simultaneous echocardiographic and hemodynamic evaluation. For the purpose of the study, according to the published data PCWP ≥ 18 mmHg was a cut-point for E/e′ value estimation.

Results: There was statistically significant difference in mitral E/e′ ratio between ADCHF patients and in CS (27±11 vs. 13±5, p=0.001). The correlation between PCWP and E/e′ ratio was statistically significant (r=0.51; p<0.05) in CS patients. In addition there were significant correlation between IVRT and PCWP (r=0.50, p=0.047) in ADCHF patients. We observed statistically significant difference of E/e′ ratio in patients subgroups defined on PCWP value < 18 mmHg or ≥18 mmHg in ADCHF group; 19.2±5 vs. 30.5±11; p=0.0083 respectively and in CS group 11.4±2 vs. 17.7±0 p=0.0492 respectively.

Conclusion: In patients with cardiogenic shock complicating ACS and in the patient with ADCHF tissue Doppler-derived mitral E/e′ ratio may be a reliable and simple tool in predicting elevated PCWP.

**Table 1**

<table>
<thead>
<tr>
<th>ADCHF (n=34)</th>
<th>CS (n=27)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51±14</td>
<td>63±13</td>
</tr>
<tr>
<td>EF (%)</td>
<td>19±4</td>
<td>35±14</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>24±8</td>
<td>18±5</td>
</tr>
<tr>
<td>CI (L/m²)</td>
<td>1.6±0.4</td>
<td>2.2±0.3</td>
</tr>
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</table>

**Results:**

In total, 441 (13.4%) patients had AHF on presentation. Patients with AHF had a substantially higher in-hospital mortality rate than those without (3.9% vs. 0.6%; P<0.001); the frequency of mortality and major complication rate cumulatively increased with severity of the functional class (Figure). EIS was less frequently applied in AHF patients (75.3% vs. 57.2% in HF, P<0.001). After adjustment, AHF severity remained significantly associated with clinical outcomes in patients with NSTE-ACS (OR 2.79; 95% CI 1.78–4.37). However, EIS had no observed impact on clinical outcomes in AHF patients after adjustment (OR 1.13; 95% CI 0.64–2.01).

**Conclusion:** Patients with NSTE-ACS complicated with AHF had a significantly higher event rates, increasing with severity of functional class at presentation. In contrast, EIS was paradoxically less frequently applied in these patients, despite strong recommendation in the clinical guidelines.

**Acknowledgement/Funding:** Grant-in-Aid for Scientific Research (C)
P3479 | BEDSIDE
Copeptin and high-sensitive troponin T for the rapid diagnosis of patients with non-STE ACS and non-conclusive early after symptom onset. Therefore copeptin can be regarded as a co-efficient marker in the rapid diagnosis of patients with non-STE ACS and non-conclusive ECG.

Background: Male gender is a consolidated cardiovascular risk factor in medical literature. However, studies show most often unfavorable outcomes in women as well as underutilization of established therapeutic strategies. The time between the onset of chest pain (CP) and hospital admission (delta T) can affect therapeutic efficacy in acute coronary syndromes (ACS). This paradigm is controversial and its impact on the stratification of the probability of ACS in the emergency room is not clear.

Purpose: To compare the delta T between genders in patients with clinical suspicions of ACS and different clinical presentations.

Methods: This prospective study included 878 patients admitted to the chest pain unit (CPU) with clinical suspicion of ACS. The delta T was estimated by the interval between the onset of symptoms and admission at the CPU. Clinical presentation was classified as typical CP (definitely angina and probably angina) and atypical CP (probably not angina and definitely not angina). Patients underwent serial assessment of EKG and troponin I on admission and 6 hours later. The diagnosis of ACS was performed by ischemia detection in stress tests or in the presence of significant obstruction in coronary angiography. Statistical analysis was performed using student t-test and chi square.

Results: Mean age was higher among women (64.4±16.9y vs 62±16.1y;p=0.04), the incidence of ACS was higher in males (29.9% vs. 12.5%; p<0.001). Typical presentations were more common in women (62.3% vs 48.7%; p=0.003). There was no difference between the median delta T of both genders for the total population (men vs women=120 min vs 115 min; p=0.16), with typical DT (men vs women=120 min vs 91 min; p=0.33), or SGA (men vs women=90 min vs 69 min; p=0.36).

Conclusion: Women were admitted to CPU with more atypical symptoms and an older age. The higher incidence of ACS in men reinforces the risk in this group. There was no difference in delta T between genders, even in individuals with ACS.

P3480 | BEDSIDE
Copeptin and high-sensitive troponin T for the rapid diagnosis of non-ST-elevation acute coronary syndrome

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Background: Despite the introduction of high-sensitive troponin T (hs-TnT) as a new marker in the rapid diagnosis of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies (High-sensitivity cardiac troponin (hs-cTn) based 1h-algorithm vs hs-cTn based 2h-algorithm).

Methods: In a prospective international multicentre diagnostic study enrolling 1697 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied using the best-validated hs-cTnT assay (hs-cTnT Roche). The 1h-algorithm rule-out was defined as 0h<12ng/l and Δ0–2h<3ng/l; and the 2h-algorithm rule-out was defined as 0h and 2h<14ng/l and Δ0–2h<4ng/l. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial ECG. STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 16% of patients. The safety was very high and comparable with both algorithms (1h-algorithm: NPV 99.9%, 95% CI 99.5%–100% vs 2h-algorithm: NPV 100%, 95% CI 99.7%–100%, p=ns.). Regarding efficacy, the 1h-algorithm allowed rule-out in 60% of patients versus 64% with the 2h-algorithm (p=0.018). Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI. While the 1h-algorithm has the obvious advantage of allowing rule-out already after 1h, the 2h-algorithm tends to be slightly more effective in detecting patients eligible for rule-out.
P3483 | BEDSIDE
An updated heart fatty acid binding protein assay facilitates improved rule-out of acute myocardial infarction within 2 hours of entry to the emergency department: threshold derivation and validation

Background: The ongoing evolution of troponin assays has enabled the more accurate determination of very low troponin concentrations which assist the clinician to rule-out Acute Myocardial Infarction (AMI). The recent launch of a commercially available assay for heart fatty acid binding protein (hFABP) has enabled this biomarker to now be measured more accurately and reliably in a clinical setting, hence overcoming previous issues with rapid tests and ELISA-based assays. We tested the performance of this new hFABP assay to combine with hs-cTnI (hsTnI), hFABP and electrocardiography to rule out AMI within two hours of patients presenting with chest pain to emergency departments. We validated the derived cutpoint in a separate cohort.

Methods: hsTnI and hFABP were measured on presentation and two hours later in patients presenting to an emergency department with possible ACS with out-of-station elevation on electrocardiograph (ECG). AMI was adjudicated by cardiologists using the ECGs, local TnI results, and clinical information. hsTnI cutpoints were 16 ng/L for females and 34 ng/L for males. A positive index test was an ECG positive for new or evolving ischemia or an hsTnI above the cutpoint. In the development cohort we calculated the hFABP cutpoint at which an addition of hFABP to the index test the sensitivity exceeded 99% and determined the proportion of low risk patients who could potentially be discharged from ED into the care of their general physician without re-testing. We validated the derived cutpoint in a separate cohort.

Results: In the development cohort AMI was diagnosed in 227 (23.1%) of 981 presentations. The index test identified 638 patients (65.0%) as negative of whom 12 were false negatives (sensitivity 94.7% [95% CI 91.0% to 97.0%]). A sensitivity of >99% (98.8% to 99.8%) was achieved with the addition of hFABP at a cutpoint of 4.35 ng/mL (415 (42.3%) presentations were negative (low risk) of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 5 were false negatives (sensitivity 90.0% [78.6% to 97.9%]). The addition of hFABP at a cutpoint of 4.35 ng/mL reduced the number of false negatives to 3 (sensitivity 93.8% [83.2% to 97.9%]) all of which had an hFABP >3.9 ng/mL. 39.0% remained low risk.

Conclusion: The addition of hFABP at a cutpoint of 4.3 ng/mL to the index test comprising hsTnI and ECG reduced the rate of false negatives whilst maintaining a clinically useful proportion of low risk patients at around 40%.

Acknowledgement/Funding: hFABP assay kits were provided free of charge by Randox Cardiology. Funding by the Health Research Council of NZ and the Christchurch Heart Institute.

P3484 | BEDSIDE
Direct comparison of the safety and efficacy of two rule-out strategies for acute myocardial infarction: undetectable levels of cardiac troponin at presentation versus 1h-algorithm

Purpose: Addressing the increasingly recognised, yet unmet clinical need for rapid and accurate acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies (LOD: Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) at presentation versus the 1h-algorithm based on hs-cTn).

Methods: In a prospective international multicentre diagnostic study enrolling 2213 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied once ST elevation MI (STEMI) has been excluded by the initial ECG, STEMI independent from the hs-cTn assay used. As both strategies should only be applied once STEMI has been excluded, we evaluated the performance of the index test (hsTnI) in the development cohort. To directly compare the safety and efficacy of two previously defined strategies (LOD: Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) at presentation versus the 1h-algorithm based on hs-cTn).

Results: In the development cohort AMI was diagnosed in 227 (23.1%) of 981 presentations. The index test identified 638 patients (65.0%) as negative of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. 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In contrast, 65 yo and older patients with hs-TnT elevation at ED has more often other final diagnosis different than MI, especially “non cardiac elevation”.

P3487 | BEDSIDE
Underlying cause for pre hospital cardiac arrest - incidence of culprit lesions after successful resuscitation and their predictability by ECG recordings

Purpose: An acute coronary syndrome is suspected to be the leading cause of out of hospital cardiac arrest (OHCA). In our present study we examined the reliability of the ECG in predicting an acute coronary syndrome (culprit lesion at angiography) as the underlying mechanism for OHCA.

Methods: We retrospectively analysed all successful resuscitation attempts from our mobile ICU from 2007 to 2012. Patient charts and electronic databases were reviewed including ECG’s and coronary angiograms from patients admitted to our hospital.

Results: We found 767 out of hospital resuscitation attempts. 220 (28.7%) where successful, 166 (21.6%) were admitted to our hospital. In 83 out of the 166 patients coronary angiography was performed. Pre-hospital or hospital ECG recording where diagnostic for STEMI in 39 cases (group A) and not diagnostic for STEMI in 44 cases (group B). Culprit lesions were found in 77% in group A and in 48% in group B. Overall, acute coronary syndrome confirmed through angiography was found as the underlying mechanism in 38.4%, chronic coronary artery disease and reduced ejection fraction in 15%, other final diagnosis different than MI, especially “non cardiac elevation”.

Conclusion: Acute coronary syndrome was found in 38% of cases as underlying mechanism in survivors from out-of-hospital cardiac arrest. ECG recording was a reliable predictor of culprit lesions (correctly in 77%), but culprit lesions were also found in 48% of cases with non-diagnostic ECG’s. Our data support an early invasive strategy after successful resuscitation from OHCA even in the absence of ECG recordings for STEMI.

ACUTE INTENSIVE CARDIOVASCULAR CARE III

P3488 | BEDSIDE
Therapeutic hypothermia in patients resuscitated from out-of-hospital cardiac arrest: a meta-analysis of randomized controlled trials
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Background: Therapeutic hypothermia (TH) is recommended by current guidelines for survivors of out-of-hospital cardiac arrest (CA). The supportive evidence showing beneficial outcomes is limited.

Purpose: We performed a meta-analysis of randomized controlled trials (RCT) to assess the efficacy and safety of TH in patients successfully resuscitated from CA.

Methods: We conducted electronic search of RCT. The primary endpoint was all cause mortality. Secondary endpoints included favorable neurological recovery and new onset arrhythmias or re-arrest. Odds ratios (OR) and 95% confidence intervals (CI) were computed using the Mantel-Haenszel (MH) method. Fixed-effect model was used; if heterogeneity (I2) ≥ 40, effects were analyzed using a random model.

Results: Five RCT (n=1,358 patients) were included. Overall survival was 51.7% and full neurological recovery was 45.7%. Pooled data demonstrated no significant difference from TH for the primary outcome of all-cause mortality (OR 0.95 [95% CI 0.91–1.00], p=0.76). No significant difference was seen for the secondary outcomes of favorable neurological recovery (OR 1.45 [95% CI 0.86–2.44], p=0.18) and new onset arrhythmias or re-arrest (OR 0.95 [95% CI 0.71–1.26], p=0.73). Exclusion of a single study from the analysis did not alter the overall result.

Conclusion: Our meta-analysis showed that TH in patients resuscitated from out-of-hospital CA does not improved mortality, favorable neurological outcomes, new onset arrhythmias or re-arrest. Overall survival rate and odds of neurological re- através in these patients, indicating that alternative therapeutic strategies need to be developed.

P3489 | BEDSIDE
Peak systolic velocity by tissue Doppler detects changes in myocardial contraction related to inotropic effects of levosimendan in patients with acute heart failure complicating myocardial infarction
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Purpose: Peak systolic velocity (PSV) by tissue Doppler imaging (TDI) has been proposed for serial non-invasive assessment of myocardial contraction in patients receiving inotropic therapy due to its relative load- and heart rate-independent properties. However, this hypothesis has so far not been tested in a clinical setting. We therefore examined the ability of PSV by TDI to detect changes in contraction in a substudy of the LEVosimendan in Acute heart Failure following myo-cardiac infarction (LEAF) trial (NCT00324766).

Methods: A total of 61 patients developing clinical signs of heart failure within 48 hours after a primary percutaneous coronary intervention-treatment ST-elevation myocardial infarction (including cardiogenic shock), were randomized double-blind to a 25 hours infusion of levosimendan or placebo. Levosimendan is an inodilator where the effects, due to active metabolites with very long half-lives, last for several days after end of the infusion. Echocardiography was performed before infusion (baseline), on day 1, on day 5 and after 6 weeks. PSV (mean of septal, lateral, anterior and posterior mitral annular peak systolic velocity) measured by tissue velocity imaging, and global longitudinal strain (GLS) of the left ventricle measured by speckle tracking were analyzed at all time-points.

Results: There was significantly larger improvement in PSV from baseline to day 1 (P<0.007) and day 5 (P<0.001) in the levosimendan group compared to placebo (levosimendan 4.70 cm/s ± 1.34 to 5.74 cm/s ± 1.47 (day 1) and 6.07 cm/s ± 1.47 (day 5) vs. placebo 4.77 cm/s ± 1.02 to 5.08 cm/s ± 1.35 (day 1) and 4.90 cm/s ± 1.26 (day 5)). No significant differences were found in PSV after 6 weeks or in GLS at any time-point between the treatment groups. We have previously shown that levosimendan improved left ventricular function measured as changes in wall motion score index (WMSI) from baseline to day 5 compared to placebo (p=0.031, primary endpoint of the LEAF trial), however no significant changes in WMSI were found on day 1 or after 6 weeks between the treatment groups.

Conclusion: PSV by TDI seems to be a more sensitive echocardiographic method to detect changes in myocardial contraction during inotropic stimulation with levosimendan than WMSI and GLS. These results suggest that PSV by TDI can be used for assessment of changes in contraction in patients hospitalized for acute heart failure receiving inotropic therapy.

P3490 | BEDSIDE
Role of copeptin in the postoperative management of patients after on-pump cardiac surgery
E. Angeloni, G. Melina, S. Reffice, A. Roscitoano, F. Capuano, C. Comito, R. Sinatra. Sapienza University of Rome, Sant’Andrea Hospital, Rome, Italy

Background: Copeptin is rapidly emerging as a fast and reliable tool in detecting myocardial ischemia. However, to date, predictive power of Copeptin has only been tested in the settings of acute coronary syndromes and heart failure.

Purpose: To investigate the predictive power of Copeptin among patients who underwent cardiac surgery.

Methods: A total of 166 patients (mean age 71±6 years, 66% male) scheduled for first-time, elective, on-pump cardiac operations between September and December 2014 were enrolled, with recent myocardial infarction being an exclusion criteria. Blood samples were collected at the time of surgery (T0), at the end of...
Further studies are warranted to confirm these findings.

Postoperative development of complications such as LOS, and MACCE. The latter

Conclusion: Copeptin dosage following CABG early and reliably identifies the postoperative development of complications such as LOS, and MACCE. The latter permits timely interventions in order to limit or prevent postoperative morbidity. Further studies are warranted to confirm these findings.

P3491 | BEDSIDE

Ventricular conduction defects - prevalence and impact on survival in cardiac shock

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Background: Conduction abnormalities are common and affect survival in acute heart failure and myocardial infarction, but their role in cardiac shock (CS) is not clear.

Purpose: The aim was to investigate the prevalence of conduction abnormalities and evaluate their association with survival in patients with CS.

Methods: We analyzed the baseline ECG of 197 patients included in a multinational prospective cohort study of CS (n=219) conducted in 2010–2012 with 1-year all-cause mortality follow-up. The multivariate models were calculated using logistic regression adjusting for age, gender, and comorbidities.

Results: The CS was caused by acute coronary syndrome (ACS) in 175 (81%) patients. The overall mortality within one year was 40%, most of the deaths occurring during the hospital stay. Mortality was higher in ACS (42%) than in non-ACS patients (24%; p<0.05). More than half (n=102, 53%) of the patients had a ventricular conduction defect; the most common were IVCD (QRS>110ms without specific partial or complete block) 19.1%, LBBB 18.6%, and RBBB 12.4%. LBBB (4.6%) and LPHB (6.7%) were less common. One-year mortality was higher in all patients with a conduction defect (Figure). In the multivariate model, isolated hemiblock (LBBH or LPHB) independently predicted mortality (adjusted OR 2.6, CI 1.1–6.4, p=0.03), and IVCD had a similar trend (adjusted OR 2.2 CI 0.9–5.2, p=0.08) compared to those with normal ventricular conduction. Both findings were pronounced in ACS: for isolated hemiblock the adjusted OR was 4.5 (CI 1.6–12.7; p=0.004), and for IVCD the adjusted OR was 2.8 (CI 1.1–7.4; p=0.04).

Conclusions: Ventricular conduction defects are common in patients with CS and are associated with increased mortality. In particular in CS caused by ACS, hemiblocks and IVCD predict death.

P3492 | BENCH

Effects of hyperthermia and mild hypothermia on myocardial function in pigs: comparison to dobutamine

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Background: The optimal target temperature in resuscitated patients after cardiac arrest is unclear at present. We assessed the effect of hyperthermia (HT, 40.5°C), normothermia (NT, 38.0°C) and mild hypothermia (MH, 33.0°C) on systolic left ventricular (LV) function in healthy pigs and compared it to dobutamine infusions. The pressure-volume loop (P-V) was recorded at a constant aortic pressure of 100 mmHg (LVV-Pes100) as a parameter of LV contractility.

Methods: 9 anaesthetized, closed-chest pigs (67±2 kg) were acutely instrumented for invasive pressure-volume analysis. Temperature was controlled by an intravascular device. After baseline measurements at HT, intravenous dobutamine infusion was titrated to double LV dp/dtmax. Pigs were then cooled to NT and further down to MH and, at each temperature step, titrated dobutamine infusion was repeated. LV function was assessed by pressure-volume relationships derived from short aortic occlusions. The calculated diastolic LV pressure at an end-systolic LV pressure of 100 mmHg (LVV-Pes100) was taken as a parameter of LV contractility (lower values indicate increased contractility).

Results: Heart rate and cardiac output decreased with cooling from HT to MH, while LV contractility increased (graph). The effect of cooling on LVV-Pes100 was of comparable effect size as dobutamine at a given temperature.

Conclusions: Ventricular conduction defects are common in patients with CS and are associated with increased mortality. In particular in CS caused by ACS, hemiblocks and IVCD predict death.

P3493 | BEDSIDE

Culprit-only or complete revascularization in patients with non-ST segment elevation acute coronary syndrome: a propensity score matching-based analysis


Background: In patients with non-ST elevation acute coronary syndrome (NSTE-ACS) and multivessel coronary artery disease (CAD), the strategy of index hospitalization full, multivessel revascularization by percutaneous coronary intervention (PCI) versus a strategy based solely on culprit-vessel only PCI has not been properly investigated.

Aims: We examined the 3-year mortality rates of NSTE-ACS patients with multivessel disease treated with culprit vessel-only PCI (incomplete revascularization, IR) compared to multivessel PCI with a view to complete revascularization, CR. Methods: We studied 3,782 consecutive patients admitted with an ACS to a coronary care unit and discharged alive. The NSTE-ACS study sample had a total of 460 multivessel CAD patients, after exclusion of clinical indications for CR. After implementing a multiple imputation technique, multivariate logistic regression and Cox proportional hazards models were used to assess predictors of CR and mortality and the impact of PCI strategy on outcomes (3-year all-cause mortality). Afterwards, a propensity score matching (PSM) methodology with a 1:1 matching and a 0.3 caliper was used; subgroup analyses were focused on predetermined higher risk groups for mortality/morbidity.

Results: A strategy of CR was performed in 128 (28%) of NSTE-ACS patients. Cardiovascular risk factors were similar between groups, except for higher hypertension prevalence and a lower proportion of diabetes and peripheral artery disease in CR patients. Patients undergoing CR had lower GRACE risk scores, higher systolic blood pressure and left ventricular ejection fraction, and less severe anatomic disease. Although there was a numerical difference, no statistically significant impact was found on 3-year all-cause mortality, even after adjustment (HR 2.0% vs. CR 2.0%, Log-rank p=0.365). After PSM, 180 patients were paired (90 CR patients and 90 IR patients); no imbalance was identified on 3-year mortality (8.9% vs. 4.4%, p=0.244). In subgroup analysis, no interaction was found between the revascularization strategy and age, ejection fraction, diabetes mellitus or renal failure. However, a significant interaction (p=0.008) was found between CR revascularization and ACS subtype, with patients suffering a NSTEMI having a much lower mortality than UA patients when subjected to a CR strategy (HR 0.231, 95% CI 0.057–0.925, p<0.05).

Conclusion: In this selected population of NSTE-ACS patients, CR was not associated with better long-term mortality, although the NSTEMI subgroup patients seemed to derive more benefit.
Long-term outcome after extracorporeal membrane oxygenation due to refractory cardiogenic shock

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Background: In patients with cardiogenic shock refractory to standard treatment, implantation of left ventricular assist devices such as extracorporeal membrane oxygenation (ECMO) may be the only option to achieve hemodynamic stability. Despite its growing use, data on long-term prognosis in patients treated with ECMO in clinical routine are lacking. Here we report first data on long-term outcome after using ECMO implantation due to refractory cardiogenic shock in a high volume tertiary care centre.

Methods: Eighty patients with refractory cardiogenic shock underwent femoral percutaneous arteriovenous ECMO implantation performed by interventional cardiologists. A detailed set of clinical, therapeutic and laboratory parameters was assessed in all patients. Clinical follow-up was conducted via a structured questionnaire by telephone, contacting the patients or their relatives. Data were verified by hospital charts, direct contact with the treating physician or contact with the local government registration. Good clinical outcome was defined as survival with a cerebral performance category (CPC) of 1-2.

Results: Mean age was 60.5±14.7 years (range 23-84) and cardiopulmonary resuscitation prior to ECMO implantation was performed in 43 patients (54.4%). Indications for ECMO were cardiogenic shock complicated by acute coronary syndrome (n=51, 63.8%), acute non-ischemic heart failure (n=24, 30.0%) and interventional cardiology (n=5, 6.3%). ECMO survival at 7 days was 70.0% as only 24 patients were alive at discharge. Long-term follow-up was performed in median 20 months (interquartile range 12–30) after ECMO-implantation. Of the 24 patients alive at hospital discharge, 9 (37.5%) died within follow-up and 5 (20.8%) were classified to a CPC ≥3. Thus, out of all 80 patients initially undergoing ECMO-implantation only 10 patients (12.5%) were alive at follow-up with a CPC of 1–2.

Conclusion: Despite ECMO support, long-term prognosis of patients with cardiogenic shock undergoing ECMO implantation remains poor. However, ECMO is a therapeutic option in this otherwise futile situation with an acceptable long-term outcome in approximately one out of eight patients.

The immediate percutaneous intervention after bypass surgery complicated by periprocedural myocardial infarction may improve clinical outcomes

J. Zalewski, K. Krawczyk, K. Janowiec, A. Flis, J. Nessler. Jagiellonian University Medical College, John Paul II Hospital, Krakow, Poland

Background: Coronary artery bypass surgery (CABG) complicated by periprocedural myocardial infarction (MI) is associated with extremely high risk of in-hospital death and is usually treated with inotropes and the systems for mechanical circulatory support.

Purpose: We sought to investigate whether percutaneous coronary intervention (PCI) after CABG complicated by periprocedural MI may reduce short and long-term mortality rate.

Methods: We studied 100 CABG patients with periprocedural MI who underwent immediate percutaneous intervention, including 32 with coronary angiography only (ANGIO) and 68 with PCI due to incomplete revascularization or graft failure, and 80 patients with periprocedural MI without immediate intervention (no-CATH) matched for demographics, risk factors, left ventricular ejection fraction before CABG and 68 with PCI due to incomplete revascularization or graft failure. The mortality rate was determined 18 to 130 (median 48) months after CABG.

Conclusion: Our findings indicate that immediate revascularisation after CABG complicated by periprocedural MI may improve clinical outcomes. This observation needs to be confirmed in a larger group of patients.

ECHOCARDIOGRAPHIC MODIFICATIONS IN EVOLUTION AND TREATMENT OF VALVULAR HEART DISEASE

P3496 | BEDSIDE

Differences in left ventricle mass regression in patients with aortic valve stenosis treated with transcatheter or surgical aortic valve replacement: an echocardiographic study

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Introduction: Certain high-risk patients with severe aortic valve stenosis (AS) can be considered for treatment with either transcatheter (TAVR) or surgical aortic valve replacement (SAVR). Little is known about the effect on left ventricle mass regression after TAVR vs. SAVR. This study was an echocardiographic substudy of the NOTION trial, a randomized comparison of TAVR vs. SAVR in patients above 70 years of age with no need for coronary artery revascularization.

Purpose: To compare left ventricular (LV) remodelling in patients with AS after treatment with TAVR vs. SAVR.

Methods: Transthoracic echocardiographic studies were performed before and 12 month after TAVR and SAVR.

Results: 232 patients were included in the study at our institution, 120 were randomized to TAVR and 112 to SAVR. From baseline to 12 months after the procedure, the aortic valve area (AVA) changed from 0.77±0.04 to 1.32±0.08 cm² (p<0.0001) in the SAVR group compared to 0.74±0.04 to 1.65±0.09 cm² (p<0.0001) in the TAVR group. The increase in AVA was significantly (p<0.0001) larger in the TAVR group. At 12 months, LV mass regressed from 215±12 to 200±13 g (p<0.01) in the TAVR group and from 221±13 to 182±12 g (p<0.0001) in the SAVR group. The reduction in LV mass was largest in the SAVR group (p<0.0002). The difference in LV mass regression between groups was correlated with differences in diastolic volume (EDV). In the TAVR group at 12 months, EDV increased from 87±6 to 96±8 ml (p<0.0001) and in the SAVR group, EDV decreased from 89±7 to 73±5 ml (p<0.0001) with a significant difference between the two groups (p<0.0001). At 12 months, 27% of the TAVR patients had no or trace paravalvular leak (PVL), 59% had mild PVL and 14% had moderate PVL. Among the SAVR patients 82% had no or trace PVL and 18% had mild PVL. Changes in EDV were correlated with the degree of PVL. In TAVR patients, EDV was unchanged in patients with no or trace PVL, but EDV increased by 13±6 ml (p=0.02) in those with mild or moderate PVL. In SAVR patients with no or trace PVL, EDV decreased by −17±6 ml (p<0.001), and in those with mild PVL by −9±9 ml (p<0.001).

Conclusion: Patients treated with TAVR have a larger AVA compared to those treated with SAVR. However, patients undergoing SAVR had larger LV mass regression, which correlated to a more pronounced reduction in EDV. Even mild to moderate PVL were associated with diminished LV mass reduction after TAVR. Current development in transcatheter valve technology to minimize paravalvular leak may be important to optimize long-term results after TAVR.
T. Machino, Y. Seo, K. Sato, A. Sugano, M. Yamamoto, Y. Harimura, T. Ishizu, K. Aonuma. University of Tsukuba, Tsukuba, Japan

Background: The functional mitral regurgitation (FMR) in lone atrial fibrillation (AF) is caused by morphological changes of mitral valve (MV) associated with the atrial remodeling; however, little is known about the precise mechanism of that.

Purpose: We aimed to clarify what morphological features of MV contributing to aggravation of FMR in patients with lone AF.

Methods: The lone AF patients who underwent three-dimensional transesophageal echocardiography with appropriate image quality (n=1124) were retrospectively screened. Of these, we picked up 25 patients showing moderate or greater FMR despite normal left ventricular function (significant-MR group). Twenty-five patients without MR (controls) and 25 patients with mild FMR (mild-MR group) were randomly selected as references from the left cohort. The following parameters were measured during systole: (1) MA area and its fraction, representing the MA sphincterlike contraction; (2) nonplanarity angle (NPA), representing the degree of saddle shape; (3) the ratio of total leaflet area to MA area, representing the degree of mitral leaflet adaptation; and (4) tethering angle of both leaflets.

Results: As shown in Table, MA area, NPA, and tethering angle of posterior mitral leaflet (PML) were the largest and MA area fraction was the smallest in significant-MR group compared to others. In multivariate models, Left atrial volume index, MA area fraction, PML angle and PML angle independent from other factors to determine effective regurgitant orifice area of FMR (adjusted R2: 0.51, P<0.001).

Conclusion: FMR related to AF might be caused by multiple factors including reduced sphincterlike MA contraction, flatter annulus and PML tethering.

P3498 | BEDSIDE
Dynamic 3-dimensional echocardiographic assessment of mitral valve in patients with functional mitral regurgitation caused by lone atrial fibrillation

T. Machino, Y. Seo, K. Sato, A. Sugano, M. Yamamoto, Y. Harimura, T. Ishizu, K. Aonuma. University of Tsukuba, Tsukuba, Japan

Background: The functional mitral regurgitation (FMR) in lone atrial fibrillation (AF) is caused by morphological changes of mitral valve (MV) associated with the atrial remodeling; however, little is known about the precise mechanism of that.

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Conclusion: FMR related to AF might be caused by multiple factors including reduced sphincterlike MA contraction, flatter annulus and PML tethering.

P3499 | BEDSIDE
Predictive factors of left ventricular outflow tract obstruction after aortic surgery in patients with severe aortic stenosis


Background: Asymmetric septal hypertrophy frequently coexists with severe aortic stenosis and can be unmasked after successful aortic valve surgery, jeopardizing the clinical and echocardiographic results. Left ventricular outflow tract obstruction (LVOTO) appears to be a marker for increased postoperative morbidity and mortality. The purpose of this study is to evaluate the predictive factors associated with LVOTO after surgical treatment for aortic stenosis.

Methods: Sixty seven patients with severe aortic stenosis were studies retrospectively before and after surgery by transthoracic and transesophageal echocardiography. We measured interventricular septum wall thickness in diastole (IVSd), the minimum diameter of the left ventricular outflow tract (MDOT), aortic annulus diameter, aorto-septal angle (ASA), including conventional echocardiographic parameters. Patients were divided into two groups based on the presence of LVOTO or absence of LVOTO. Sixteen patients had significant LVOTO and 51 patients did not have LVOTO. We analyzed the IVSd, MDOT, aortic annulus diameter and ASA with the receiver operating characteristic (ROC) curve.

Results: IVSd was significantly larger in obstruction group (p=0.0039). MDOT was significantly smaller in obstruction group (p=0.0025). Aortic annulus diameter was significantly smaller in obstruction group (p=0.047). There was no significant difference in ASA between two groups. The optimal cut-off value of the MDOT in predicting presence of LVOTO was 15.2 mm as calculated using ROC curve analysis. Patients with MDOT <15.2 mm were associated with sensitivity of 87.5% and specificity of 80.8% for LVOTO. Patients with IVSd ≥17.5 mm were associated with sensitivity of 43.8% and specificity of 94.1% for LVOTO.

Conclusion: Our study suggested that MDOT and IVSd were useful predictive factors of left ventricular outflow tract obstruction after aortic valve surgery for severe aortic stenosis. Concomitant myectomy may be considered treatment of choice for aortic stenosis.
Materials and methods: A total of 210 patients (120 patients for non-direct TAVI and 90 patients for direct TAVI) with severe aortic valve stenosis were analysed. All patients underwent transthoracic echocardiogram prior to the procedure and before discharge.

Results: The direct group had less moderate/severe paravalvular leakage (PVL) post TAVI compared to the non-direct group (8% vs 27%, p < 0.01). Both groups had similar 1-year mortality rates (15% in non-direct versus 11% in direct, p = 0.5).

Table 1: Mitral valve parameters before and after AV repair

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before AV repair</th>
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<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterolateral-posterior mediolateral angle (°)</td>
<td>41.6±6.0</td>
<td>39.0±8.4</td>
<td>0.10</td>
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<tr>
<td>Anteroposterior mediolateral angle (°)</td>
<td>36.5±15.8</td>
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<td>Aortic annulus height (mm)</td>
<td>10.3±2.2</td>
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<td>&lt;0.001</td>
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<tr>
<td>Aortic annulus height to commissural width ratio</td>
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<tr>
<td>Coaptation height (mm)</td>
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<td>0.002</td>
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<tr>
<td>Tenting area (mm²)</td>
<td>109.1±43.3</td>
<td>53.4±30.3</td>
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<tr>
<td>Aorto-mitral angle (°)</td>
<td>112.8±9.6</td>
<td>121.1±8.3</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Conclusions: Patients undergoing direct TAVI had less moderate/severe paravalvular leakage and similar mortality rates compared to patients with non-direct TAVI.

P3504 | BEDSIDE

Impact of aortic valve repair and valve-sparing procedures on the mitral annular geometry assessed by 3-dimensional transesophageal echocardiography

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Background: Annular non-planarity, referred as the "saddle-shape" of the mitral valve (MV) annulus, minimizes leaflet stress and plays a role in preserving adequate valve function. Aortic valve (AV) repair is an attractive approach increasingly used to treat young patients with severe aortic regurgitation (AR). However, the

Abstract P3504 - Table 1. Mitral valve parameters

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Conclusions: When compared to TEE performed days after AV repair, TEE under-diagnosed absence of AR. This might be explained by a lower BP immediately after AV repair, compared to follow-up, as well as mild short-term progression of AR.

Acknowledgement/Funding: Portuguese Foundation for Science and Technology Grant HMSP-ICS/007/2012

P3505 | BEDSIDE

Assessing aortic regurgitation after TAVI: overcoming diagnostic pitfalls

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Introduction: Aortic regurgitation (AR) after transcatheter aortic valve implanta-

tion (TAVI) negatively affects prognosis, but the best method and optimal timing for detecting the presence and severity of AR remains unclear. In this study we aimed to compare preprocedure transesophageal echocardiography (TEE) with post procedure transthoracic echocardiography (TTE) for the diagnosis of AR.

Methods and results: Among 163 patients undergoing TAVI under TEE guid-

ance, TEE and TTE images were reviewed separately and blinded to each other. The median time between TEE/TAVI and TEE was 4 days (IQR=10). After TAVI, 48% had at least trace AR by TEE, while the same finding was present in 56% of patients by angiography and in 67% by TTE. The majority (78%) of AR was paravalvular. More patients were classified with mild-moderate AR by TEE than by TEE (44% vs. 22%, p < 0.01). There were no cases of severe AR. During TTE, patients had higher systolic (mean ΔSBP= 9±4 mmHg, mean ΔDBP=6±2mmHg, p < 0.01) and diastolic blood pressures (mean ΔDBP= 5±2 mmHg, p < 0.01) when compared to TEE. When ex-
amining the 46 patients with AR by TEE which was not detected during TEE/TAVI,

both SBP and DBP were significantly higher during TEE than during TEE (Figure; mean ΔSBP= 9±4 mmHg, mean ΔDBP=6±2mmHg, p < 0.01 for both). No differ-

cences in BP between TEE and TTE were found among patients with no AR or those who had AR on both studies. At median follow-up of 185 days death or cardiovascular hospitalizations occurred in 36% patients, but the presence of AR was not predictive of such events.

Conclusions: Patients undergoing direct TAVI had less moderate/severe paravalvular leakage and similar mortality rates compared to patients with non-direct TAVI.

P3502 | BEDSIDE

Left atrial volume changes and left atrial 2D strain measurements for diagnostic and prognostic evaluation of heart failure patients with MR undergoing mitral clip procedure

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Methods: 75 heart failure patients (NYHA class 2-3) with significant mitral regur-
gitation (MR ≥2+) undergoing percutaneous mitral valve (MV) repair using mitrilclip were investigated. Conventional 2D echocardiography including speckle-tracking analysis were performed to determine LA volumes and function at baseline (BL) and at six-months follow-up (FU).

Results: Primarily, mitral clip procedure resulted in significant reduction of MV regurgitation (BL 2.5±0.4 vs. FU 1.4±0.7, p < 0.001) and ameliorated NYHA functional class (3.0±0.5 vs 2.3±0.5, p < 0.001). Echocardiographic revealed re-
duced left atrial (LA) minimal (75±31 vs. 70±32ml, p < 0.01) and maximal vol-
uumes (106±339 vs 96±359 ml, p < 0.01), reduced LA volume index (57±19 vs. 51±19 mm²/m², p < 0.01) accompanied by decreased pulmonary systolic artery pressure (PASP, 52±12 vs. 44±14 mmHg, p < 0.01) and increased LA systolic strain (10.2±4.1 vs. 12±3.6%, p < 0.01). Active emptying fraction showed no sig-
nificant change suggesting the improvement of LA conduit function. However, patients with preserved ejection fraction (EF ≥50%) showed an increase in LA systolic strain (11.3±2.6 vs 13±5±5%, p < 0.01), LA early diastolic strain rate (−0.73±0.33 vs. −0.61±0.27, p < 0.01) and LA late diastolic strain rate (−0.49±0.35 vs. −0.37±0.24, p < 0.01). Patients without preprocedural atrial fibrillation (preAF) exhibited, independently from LVEF, a significant increase in LA systolic strain after mitral clip deployment (10.2±4.1 vs 12.6±6.6%, p < 0.01), whereas patients with preAF showed no significant change in LA strain values. Patients with preserved EF and without preAF demonstrated considerable increase in LA systolic strain (11.4±4.9 vs. 14.4±6.2%, p < 0.01), LA early diastolic strain rate (−0.69±0.24 vs. −0.58±0.26%, p < 0.01) and late diastolic strain rate (−0.54±0.35 vs. −0.43±0.33%, p < 0.01). According to multivariate logistic regression analysis neither LA volumes nor strain parameters provided to be an independent pre-
dictor of clinical recovery after mitral clip procedure.

Conclusions: In heart failure patients percutaneous MV repair results in a signif-
ificant reduction in LA volumes accompanied by an increase in LA systolic strain. These parameters are strongly associated with the severity of MV regurgitation, PASP and NYHA functional class. In regard to LA function heart failure patients with preserved left ventricular ejection fraction and with permanent atrial fibril-
lation are especially advantageous demonstrating a considerable improvement of conduit, reservoir and contractile function. Hence, LA volumes and strain parameters are useful and reliable follow-up markers of clinical recovery.
impact of AV repair and sparing procedures on MV annular geometry and function is unknown.

**Purpose:** We aimed at assessing the impact of AV repair on the MV annular geometry.

**Methods:** 2D and 3D transesophageal echocardiography (TEE) of the MV apparatus was acquired pre-operatively and immediately after surgery in 14 patients with severe AR (13 bicuspid, 1 tricuspid;12 males; age 45±11.4), and in 16 controls with normal TEE (9 males; age 60±13.3). MV annular morphology was retrospectively assessed by dedicated quantification software.

**Results:** Success of valve-sparing root replacement with AV reimplantation and cusp repair in 12 patients, and external ring annuloplasty and cusp repair in 2. MV parameters are summarized in Table 1. Pre-operative MV parameters did not differ from those of the normal subjects. The annular height and annular area were significantly lower in the control group. The cusp annular angle was significantly decreased after AV repair, as were the coaptation height and tenting area. The aorto-mitrall angle was increased after AV repair/sparing procedure.

**Conclusions:** AV repair procedures decrease the non-planarity of the MV annulus and the height of coaptation of the MV leaflets. These alterations could have long-term implications on MV function.

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**References:**

1. G. Bonzani, A. Battistelli, G. Casti, A. C. Zerbi, C. Grassi, M. D. Zauli, E. DeMaria, A. D. Anderl, G. Banzoni, P. Caso. AO dei Colli-Monaldi Hospital, Department of Cardiology, Naples, Italy


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**P3505 | BEDSIDE**

**Mitrail/aortic velocity flow integral ratio as a simple and useful index to evaluate residual mitral regurgitation after MitraClip implantation**

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**Background:** Percutaneous mitral valve repair using MitraClip (MC) has emerged as a therapeutic option for pts with functional severe mitral regurgitation (MR) at prohibitive surgical risk. The echocardiographic semiquantitative assessment of MR after MC implantation is challenging because the traditional semiquantitative and quantitative echocardiographic methods, commonly used to assess MR severity, have important limitations in this setting.

**Purpose:** The aim of this study was to assess the accuracy and reliability of a simple Doppler index, the mitral/aortic flow velocity integral ratio (MAVIR), to evaluate residual MR severity after MC implantation.

**Methods:** From June 2012 to December 2014, 85 heart failure patients (age mean 64±11.5 years; 69 M, 16 F) with functional MR and LV dysfunction (LVEF ≤40%) were included. MR was quantified on the basis of two quantitative parameters of MR severity: the vena contracta width (VC) and the effective regurgitant orifice area (EROA). VC width was measured on a magnified parastral longitudinal view (PVL). EROA was measured using the PISA method. MAVIR was expressed as the ratio of mitral and aortic time velocity-integral (TVI) values. Mitral TVI was obtained with pulsed wave Doppler (PW) at mitral annulus level in four-chamber view whereas the aortic TVI was obtained at level of LVOT in the apical long-axis view. On the basis of VC, used as reference standard, 27 pts had mild MR (VC <3 mm), 33 pts had moderate MR (VC 3–6 mm) and 25 pts had severe MR (VC ≥7 mm). According to MR severity (VC ≥7 mm), 25 patients underwent MC implantation and at 6 months a complete echocardiographic follow-up was performed.

**Results:** A significant linear relationship was found between MAVIR and both VC (r=0.74) and EROA (r=0.64). A MAVIR >1 identified pts with severe MR with a sensitivity of 86.7% and a specificity of 90.9%. At 6 months echocardiographic follow-up, after MitraClip implantation, we observed an significant reduction of LAVI (77.2±14.8 ml vs. 68.5±13.0 ml; P<0.03), LVED (2549±52 ml vs. 242±89 ml; P<0.001), LVEF and LV systolic function (LVEF improved (29.4±7.3% to 32.3±8.9%; P<0.001). MAVIR significantly decreased at follow-up after MC implantation (1.2±0.2 vs. 1.0±0.1; P<0.003) and its decrease showed a significant linear relationship with LAVI reduction (r=0.79).

**Conclusions:** Our data show a closer relationship between MAVIR and traditional indexes of MR severity in patients with functional MR. This Doppler index, easy to obtain, seems applicable after MC implantation when traditional echocardiographic index of MR severity show significant limitations.

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**References:**


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**P3506 | BEDSIDE**

**Mitral/aortic velocity flow integral ratio as a simple and useful index to evaluate residual mitral regurgitation after MitraClip implantation**

G. Palmiero, L. Ascolle, C. Sordelli, V. Monra, R. Ascolle, A. D’Andrea, G. Bonzani, P. Caso. AO dei Colli-Monaldi Hospital, Department of Cardiology, Naples, Italy

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**P3507 | BEDSIDE**

**Outcome by treadmill exercise echocardiography in patients with low pre-test probability of coronary artery disease**

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**Purpose:** Recommendations for testing in patients with low pre-test probability of (LPP) of coronary artery disease (CAD) differ current guidelines from no testing at all for renal transplantation, and revascularizations during follow-up (FU) were searched for each group. Coronary angiographies and specific causes of mortality were investigated in the Clin+ECG group. CAD was defined as a maximal luminal narrowing ≥50% by visual estimation in a coronary artery or major branch.

**Results:** Among 7,174 patients with a normal ExE, 102 patients (1.4%) belonged to the Clin+ECG group, and 922 (17.7%) were collected on data with a normal ExE, and 922 (17.7%) were collected on data with a normal ExE, and 321 M2 (annualized MI rates of 1.2%, 0.7%, and 0.7%, for the Clin+ECG and All- groups, respectively, p<0.001). Although the independent predictors of either overall mortality or MI did not include clinical or ECG positivity or their combination, revascularizations during follow-up were more frequent in the Clin+ECG group either within 3 months or within 1 year (P<0.001). The annualized revascularization rates of 9.2% vs. 3.1% in the Clin+ECG group and 1.4% in the All- group, p<0.001. Causes of death in 10 Clin+ECG group patients were cardiovascular in 3 (cardiac failure in 2, mesenteric thrombosis in 1). Coronary angiography performed in 48 of the 102 patients in the Clin+ECG group (29 without history of CAD), showed CAD in 33 (18 without history of CAD), with multivessel disease in 14 patients. Proximal severe left anterior descending CAD (≥75%) was found in 7 patients, left main CAD in no one, and 3-vessels CAD in 4. Among the 19 patients with single vessel CAD, the diseased area was more likely to be the left anterior descending artery (present in 62% of the patients).

**Methods:** Retrospective analysis of prospectively collected data on 1,481 patients with LPP of CAD (<15%) that underwent a first treadmill ExE in our institution from March 1995 to January 2015. Data were extracted from a database of 18,031 cases. Outcome (overall mortality, myocardial infarction [MI] before any revascularization, and revascularizations) during follow-up (FU) was assessed. Patients with LV ejection fraction <45%, at least moderate valve disease, congenital heart disease, or hypertrophic cardiomyopathy were excluded. Ischemia was defined as the development of new wall motion abnormalities (WMAs) with exercise (HRE ≥15% (ESC) or ≥10% (NICE) to exercise ECG, stress echocardiography or computed tomography (ASC). Our aim was to assess the value of peak treadmill exercise echocardiography (CAD) to define outcome in these patients.

**Results:** Mean age was 50±12 years and 1,349 patients were women (91.1%). A fixed WMA was seen in 23 patients (1.7%) and ischemia in 115 (7.8%). During FU of 6.7±5.2 years 42 patients died (annualized death rate 0.42%), 27 patients experienced MI (annualized rate 0.26%), and 52 patients underwent revascularization (annualized revascularization rate 0.47%). Independent predictors of combined overall mortality and MI in 62 patients were the presence of atrial fibrillation at the time of the ExE (Hazard ratio [HR]= 4.81, 95% Confidence Interval [CI]=1.99–11.65, P<0.001), product heart rate (HRP) by blood pressure product at rest (HR=1.13,95% CI: 1.02–1.25, P<0.02), maximal achieved workload in Metabolic Equivalents (HR=0.86, 95% CI: 0.78–0.95, p=0.003), % achieved of the maximal age-predicted HRate (HR=0.97, 95% CI: 0.94–0.99, p=0.009) and Δ in wall motion score index with exercise (HR=6.98, 95% CI: 1.63–29.88, p=0.009; incremental prognostic value of ExE, p=0.03). Clinical or ECG testing positivity was not predictive. The incidence of ExE required to detect an ischemic case was 12.9.

**Conclusions:** Exercise testing information in patients with LPP of CAD although the number of studies needed to detect a patient at risk is very high.

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**References:**


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in patients referred for exercise testing. We hypothesized that a negative peak supine bicycle exercise stress echocardiography (ESE) might be able to identify a selected relatively healthy subpopulation among potential kidney transplant recipients with favourable cardiac prognostic course. However, there are currently no data to support this strategy in clinical practice.

Objectives: To assess the value of a comprehensive risk stratification prognostic strategy based on negative ESE in patients with end-stage renal disease (ESRD) awaiting renal transplantation (RT).

Methods: Retrospective analysis of a series of ESRD (with no active cardiac conditions and sufficient predicted functional status to perform exercise) awaiting RT undergoing normal ESE as part of a preoperative cardiac screening strategy regardless of the presence of coronary artery disease risk factors.

Results: Of 64 patients undergoing ESE, 59 had a normal exam (43 men, mean age 55.9±8.7 years). After a mean follow-up period of 3.8±2.4 years, one patient had cardiac death. Thirteen patients (22%) had hospitalizations for non-fatal acute coronary syndrome (5.7% per person-year of follow-up). Predictors of future cardiac death and non-fatal events included diastolic duration, smoking, previous PCI, peripheral vessel disease, low HDL level, and worsening diastolic dysfunction. Eighteen patients (30.5%) underwent renal transplantation at a median of 21.5 (25th-75th percentile 4.7–36.0) months after negative ESE and only one developed perioperative myocardial infarction.

Conclusions: In potential kidney transplant ESRD recipients a negative ESE may effectively predict adverse outcome, which can be identified by assessment of systolic function reserve and diastolic relaxation reserve during SE.

P3509 | BEDSIDE
Blunted stress upregulation of stroke volume index is related to impaired end-diastolic volume recruitment
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Background: In the normal heart, when exercise is performed, left-ventricular end-diastolic volume (EDV) increases slightly, whereas end-systolic volume (ESV) decreases significantly. Little is known of end-diastolic volume (EDV) recruitment during exercise, dipyridamole and dobutamine stress echocardiography (SE).

Aim: To assess the dependence of stroke volume (SV) upon LVEDV changes during physical or pharmacological stress in patients with negative SE and all ranges of resting LV function.

Methods: We analyzed interpretable data obtained in 891 patients; 593 men; age 63±12 years, ejection fraction 47±12%, 338 normal or hypertensive; 229 coronary artery disease; 324 dilated cardiomyopathy, studied with SE during exercise (n=172), dipyridamole (n=482) or dobutamine (n=237). By selection, all patients had negative SE during follow-up and one of those who eventually underwent RT had perioperative myocardial infarction. However, the incidence of future non-fatal acute coronary syndrome continues to be a major limitation despite negative ESE both in patients in waiting list and after the transplant.

Results: For the overall population, SV index increased from 29±10 to 32±11 ml/m². A significant positive linear relationship between SV changes and EDV augmentation during follow-up (Fig. Middle panel) was present. The SV recruitment was maximal in patients with a positive SE response to dipyridamole (n=482) or dobutamine (n=237).

Conclusions: Patients with negative stress echocardiography may experience an adverse outcome, which can be identified by assessment of systolic function reserve and diastolic relaxation reserve during SE.

P3511 | BEDSIDE
Impact of pre-operative dobutamine stress echocardiography on outcomes in patients undergoing orthotopic liver transplantation
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Background: Coronary artery disease (CAD) increases mortality in patients that undergo orthotopic liver transplantation (OLT). Due to chronic vasodilatory state and poor exercise tolerance, dobutamine stress echocardiography (DSE) is preferred for preoperative evaluation of CAD prior to OLT.

Purpose: We sought to a) study the incidence of positive DSE results and b) assess the role of preoperative DSE in outcomes in patients undergoing OLT.

Methods: We studied 460 patients that underwent DSE within 1 year prior to OLT between 2004–2011. Clinical and DSE data was recorded. Primary outcome included death, stroke and myocardial infarction at 30 days post-OLT. We also recorded long-term deaths.

Results: Clinical and DSE data are shown in Table 1. 30-day events occurred in 14 (3%) patients of DSE positive and 4 (0.9%) deaths at 4.6±2 years of follow-up. No patient with an abnormal DSE had an adverse 30-day event. On Cox survival analysis, only baseline left ventricular ejection fraction (HR 0.90 [0.85–0.96], p <0.001) and not ischemia on DSE (HR 1.05 [0.83–1.33], p=0.7) was associated with long-term deaths.

Table 1. Data of study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>(N=460)</th>
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<tr>
<td>Age</td>
<td>58±7 years</td>
</tr>
<tr>
<td>Men</td>
<td>324 (70%)</td>
</tr>
<tr>
<td>MELD score 7</td>
<td>216±4</td>
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<tr>
<td>Etiology for OLT</td>
<td></td>
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<tr>
<td>Hepatitis C</td>
<td>167 (41%)</td>
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<tr>
<td>Alcohol</td>
<td>122 (27%)</td>
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<tr>
<td>NASH</td>
<td>85 (18%)</td>
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<tr>
<td>Other</td>
<td>66 (14%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>114 (25%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>161 (35%)</td>
</tr>
<tr>
<td>% %MPHR on DSE</td>
<td>84±9%</td>
</tr>
<tr>
<td>Max rate pressure product</td>
<td>18489±4007</td>
</tr>
</tbody>
</table>

Conclusion: Patients with negative stress echocardiography may experience an adverse outcome, which can be identified by assessment of systolic function reserve and diastolic relaxation reserve during SE.

P3510 | BEDSIDE
End-systolic volume and end-diastolic volume reserve predict cardiac events in patients with negative stress echocardiography
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Background: The potentially prognostically relevant information on left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) changes in patients with negative SE for heart-failure-related events is unsettled.

Aim of this study was to assess the prognostic value of stress-induced variation in LVEDV and LVESV changes in patients with negative SE.

Methods: We enrolled 890 patients (593 males, age 63±12 years, ejection fraction 47±12%, with negative (exercise 172, dipyridamole 481, and dobutamine 237) SE result. Cardiac index (CI) was evaluated at rest and peak stress from raw measurement of heart rate by EKG, LVEDV and LVESV by biplane Simpson rule from 2D-echo. Changes from rest to peak stress (reserve) were tested as predictors of combined death and heart failure hospitalization.

Results: For the overall population, CI increased from 2.05 to 3.33 L/min/m². At peak stress, 181 patients decreased the LVESV and increased the LVEDV (Group I) with a higher CI increase (+ 1.89 L/min/m² vs. rest); 573 patients decreased the LVESV and the LVEDV (Group II-III, loss of systolic function and decreased relaxation; CI + 1.17 L/min/m² vs. rest); 136 patients increased the LVESV during stress (Group III, decreased systolic function and decreased relaxation; CI +0.90 L/min/m² vs. rest); p<0.05 between Groups (Figure). During a median follow-up of 19 months (interquartile range 8–36), 50 deaths and 84 hospitalization occurred. The overall event-free survival for the Group I subjects was 89%, compared with 86% (Group II) and 76% (Group III) patients, p=0.02.

Conclusions: The potentially prognostically relevant information on left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) changes in patients with negative SE for heart-failure-related events is unsettled.

Response to DSE Ischemic 4 (0.9%) Nondiagnostic 96 (21%) Normal 360 (78%)

Conclusion: In patients undergoing preoperative DSE prior to OLT, there is a low incidence of ischemia on DSE; and it has no association with 30-day events. Ischemic response on DSE does not predict long-term outcomes following OLT.
Conclusions: Angina were the first abnormal manifestation of myocardial ischemia in 9 (22%), 73 (95%), 62 (80%) and 64 (83%), respectively. Forty patients (52%) developed DST-induced myocardial ischemia, which can variably be manifested initially by strain rate were the best predictors of cardiac death \[HR: 2.4 \pm 0.095 \text{ (95\% CI: 1.5–3.7)}\] < \(x^2=86.15\) and \(x^2=84.06\) to \(x^2=87.3\) after inclusion of LVEF, LVVTI, longitudinal strain (or strain rate), an independent and additive predictive value in a model including age, sex, resting LVEF, LVVTI, longitudinal strain (or rate), \(\Delta\)EF, \(\Delta\)LVVTI (as measures of contractile reserve) and the type of cardiomyopathy (model \(x^2=84.06\) increased to \(x^2=86.15\) and \(x^2=84.06\) to \(x^2=87.3\) after inclusion of \(\Delta\) longitudinal strain and strain rate, respectively, \(p\) for change < 0.001).

Conclusion: In severe chronic systolic heart failure, the longitudinal, circumferential, and radial deformation are related with cardiac death. The dobutamine-induced changes in longitudinal myocardial ischemia detection of LV function are the best predictors to stratify the risk for cardiac death.

Conclusions: In this study of postmenopausal women at low to intermediate risk for coronary artery disease (SMART study), 5 year outcome

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Purpose: To determine the value of contrast stress echo (CSE), stress ECG (sECG) & novel biomarkers for major adverse cardiovascular events (MACE) prediction in postmenopausal women at low-intermediate risk for CAD.

Methods: 366 postmenopausal women [age 54±5 yrs, Framingham risk 7±4%] were prospectively studied during simultaneous CSE & sECC. Abnormal CSE was defined as new or worsening WM abnormalities at stress; abnormal sECC was defined as ≥1 mm horizontal downsloping ST segment depression/elevation (80 ms). All patients underwent resting labs: Brain Natriuretic Peptide [BNP], Atrial Natriuretic Peptide [ANP], Endothelin & high sensitivity C-reactive protein (hsCRP). MACE outcomes [mailed questionnaire] included: mortality, myocardial infarction (MI), chest pain hospitalization (CP) and revascularization (REVASC). Adjusted Cox hazards ratios [HR:95\% CI] were reported.

Results: Followup (4.4±1.2 yrs) was available in 315 (86\%) women [78\% exercise-CSE, 22\% dobutamine-CSE]. Abnormal CSE was in 33 (11\%) while sECC was in 21 (7\%) women. In 33 women with abnormal sECC, CSE was abnormal in 7 (21\%), \(p=0.003\). Total of 27 (9\%) women had MACE: 8 deaths, 4 REVASC, 2 MI, and 13 CP. MACE occurred in 73\% (21\%) vs 20/282 (7\%) of women with abnormal vs. normal CSE, P=0.014 and 82/318 (26\%) vs 18/293 (6\%) of women with abnormal vs. normal sECC, \(p=0.001\). Figures. m, higher in women with MACE vs. without [BNP, pg/ml: 70±106 vs 33±39, \(p=0.001\)]. Abnormal sECC was an independent predictor of MACE [HR 10.3 (1.9–61.4), \(p=0.007\)]; while abnormal CSE was not [HR 2.5 (0.8–31.7), \(p=0.539\)]. Only resting sECC was associated with MACE [HR 2.9 (1.1–7.3), \(p=0.028\)].

Discriminant function analysis revealed that DSR can be used to classify patients into low (<1.7 l/s) and high (≥1.7 l/s) risk of CAD with high accuracy: sensitivity 89\%, specificity 86\%, PPV 79\% and NPV 98\%.

Introduction: Value of early longitudinal diastolic strain rate (DSR) at rest in determining coronary stenosis has been shown in previous studies. However, little is known about the value of early and late DSR during dobutamine stress echocardiography (DSE) while their value can be substantial.

Purpose: To determine the diagnostic value of speckle-tracking echocardiography (STE) derived DSR parameters during DSE to determine significant coronary artery stenosis validated by adenosine magnetic resonance imaging (AMRI) in patients with moderate and high probability of coronary artery disease (CAD).

Methods: 46 patients (mean age 65±8, 7 years) with moderate and high probability of CAD were evaluated by DSE. CAD was defined as having a ≥70\% diameter stenosis on coronary angiography validated as hemodynamically significant by AMRI. Patients were divided into two groups based on the absence or presence of CAD (CAD (-) n=22 vs. CAD (+) n=22). Diastolic longitudinal, circumferential, and radial early and late DSR parameters and their changes from rest (BASE) to low stress (MIN), peak stress (MAX) and recovery (REC) were analyzed using 2D STE.

Results: There were no significant differences in the clinical characteristics, results of conventional echocardiography and DSR parameters between the two groups at rest. From BASE to MIN lateral DSR significantly increased in the CAD (-) group \(\Delta\) (−1.86 l/s to −2.88 l/s, \(p=0.012\)) though not in the CAD (+) group \(\Delta\) (−1.95 l/s to −2.28 l/s, \(p=0.754\)). Same tendency was observed in late longitudinal DSR (CAD (-) 1.27 l/s to 1.53 l/s, \(p=0.001\); CAD (+) 1.27 l/s to 1.41 l/s, \(p=0.074\)). Discriminant function analysis revealed that DSR can be used to classify patients to both groups by 100% accuracy. DSR parameters used were: early longitudinal \(\Delta\)BASE to MIN, early longitudinal \(\Delta\)BASE to MIN, late circumferential \(\Delta\)BASE to MIN, early circumferential \(\Delta\)MIN to MAX, late radial \(\Delta\)MIN to MAX.

Conclusions: Early and late circumferential, circumferential and radial DSR are important markers of validated by perfusion defects hemodynamically significant CAD.

Acknowledgement/Funding: This research was funded by a grant (No. MIP-037/2013) from the Research Council of Lithuania.
Conclusions: Inhaled iloprost acutely reduces RA size, RV systolic volume and RV E/e' in patients with PAH. It also significantly increases the magnitude of RA contraction during RV systole as well as making it occur earlier in RA filling phase. This suggests that iloprost might improve RA mechanical performance and lower right ventricular filling pressures. These results must be corroborated in a larger cohort using invasive measurements.

Acknowledgement/Funding: Fondecyt 1141198

P3519 | BEDSIDE Myocardial scar evaluation by 2D contrast echocardiography
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Background: Scar identification and extension in ischemic cardiomyopathy is of paramount relevance. At present, cMR is the gold standard technique, but it has limited availability or may be in a subset of patients contra-indicated. Thus, alternative noninvasive methods would be desirable.

Methods: In this study we evaluate whether 2D contrast echocardiography (2D-CE-Echo) could be used to identify myocardial scar and its trans-mural extent. We used cardiac magnetic resonance (cMR) as a reference standard technique. Methods: We retrospectively enrolled 38 subjects (76% affected by ischemic cardiomyopathy) who underwent cMR and 2D-CE-Echo for clinical indications. Two-dimensional echocardiographic images were acquired with a low mechanical index (MI=0,1) so that normal myocardium appears hypo-echoic, whereas region with scar brighter. We used transpulmonary contrast agent to improve border definition and evaluate the trans-mural extent of scar.

Results: In 2D-CE-Echo, a total of 139 segments (25% with scar) were evaluated. On a per-segment analysis, 2D-CE-Echo allowed the identification of cMR scars with a sensitivity of 60% and a specificity of 99%. When the presence of a scar is detected, 2D-CE-Echo discriminates with accuracy transmural (sensitivity=88%, specificity=71%) from subendocardial (sensitivity=74%, specificity=84%) infarct.

Discussion: Disagreement between 2D-CE-Echo and cMR was principally due to false negative (60 segments) than false positive segments (6 segments). At univariate analysis, thin segments (<6 mm) and scar localization in anterior, anterolateral wall and apical segments, were predictors of disagreement.

Conclusions: This study shows that 2D-CE-Echo could be used to evaluate the presence and trans-mural extent of scar in patients with ischemic cardiomyopathy. In clinical practice, this technique can be used as alternative method when cMR is contra-indicated or not immediately available.

P3520 | BEDSIDE Assessment of an echocardiographic model to predict significant paravalvular regurgitation after TAVI
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Aim: Paravalvular regurgitation is a major concern when performing transcatheter aortic valve implantation (TAVI), as it has been associated with adverse outcomes. Our aim was to develop a simple calculator to predict the risk of significant paravalvular regurgitation after TAVI.

Methods: We analyzed 217 consecutive patients with severe symptomatic aortic stenosis who underwent TAVI in a single center from 2009 to 2014. Prior to the procedure and immediately after valve deployment all patients underwent transesophageal echocardiography. The echocardiographic image of the aortic valve.

Thickness of the aortic leaflets, mobility and calcium distribution was assessed at 45° and 120–140° views in end diastole. Valve calcification were classified as either mild (1) [mean leaflet thickness <3mm, absence of nodules at the cusps and
annulus calcification), moderate (2) [mean thickness 3–5 mm with small calcium nodules at the cusps and localized calcification at the aortic annulus], or severe (3) [leaflet thickness > 5 mm, large nodules and diffuse calcification of the aortic annulus]. Mobility of aortic cusps was classified as slightly restricted (1) [all commissures seemed to be open], moderately restricted (2) [one fused commissure], or severely restricted (3) [two or more fused commissures]. Prosthetic nominal loss was calculated with the following formula: (nominal prosthesis diameter – maximal unfolding)/nominal prosthesis diameter.

The primary endpoint was significant paravalvular regurgitation, defined as grade ≥ 2 according to VARC-2 criteria.

Results: Mean age was 82.7±6.5 years, and 65% were female. Significant paravalvular regurgitation after TAVI was observed in 9 patients (4.2%). A univariable analysis for paravalvular regurgitation ≥ 2 was performed, and those echocardiographic measurements were used to develop a multivariable prediction model.

Conclusions: We found that echocardiographic factors (mobility, calcification of the native valve, and prosthetic nominal loss) were independently associated with paravalvular regurgitation. The risk for significant paravalvular regurgitation after TAVI was calculated with the following formula: (nominal prosthesis diameter – maximal unfolding)/nominal prosthesis diameter.

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P3521 | BEDSIDE
A new echocardiographic evaluation of ascending aorta elasticity in patients with bicuspid aortic valve
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Background: Bicuspid aortic valve (BAV) is one of the most common congenital heart diseases, frequently associated with diffuse alterations of aortic wall. The aim of this study is to detect whether increased aortic stiffness, very often found in these patients, and traditionally evaluated through echocardiography, has a correlation with aortic strain, evaluated by speckle tracking imaging (STI) technique.

Methods: We enrolled 43 patients (mean age 36.5±16.2 years) with BAV and 13 normal subjects (mean age 30.9±16.0 years), with comparable age and body surface area (BSA). We obtained all the measurements of aortic diameters (annulus, sinus of Valsalva (SV), sinu-tubular junction (STJ) and ascending aorta) by a parasternal long-axis view and indexed them for BSA. Aortic stiffness was calculated using the formula [ln(SBP)/(ΔP)·[Systolic Pressure – Aortic Pressure)].

Results: Ascending aorta was larger in BAV patients than in controls (17±7.7 mm/m² vs. 10.5±6.2 mm/m², p=0.001). Aortic stiffness was increased in BAV patients compared to controls (8.6±7.3 vs 3.7±7.15, p=0.003), whereas LS by STI was significantly reduced (22.9±7.7 vs 6±7.13, p=0.001). In overall population, aortic stiffness was inversely related with left ventricle ejection fraction (r=−0.4, p=0.007) and aortic LS, estimated by STI (r=−0.46, p=0.014), whereas it was directly related with age (r=0.55, p<0.001) and aortic diameters (r=0.36, p<0.01; r=0.50, p=0.001; r=0.42, p=0.005 for SV, STJ and ascending aorta, respectively). An inverse relation has been found also between CS, estimated by STI, and aortic diameters (r=−0.35, p=0.019; r=−0.41, p=0.004; r=0.38, p=0.009, for SV, STJ and ascending aorta, respectively).

Conclusions: BAV is often associated with aortic elasticity impairment. Aortic LS and CS by STI well correlate with aortic dimensions and stiffness. STI allows a new evaluation of aortopathy that could be applied in different BAV types which probably cause a different aortic walls strain.

P3522 | BEDSIDE
Accuracy of adenosine 2D strain stress echocardiography in the detection of coronary artery disease in patients with chest pain

Introduction: Stress echocardiography (SE) with vasodilators or Dobutamine is a valuable tool for noninvasive investigation of coronary artery disease (CAD). Adenosine is easy to administrate, well tolerated and induces little increase in heart rate. Dynamic semi-automated techniques allow quantification of the myocardial deformation and aid in the identification of an abnormal stress response. Global longitudinal strain (GLS) obtained with speckle tracking is recognised as a robust and useful marker of left ventricular function in various pathological conditions.

Purpose: To determine if endocardial GLS (eGLS) in Adenosine SE could identify significant coronary stenoses in patients with chest pain.

Methods: 155 patients with chest pain, suspected for CAD and scheduled for invasive coronary arteriography (CA), were consecutively included. One week before CA, the patients underwent SE with Adenosine 140 μg/kg/min on a Vivid 7 scanner, GE. The CAs were analysed quantitatively in QAngio XA version 7.1, (Medis Medical Imaging Systems) by an experienced reader and the rest and stress echocardiograms were analysed offline with in EchoPac, ver. 113 blinded to the results of the CA. Seven (4%) patients dropped out and 16 (10%) were excluded due to poor acoustic signals yielding 132 patients (mean age (sd) 62.6 (9) years, 70% male)/2376 segments for analysis. Speckle tracking was successfully performed in 98.1% of the segments at rest and 97.7% during stress (p<0.02).

Conclusions: Adenosine GLS during Adenosine SE may be used as a noninvasive tool to stratify patients suspected of CAD. However, there seems to be a wide overlap in the increase in stress induced by Adenosine in patients with and without significant stenoses.

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P3523 | BEDSIDE
Stress speckle tracking; an underestimated tool in detecting myocardial viability
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Introduction: The local deformation properties of viable and nonviable myocardium in response to dobutamine challenge have been well established but there are limited data on the feasibility of strain and strain rate in exercise stress echocardiography.

Objective: To detect the feasibility of stress speckle tracking to detect myocardial viability in comparison to cardiac MRI in post-STEMI patients.

Methods: 54 patient enrolled in our study, Dobutamine stress echocardiography was performed 4 days post-infarction accompanied with automated functional imaging (Speckle tracking) analysis of left ventricle during rest and during low dose stress. All patients underwent a follow up stress echocardiography at 6 weeks with concomitant speckle tracking analysis. Cardiac MRI took place at 4 days and 6 weeks post-infarction as well. We carried out an assessment of re-admission with ACS in a period of 12 months.

Results: The usual cardiac risk factors including hypertension, DM and smoking had no impact on the global and regional longitudinal stress strain rate obtained with speckle tracking. Global stress strain rate value of −10.35 at 6 weeks was able to differentiate viable myocardium with 85% sensitivity and 75% specificity in comparison to cardiac MRI. Accordingly regional stress strain rate of 3.5 at 6 weeks had 90% sensitivity and 80% specificity in viability assessment. Global and regional stress strain rate values of −9.5 and 4 were significant to predict re-infarction at 12 months, p-value <0.05.
of the 3rd tertile exhibited the worst LV EF (%) (26.6±3 vs 32.5±5 vs 34.5±8; p < 0.0001); VO2 max (13.4±2 ml/kg/min vs 16.4±4 ml/kg/min vs 20.5±5 ml/kg/min; p < 0.0001) and E/e’ (1625±12 vs 18±12;p = 0.0003) with respect to those of the 2nd and 1st tertile.

Conclusion: CPOM is an integrated measure of LV pumping capability that may be important to stratify patients with adverse LV remodeling with potential additional prognostic information either in association with resting echocardiographic studies or cardiopulmonary exercise testing.

CARDIAC MECHANICS AND VALVULAR HEART DISEASE

P3525 | BEDSIDE

Edge-to-edge repair in patients with secondary mitral regurgitation: effect of echocardiographic speckle tracking analysis

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Purpose: To evaluate the effect of catheter-based edge-to-edge mitral valve repair (MVR) with the Mitraclip-System on left ventricular (LV) systolic function as measured by echocardiographic speckle tracking analysis (STA) in addition to standard parameters.

Methods: There were 20 deaths and 3 VAD implantation during a mean follow-up of LV mechanics, constant despite changing inotropic and chronotropic challenge. However, in our population with severe LV dysfunction and sMR it seems that MR reduction by MVR did not lead to significant LV size reduction.

Conclusions: Endystolic rotation as well as twist of the LV are intrinsic features of LV mechanics, constant despite changing inotropic and chronotropic challenge. Endystolic rotation and twist of the LV are intrinsic features of LV mechanics, constant despite changing inotropic and chronotropic challenge.

Conclusions: STA offers sensitive measures of both global and regional LV function. However, in our population with severe LV dysfunction and sMR it seems that MR reduction by MVR did not lead to significant LV size reduction.

P3527 | BEDSIDE

Back to the future: head to head comparison of hemodynamically re-validated Doppler end-diastolic pulmonary regurgitant gradient and ASE-AECVI algorithm for the estimation of pulmonary wedge pressure

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Purpose: The echocardiographic continuous-wave Doppler edge-to-diastolic pulmonary regurgitant pressure gradient (PVRG) has long been validated to calculate pulmonary arterial wedge pressure (PAWP) when vascular resistances are normal. We validated PVRG in patients undergoing diagnostic catheterization and used it as reference for the ASE-AECVI algorithm (ALGO) to predict increased PAWP in a large non-selected population.

Conclusions: STS offered sensitive measures of both global and regional LV function. However, in our population with severe LV dysfunction and sMR it seems that MR reduction by MVR did not lead to significant LV size reduction.

Methods: We examined 183 patients (age 68±11 y.; NYHA: 2.4±.6; n=63, coronary artery disease; n=52, dilated cardiomyopathy; n=68, aortic stenosis) in a Foundation IRCCS Polycyclic Sam Matteo, Medical Clinic II – University of Pavia, Pavia, Italy; 2Department of Cardiology, Astana, Kazakhstan;

Background: Cardiac power output (CPO), which is the product of mean arterial pressure (MAP) and cardiac output (CO), is a measure of cardiac energy delivery. Echo-derived peak cardiac power output-to-mass (CPOM) is a variable that couples CPO with LV mass at peak exercise or during maximal inotropic stimulation. Since it is a measure of the rate at which cardiac work is delivered with respect to the potential energy stored in LV mass, it provides indirect information about the efficiency of such transformation.

Aim: To assess the influence of patients with chronic stable heart failure (HF) submitted to exercise echocardiography (ESE) to test exercise echocardiography (ESE).

Methods: A symptom-limited graded bicycle semi-supine ESE was performed in 125 patients (age: 61±11 years, 20% female) with LV systolic dysfunction (LV ejection fraction [EF]= 30±6%). A complete echocardiographic study, including the assessment of ratio of mitral to myocardial early velocities (E/e') as a surrogate of mitral to LV filling pressure, was performed. CPOM was calculated as the product of a constant (K=2.2×1011) with CO and MAP divided by LV mass (M) to convert the units to watts/100 g: CPO = K × CO (l/min) × MAP (mmHg) × M (g). Patients were followed-up for the endpoint of all-cause mortality or ventricular assist device (VAD) implantation.

Results: There were 20 deaths and 3 VAD implantation during a mean follow-up of 819 days. In a multivariate proportional hazards survival model, CPOMP (HR 0.17, 95% CI 0.02–0.16, p = 0.0004) was selected as the most powerful independent predictor of mortality or ventricular assist device (VAD) implantation. CPOMP was 44% in patients of the 3rd tertile (CPOMP < 0.60 watts/100 g), 87% in patients of the 2nd tertile (between 0.60 and 1.0) and 92% in those of the 1st tertile (CPOMP > 1.0 watts/100 g) (Log rank: 35.6; p = 0.0001). Patients of the 1st tertile (COPM ≤ 0.35 g), 87% in patients of the 2nd tertile (between 0.60 and 1.0) and 92% in those of the 3rd tertile exhibited the worst LV EF (%) (26.6±3 vs 32.5±5 vs 34.5±8; p < 0.0001), VO2 max (13.4±2 ml/kg/min vs 16.4±4 ml/kg/min vs 20.5±5 ml/kg/min; p < 0.0001) and E/e’ (1625±12 vs 18±12;p = 0.0003) with respect to those of the 2nd and 1st tertile.

Conclusion: The quantitative assessment of the rotation and twist of the left ventricle during dobutamine stress echocardiography—comparison between patients with and without significant coronary artery stenosis

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Background: Rotation (R) and twist (T) of the left ventricle (LV) can be assessed quantitatively by speckle tracking echocardiography (STE). Although evaluated in various clinical settings at rest it is poorly validated during stress echocardiography.

Aim: Our aim was to calculate and compare rotation at basal and apical levels of LV and twist of LV at rest (0), at peak stage (1) and recovery (2) of dobutamine stress echocardiography (DSE) in patients without (non-CAD) and in patients with coronary artery disease (CAD).

Methods: We analyzed 44 patients with angiographically excluded significant coronary stenosis (27 female, mean age 62±10 years) in whom CPO was performed and 50 patients with significant lesions in coronary arteries confirmed in coronaryography (18 female, mean age 61±9 years). Rotation was measured at basal and apical levels of LV. We compared rotation measured at aortic valve closure (AVC) and twist (T) calculated as a difference of basal and apical RAVC. Heart rate at all stages of DSE was similar in compared groups.

Results: Neither endystolic rotation nor twist changed significantly during DSE in both groups. Nevertheless, apical rotation at the peak stage of DSE and at recovery were higher in CAD patients whereas absolute value of basal rotation at peak stage was higher in non-CAD, see Table Rotation and twist parameters during DSE

Parameter Non-CAD CAD p

Ravc basal segments (0) -2.91±3.33 -2.47±2.02 ns
Ravc apical segments (0) 3.62±3.33 4.83±1.16 ns
Twist (0) -6.94±4.48 7.3±3.87 ns
Ravc basal segments (1) -3.17±3.94 -2.79±3.25 ns
Ravc apical segments (1) -3.17±3.52 1.5±4.45 p<0.01
Twist (1) -6.73±5.3 8.22±3.13 ns
Ravc basal segments (2) -3.87±3.37 -2.63±2.42 p<0.03
Ravc apical segments (2) 2.67±2.73 5.05±3.65 p<0.01
Twist (2) 6.27±4.61 7.68±4.72 ns

Conclusions: STS offers sensitive measures of both global and regional LV function. However, in our population with severe LV dysfunction and sMR it seems that MR reduction by MVR did not lead to significant LV size reduction.

P3525 | BEDSIDE

Value of peak cardiac power output-to-left ventricular mass to risk stratify patients with chronic systolic heart failure

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Background: Cardiac power output (CPO), which is the product of mean arterial pressure (MAP) and cardiac output (CO), is a measure of cardiac energy delivery.
negative predictive values (NPV 55%). In the PROS study, feasibility was high (PWPe 75%; E/E' 90%, LAVi 93%, E/A 95%, Edec 90%, SF 91%, PSPe 92%). Using the ALGO, 16% of patients were unclassified, prevalently secondary to combined E/e' = 9–13 range and LAVi >34 ml/m². In the remaining (84%) patients, utility of ALGO to predict high PWPe was impaired by low PPV (EF <50% = 18%, EF >50% = 85%) whereas NPV was good (EF 50% = 98%, EF >50% = 84%). Further, when E/e' alone was tested in the same patients at ROC analysis (cutoff=15; AUC=0.72; CI: 0.6-0.8), accuracy was still impaired by a low PPV (53%), albeit a fair negative predictive value (NPV, 79%). Correlation of E/e' with PWPe was poor even when EF >50% (r=0.4, p<0.001) at regression analysis. E/e' was independently determined by age and mitral regurgitation in all patients, and by LV end-diastolic volume in EF <50% (r=0.7, p<0.001), and LV mass index in EF >50% (r=0.64, p<0.001).

Conclusions: PWPecho performs better than ALGO in estimation of PWP in unselected patients. The ALGO is limited by a low PPV irrespective of EF%, and utility of E/e' is limited by influence of patient age, preload and LV mass.

P3528 | BEDSIDE
Determination of the compensatory mechanism in HCM and severe aortic stenosis patients with preserved LV ejection fraction by 2D myocardial multi-layer speckle tracking strain echocardiography

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Background: Multi-layer speckle tracking transthoracic echocardiography (STTE) can quantitate strain measure in the endocardial and epicardial layers of the left ventricle (LV).

Purpose: To evaluate compensatory mechanisms in hypertrophic cardiomyopathy (HCM) and severe aortic stenosis (AS) subjects with a preserved LV ejection fraction (EF) >50%. We measured 2D LV global longitudinal strain (GLS) and segmental myocardial multi-layer speckle tracking strain echocardiography (2D SRS) 0.50 3.82±9.9 31.3% 0.39 −0.45±10.49 31.9% 0.215

Conclusions: In HCM and severe AS with preserved LEVF, all GLS values were significantly smaller than in controls. We speculate that in such subjects, endocardial GCS is maintained in compensation for GLS decrement, and may contribute to maintaining LEVF.

P3529 | BEDSIDE
The impact of significant tricuspid regurgitation on echocardiographic assessment of right ventricular performance

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Background and purpose: Right ventricular (RV) function is a known predictor of outcome in a variety of cardiovascular diseases. It is important to measure right ventricular function accurately. However, many echocardiographic parameters of RV performance is known to be susceptible to TR grading.

Conclusions: In HCM and severe AS with preserved LEVF, all GLS values were significantly smaller than in controls. We speculate that in such subjects, endocardial GCS is maintained in compensation for GLS decrement, and may contribute to maintaining LEVF.

P3530 | BEDSIDE
Impact of global and segmental hypertrophy on 2D and 3D strain in hypertrophic cardiomyopathy: comparison with healthy subjects

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Objectives: We studied the impact of hypertrophy on global and regional 2D and 3D strain in primary HCM as compared with controls.

Methods: A comprehensive resting 2D and 3D echocardiography was performed in 40 HCM and in 50 controls with a comparable distribution of age, gender, and left ventricular ejection fraction (LVEF). LV global (G) and segmental (S) measurements of all 2D and 3D peak strain components (longitudinal: GLS, SLS, circumferential: GCS, SCS, radial: GRS, SRS and area: GAS, SAS) and 3D indexed LV end-diastolic myocardial mass (3D LVED mass) were obtained from all patients. LV wall thickness (LWWT) was assessed in short-axis views and classified in 4 quartiles (<10.5 mm, 10.5–13.0 mm, 13.0–16.5 mm and >16.5 mm).

Results: For global and regional 2D and 3D strain analysis results were consistent. However, reproducibility of 3D strain was similar or greater and more consistent for all strain components as compared to 2D strain analysis (table 1).

Conclusion: 3D strain is a reliable technique to assess myocardial deformation. Myocardial mass is related with 3D strain components in HCM patients. Circumferential deformation, as compared to longitudinal, seems to be the main determinant of the systolic function in HCM patients.
uniformity shortening are common histological features of HCM even in the presence of normal left ventricular ejection fraction. Abnormalities in 2D speckle tracking echocardiography-derived parameters have been described in HCM patients showing a significant correlation with myocardial fibrosis. However, values of 3D speckle tracking parameters in this population have not been fully studied. The aim of our study was to evaluate LV 3D speckle tracking parameters in HCM patients and its relation to functional parameters.

Methods: Twenty-four patients with HCM and thirty controls were included in the study. All subjects underwent conventional and 3D speckle tracking echocardiography (3DSTE) using the Scanner Ardisa 4D System. Global 3D longitudinal, circumferential, radial strains and area tracking were investigated.

Results: Patients with HCM showed attenuated global longitudinal (GLS) and circumferential strain (GCS) compared to controls (HCM vs. controls, GLS: −4.2±1.4 vs. −4.8±1.1%, p<0.001; GCS: −34.9±4.1 vs. −39.4±4.6%, p<0.001 for both). 3D area tracking (AT) was also significantly impaired compared to controls (HCM vs. controls, −33.6±7.5% vs. −47.99±4.8%, p<0.001). Left atrial (LA) volumes were moderately correlated with AT (r=−0.46, p=0.05). Additionally, the degree of LV obstruction was also correlated with GCS (r=−0.43, p=0.05).

Conclusions: 3D speckle tracking LV deformation parameters are impaired in patients with HCM providing novel insight into the pathophysiology of the disease. The relation between AT and LA volumes may reflect some degree of diastolic dysfunction. Its role over 2D speckle tracking echocardiography as well as its potential to predict clinical outcomes needs further evaluation.

P3534 | BEDSIDE
Age- and Gender-related Differences on Left Ventricular Systolic Mechanics in Asymptomatic Asian Population: Special Focus on Torsion

Background: Gender may play an important role in left ventricular (LV) geometry and further contribute to LV mechanics with aging. The influence gender in age-related LV remodeling and torsion in asymptomatic Asian population remains largely unknown.

Methods: We consecutively enrolled asymptomatic subjects who underwent cardiac structure, function, and 2D-based speckle-tracking including strains and twist/torsion were all analysed.

Results: Totally 4,100 subjects were analysed (mean age: 49.9±10.8 years, 52.7% females). Advanced age quintiles was associated with greater wall thickness, higher LV mass index (all trend p<0.001). Compared to men, women showed both higher global longitudinal (~19.88 vs ~21.02%) and circumferential strains (~21.79 vs ~21.14%), greater torsion (2.13 vs 2.34°/cm) and better LV ejection fraction (61.8 vs 63.3%, all p<0.001). Graded reduction of global LV longitudinal and circumferential strains with advanced age was accompanied by greater twist/torsion (adjusted estimate 0.7° & 0.13°/cm per decade, respectively, both p<0.05), which is more pronounced in women (interaction p<0.05).

Conclusion: Advanced age is associated with greater cardiac mass and progressive contractile functional decline in terms of strains though augmented torsion, which is more obvious in women. These findings suggested a gender-specific contractile difference with aging in asymptomatic population.

P3533 | BEDSIDE
Reduction in left atrial early diastolic strain rate evaluated by two-dimensional speckle tracking echocardiography in acute ischemic stroke patients with sinus rhythm
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Background: The left atrial appendage (LAA) was reported to be a major source of cardioembolism in stroke patients with atrial fibrillation. LAA dysfunction is associated with LA thrombus formation. Recently, it was reported that left atrial (LA) strain assessed by two-dimensional speckle tracking echocardiography is a feasible parameter for evaluating LA function. There are three types of LA mechanical function: reservoir, conduit and booster pump function. The association between LA strain and LAA function remains to be fully determined.

Purpose: In the present study, we investigated whether LA strain rate of conduit function is associated with LAA dysfunction in patients with acute ischemic stroke.

Methods: We performed transthoracic and transesophageal echocardiography (TEE) in 83 patients with acute ischemic stroke in sinus rhythm (56 males, mean age 73±11 years) within 7 days of onset. We measured left atrial early diastolic strain rate (LAAe'sr) as LA conduit function by two-dimensional speckle tracking imaging in apical four- and two-chamber views. We measured left ventricular ejection fraction (LVeF) and the ratio of peak early atrial and peak diastolic velocity to E/e'. (LAAe'sr) was significantly higher in patients with LAA dysfunction than those without (~0.99±0.40 vs. ~1.35±0.64, P<0.05). LAAe'sr was correlated with LAVE (r=−0.33, p<0.05), left ventricular ejection fraction (r=−0.29, p<0.05) and E/e' (r=−0.35, p<0.05).

Multivariate logistic regression analysis showed that LAAe'sr was an independent predictor of LAA dysfunction (odds ratio 3.30, p<0.05).

Conclusion: Impaired LA conduit function evaluated by LA strain rate was a promising parameter for LAA dysfunction in patients with acute ischemic stroke.
GENETICS AND GENE THERAPY

P3535 | BENCH
The long noncoding RNA MALAT1-derived mascRNA is highly enriched in immune cells and regulates monocyte-macrophage functions

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Background: Next generation sequencing revealed that the majority of the human genome is transcribed but has no coding function. It is estimated that >30,000 long noncoding RNAs (lincRNAs) are expressed in humans but their functions are largely unknown. We searched for IncRNAs influencing antiviral capacity in patients with viral cardiovascundary cardiomyopathies and assign immunoregulatory functions to a small lincRNA-like processing product of the IncRNA MALAT1.

Methods and results: To identify functions of the MALAT1-lincRNA system in the context of cardiotoxic viral infections, we investigated its expression in immune cells and cardiomyocytes. Whereas the primary transcript MALAT1 was expressed in all cells and tissues, the small lincRNA-like product mascRNA was highly enriched in immune cells. Antisense oligonucleotide (ASO)-mediated mascotRNA ablation in monocytes led to massive induction of FASLG, TNF-a, and IL6, indicating important immunoregulatory functions of mascRNA in this cell type.

Conclusions: MALAT1-derived mascotRNA has important immunoregulatory functions. Beyond its specific lincRNA, multiple others are associated with cardiovascular diseases, but have complex cellular functions and thus are difficult therapeutic targets. Strategies to address lncRNA products with restricted functions appear more promising. MascRNA exemplifies a first target of this type and its modulation by mimetic or antisense drugs has cardiovascular therapeutic potential.

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P3536 | BENCH
A novel locus on chromosome 19p13.3 linked to arrhythmogenic cardiomyopathy

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Background: Arrhythogenic cardiomyopathy (ACM) is an autosomal dominant myocardial disorder characterized by progressive cardiomyocyte death, followed by fatty or fibrofatty replacement. It is recognized worldwide as the second most common cause of unexpected sudden death among young people and athletes. Thirteen causative genes have been identified thus far, with a central role of the desmosomal genes. Since causative mutations in ACM genes have been detected in about 50% of probands, additional and still unknown disease-genes should be involved.

Purpose: The aim of the present study is to identify a novel disease locus/gene involved in the genetic determination of ACM in a large family, in which the proband resulted negative for mutations in the major ACM genes.

Methods: The proband and additional 44 family members were genotyped by using a SNP array (370,000 markers) and a multipoint linkage analysis using an “affected-only” approach was carried out. The presence of structural variations was determined through a copy number variations analysis (CNV). Next Generation Sequencing (NGS) technology was then applied in order to identify a novel disease gene into the linkage region by sequencing the whole exome (WES) of 4 affected family members. Exons with insufficient reads (coverage <15X) of the 13 known genes and of the genes inside the critical region were further evaluated by Sanger sequencing.

Results: Parametric linkage analysis allowed to exclude linkage of ACM to markers in 8% of the genome (pLOD < -2) and yielded a single significant linkage peak on chromosome 19p13.3, with a maximum parametric LOD score of 3.85. Analysis of haplotype segregation defined a region of 2 Mb on chromosome 19 shared by all the affected individuals. After the exclusion of good candidate genes into the critical region and the presence of any large insertions/deletions (CNV analysis), WES was performed in 4 affected family members. Sequencing data didn’t reveal the presence of any novel variant shared by the 4 subjects, neither into the linkage region nor in the rest of the exome. Direct sequencing of the uncovered exons both into the critical region and in the 13 known ACM genes directly revealed the presence of additional variants except for a novel intron variant (c.766+8C>A) in TMEM43 gene. The segregation of this variant among all the available family members excludes an association with the disease phenotype.

Conclusion: In this family showing no mutations in known ACM genes segregating with the disease locus the novel disease was mapped on chromosome 19p13.3 and a critical region of 2 Mb was defined.

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P3537 | BENCH
Constitutively active phosphatase inhibitor-1 improves cardiac contractility in unchallenged mice but is deleterious in a model of pressure-overload

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Recently the phosphatase-inhibitor-1 (1-1) was identified as a distal and positive-acting mediator of ß-adrenergic (ß-AR) signaling, which inhibits the cardiac type-1 phosphatase (PP1). This pathway allows amplification of PKA-mediated effects on the phosphorylation state of regulatory proteins, e.g. phospholamban (PLB). Moreover, 1-1 was found to be markedly down-regulated and hypo-phosphorylated in experimental and human heart failure and thus likely contributes to pathogenesis of ß-AR desensitization. Aim of our study was to investigate whether adeno-associated virus serotype 9 (AAV9) -mediated cardiac-specific expression of a constitutively active, truncated inactive (1-1c) is able to ameliorate the development of heart failure following transverse aortic constriction (TAC) in mice. Therefore, AAV9 vectors containing 1-1c DNA under control of a human troponin T promoter (AAV9/I-1c) were created and 6 week-old C57BL/6 wild-type mice were subjected to TAC. Two days later 2,75E+12 AAV9/I-1c vector particles were intravenously injected into these mice (n=12). AAV9 harbouring a Renilla luciferase reporter (AAV9/hRluc) was used as a control vector (n=12). Cardiac morphology and function was evaluated weekly by echocardiography. After 28 days, pressure-volume loops, histological and molecular analyses were performed.

At day 28, both groups showed progressive deterioration of contractile function and left ventricular remodelling. Surprisingly, echocardiographic assessment revealed significantly increased myocardial hypertrophy in AAV9/I-1c-treated mice compared to AAV9/hRluc-treated controls (cardiomyocyte surface area 218±14,68±6µm2; p<0.05; 195±8,46±4µm2; p<0.05). Hearts of AAV9/I-1c-treated TAC mice showed a higher phosphorylation of PLB compared to control mice. In contrast, cardiac-specific expression of 1-1c in unchallenged animals resulted in selective enhancement of PLB phosphorylation and augmented cardiac contractility. Our data suggest that AAV9-mediated cardiac expression of 1-1c, usually associated with enhanced Ca2+-cycling, improves cardiac contractile function in unchallenged animals but failed to protect against cardiac remodeling induced by TAC in wild-type mice. We conclude, that in heart failure rather down-regulation of 1-1 may therefore be a potential strategy to treat heart failure.

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Translational regulation shapes the molecular landscape of complex disease phenotypes

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RNA transcriptional phenotypes have been studied extensively, but the extent of translational regulation in mammalian tissues remains largely unknown. To ad-}

Address this, we adapted ribosome profiling to reliably monitor genome-wide protein synthesis at single ribosome resolution in rat organ tissues. To investigate strain-specific translation, we profiled RNA expression and ribosome occupancy in heart and liver tissues in the spontaneously hypertensive rat (SHR/Ola) and the reference strain (BN-Lx). Translational variation is mostly forwarded to the translational level
Mice with cardiac specific overexpression of hDSC2 develop a biventricular cardiomyopathy associated with severe fibrosis and calcification

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Mutations of DSC2 cause arrhythmogenic cardiomyopathy (AC). DSC2 is localized within the cardiac desmosomes and contributes to the Ca2+-dependent adhesion of cardiomyocytes at the intercalated disc. However, the molecular and cellular mechanisms induced by DSC2 mutations leading to AC are widely unknown.

So far, no DSC2 mouse model mimicking an AC is described. Therefore, the aim of this study was to establish and characterize an adequate transgenic mouse model to investigate the underlying pathomechanisms in vivo.

We developed and characterized a transgenic mouse model with a cardiac-specific overexpression of hDSC2. Echocardiography and (immuno)histology were used to characterize the functional and structural defects in our DSC2 mouse model. These experiments were complemented by Western blot analysis and qRT-PCR experiments to characterize the molecular expression changes of other desmosomal genes.

Non transgenic

Analysis using echocardiography revealed that transgenic mice shortly after birth develop a severe cardiomyopathy with significantly reduced fractional shortening and ejection fractions compared to non-transgenic mice. Histopathology demonstrated that the myocardium is significantly replaced by fibrosis and fatty tissue. Furthermore, a severe calcification is detected within the myocardium. In addition, we showed that the expression of other desmosomal genes are significantly reduced in our transgenic mice compared to control mice. Thus, the established cardiac specific overexpressing hDSC2 mice are viable but develop a progressive biventricular cardiomyopathy mimicking the clinical phenotype of patients with arrhythmogenic cardiomyopathy. This novel mouse model might contribute to further understanding of the molecular and cellular pathomechanisms leading to arrhythmogenic cardiomyopathy.

Next generation sequencing in thoracic aortic aneurysms and dissections - eight novel mutations in known genes (ACTA2, FBN1, MYH11, SKI, SMAD3, and TGFBR1)

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Background: Thoracic aortic aneurysms and dissections (TAAD) are significant cause of morbidity and mortality and occur either as isolated manifestation or as part of a syndromic condition.

Purpose: The aim of our study was to define genetic background of TAAD.

Methods: In the years 2012–2014 we studied 40 unrelated TAAD patients (pts; 26 male) from a cohort of 120 pts consenting for genetic study. We performed whole exome sequencing on an Illumina HiSeq sequencer. We considered mutations located in the coding or splicing regions of one of established TAAD genes, of frequency no greater than 0.001 in any of 3 databases (1000Genomes, ESP, and ExAC), and classified as pathogenic by at least one of applied software algorithms. Mutation was considered novel when absent from HGMD database (release 2014.2). Once mutation was identified, screening was offered to consenting relatives. Whenever possible, we looked for cosegregation in the TAAD families.

Results: At the time of genetic inquest mean age of the study population was 43.5±13.4 years, 18 had familial TAAD. In 15 pts acute aortic dissection at mean age of 42.3 years was first symptom of TAAD, and 13 pts with thoracic aortic aneurysm had planned aortic surgery as first intervention at mean age of 42.8 years. Associated abnormalities included: BAV – 8 pts, 1 CoA, 1-ASD. We identified causative mutation in 14 pts (35%), 8 of them were novel. Analysis revealed 6 mutations in FBN1 gene: 3 missense variants in EGF-like calcium-binding domains (1 affecting cysteine residue), 1 nonsense, 1 splice site, and 1 in-frame deletion. Single missense mutations were found in each of TGFBR1 and TGFBR2 genes, both affecting their serine/threonine protein kinase catalytic domains. In addition, missense mutations: 1 in highly conserved domain of CHD2 domain in SMAD3, 1 within a hot spot in SKI, 2 in ACTA2, and 2 in MYH11. All detected mutations were absent from 1000Genomes, ESP, and ExAC databases with exception of TGFBR1 (<0.00002 in ExAC) and both MYH11 variants (<0.001 in ESP and ExAC). In familial TAAD, all relatives with TAAD carried identified variants.

Conclusion: The exact disease mechanisms responsible remain unclear. Based on combined clinical and genetic data, syndromic TAAD was diagnosed/confirmed in 9 pts (7-Marfan syndrome, 1-Loeys-Dietz syndrome, 1-Sprintzen-Goldberg syndrome), and nonsyndromic TAAD in 5 pts. Furthermore, we identified 17 mutation carriers among relatives. Summary: Genetic testing supports the diagnosis of inherited, both syndromic and nonsyndromic TAAD. Identification of novel causal mutations adds to heterogeneity of the genetic background of TAAD.

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Gene expression in myocardial tissue and peripheral blood cells: potential RNA-biomarkers for myocarditis identification

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Introduction: Myocardial inflammation followed by cardiomyocyte necrosis is accompanied by altered gene expression in affected cells. Development of the pathology modifies gene expression in myocardial tissues, but also might affect transcription in peripheral blood cells.

Purpose: The study was devoted to investigate modulation of gene expression in myocardial tissues and PBC of patients with myocarditis and to identify potential biomarkers for this pathology.

Methods: 15 endomyocardial biopsy (EMB) samples (M: 10, F: 5; age: 37–62) and 10 PBC samples (M: 6, F: 4; age: 26–50) were obtained from patients with myocarditis, 6 PBC samples were obtained from healthy donors (M: 3, F: 3; age: 25–50), 4 orthotopic heart transplantation autopsy samples (all males) were used as healthy controls. 30 candidate genes were selected for the study. mRNA expression profiles in EMB from male and female groups. An absence of female healthy myocardial tissue forced us not to use the data into further analysis. Expression of 10 candidate genes (NF-kB, IL2, NOTCH3, GLIPR, TMOD3, SEC24A, FCGR1G, ITGB2, SIGLEC1, ADCY7) out of 30 studied was altered in EMB of male patients with myocarditis. 6 out of 10 genes were identified in the present study, transcription level of 4 genes matched to the disease progression. Analysis of transcription in PBC revealed only 2 genes with altered expression; no correlation was found for expression of target genes in PBC and EMB samples.

Conclusion: Significant alteration of transcription was found for 10 genes in EMB samples of male patients with myocarditis. Preliminary results suggest that expression profile can be considered not only as a biomarker of myocarditis, but also for assessment of therapeutic effects and the long-term outcome prognosis for patients with myocarditis.

Strategies to normalize zebrafish specific cardiac phenotypes resembling different human myosin binding protein C3 mutations using RNA approach

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Mutations in the gene encoding myosin binding protein C3 (MYBPC3) are one of the most common mutations in arrhythmogenic cardiomyopathy and can produce varying phenotypes. The exact disease mechanisms responsible remain unknown. Zebrafish model offers unique opportunities to study human cardiovascular disease mechanisms in vivo.
We have previously recapitulated in the zebrafish model four disease causing missense mutations of MYBPC3 domain C1: Mutation1 (Arg177His), Mutation 2 (Ala216Thr), Mutation 3 (Glu258Lys) and Mutation 4 (Ser217Gly). Injection of splice donor site morpholino targets Mutation 1, 2 and 4 at exon 5 and Mutation 3 at exon 6 in zebrafish embryos induced hypertrophic cardiomyopathy similar to the human phenotype. Mutation 3 resulted in severe cardiac phenotype exhibited by 71% zebrafish morphant embryos with enlarged cardiac chambers and reduced heart rate compared to 46% of Mutation 1, 2 and 4. Since it remains unclear whether specific cardiac phenotypes in these morphant zebrafish embryos reflect primary or secondary responses of the heart caused by the accumulation of the mutant mybpc3 RNA; further studies are necessary in order to determine the early changes occur specifically in response to mutation in MYBPC3. Therefore, we assessed the RNA-based approach as a potential correction of HCM. The human MYBPC3 was cloned into pcDNA-DEST47 vector. Site-directed mutagenesis was used to create corresponding mutations mentioned above in the human cDNA followed by generation of mRNA. The wild type human mRNA was co-injected with the morpholino targeting exon 6 to test the ability to suppress the accumulation of the mutant zebrafish mRNA and revert the embryonic zebrafish mutant phenotype. However, the co-injection resulted in aberrant cardiac phenotype and induced hypertrophic cardiomyopathy similar to the morphant embryos, suggesting that this specific cardiac phenotype produced by Mutation 3 might be a secondary response of the heart caused by activation of compensatory mechanisms after the alteration of cMyBP-C. Further work is needed to understand the exact pathogenic mechanisms of these mutations.

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Detection of novel TTN truncating variants in patients with unexplained left ventricular systolic dysfunction and genotype-phenotype correlations
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Background: Recently, TTN truncating mutations have emerged as a common cause of dilated cardiomyopathy (DCM), and novel genotype-phenotype correlations are searched for.

Purpose: Patients with unexplained left ventricular systolic dysfunction (LVSD; LVEF<45%) were studied in order: (1) to identify genetic background of the disease with a focus on TTN truncating mutations and (2) to define genotype-phenotype correlations.

Methods: In the years 2012–2014, 66 unrelated patients (pts) were studied with various approaches of NGS (whole exome sequencing)/TruSight One sequencing panel/targeted sequencing of a panel of 35 genes involved in cardiomyopathies that include TTN). Of these 66 pts, 64 had dilated cardiomyopathy (DCM), diagnosed according to ESC criteria, 1 had DCM associated with left ventricular noncompaction (DCM-LVNc), and one was with LVSD due to hypertrophic cardiomyopathy (HCM-LVSD).

Results: In 18/66 (27.3%) pts we found 16 different TTN truncating variants: 7 frameshift (fs) deletions, 1 fs insertion and 10 stop variants. One variant was located in Z-disc, two in I-band region and 15 in A-band region. There were additional 26 mutation carriers among relatives, half of them were affected (6 with DCM, 6 with mild LVSD (LVEF<50%), 1 with DCM-LVNc) and the remaining half (13) had normal cardiological study. During follow-up, mean 46.2±49.9 months, major SAE occurred in 7 pts (15.9%, 6 male), 4 had HTX, 2 died of HF, 1 had LVAD. 16 patients had stable course of the disease, 10 noted significant improvement in LVEF and 11 had normal persistent LV function. Of the four male patients who had HTX, two DCM pts had stop mutation in the N2BA exon 276 (HTX at age of 33y and 30y), one DCM pt - fs mutation in exon 289, (HTX at age 43y), each in the fibronectin type III domains, A-band, and last patient with DCM-LVNc - in exon 46, in the unique sequence of TTN N2B transcript, located in I-band (HTX at 51y). Of interest, one of fs variants, located in the N2BA exon 276, was found in 3 pts (one with fulminant onset of DCM treated with LVAD to recovery, one with HCM-LVSD and one in chronic DCM with AF).

Conclusion: The presence of TTN truncating variants with different clinical presentations (DCM, HCM-LVSD, DCM-LVNc) as well as high proportion of asymptomatic mutation carriers among relatives suggest possible influence of other genetic and/or environmental factors on the course of cardiomyopathy. Male pts with the disease have worse prognosis.

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A. Bayes-Genis2, larization and innervation to ensure integration with the surrounding myocardium. Engineered bioimplants for cardiac repair require functional vasculature and nervous system connections to aid in healing. The use of decellularized pericardial scaffolds as myocardial bioimplants after myocardial infarction in swine was performed to confirm the presence of vascular and nervous ultrastructures. Immunohistochemical analysis was performed to confirm the presence of vascular and nervous ultrastructures. Results: Alamar blue assay showed a 2.5 and 3.5 fold increase in EC adhesion on SVV-conjugated scaffolds, after 3 and 6 days of culture compared to control; the effect was specific for SVV. Histology of the gradient scaffolds (H/S) showed a gradient of binding of fluorescent heparin and VEGF compatible with Heparin binding. Vascular structure with erythrocytes within the lumen, confirming functional conduits with blood flow.

Methods and results: We engineered MSCs with integrin-linked kinase (ILK), a pleiotropic protein enhancing progenitor cell homing, reversing myocardial remodeling and improving cardiac function following MI. We evaluated the therapeutic potential of ILK-MSCs in a porcine MI model established by a 90-minute balloon occlusion. These cells were iron-labeled before transplantation and were monitored in vivo by cardiac magnetic resonance imaging. Significantly enhanced homing capacity of MSCs was detected following ILK overexpression in vivo. At 15-day follow-up, intracoronary transplantation of ILK-MSCs improves global LVEF by 7.8% compared with baseline (P=0.03), and by 10.3% when compared with vehicles (P<0.018). Regional LV contractile function was also recovered, accompanied by substantially reduced scar size, myocardial remodeling, fibrosis, cell apoptosis, and increased regional myocardial perfusion and cell proliferation in ILK-MSCs treated minipigs versus vehicles (all significant). Vector-MSCs did not exhibit in significant or significant favorable effects compared with MSC-MSCs, and generated less extent of all other favorable effects compared with ILK-MSCs.

Conclusions: Based on iron-labeling and MRI-monitoring techniques, for the first time we provided visually direct evidence that intracoronary ILK-MSCs had substantially enhanced homing capacity to infarct myocardium in porcine following myocardial infarction. Intracoronary transplantation of allogeneic ILK-MSCs significantly enhanced global and regional LV functions, reversed the remodeling process and restored regional perfusion, which has great implication for cell therapy.

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The longevity gene SIRT6 switches macrophages into an anti-inflammatory phenotype and improves cardiac function after myocardial infarction in mice

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Background and purpose: Ageing has been implicated in macrophage (MQ) dysfunction, deterioration of myocardial homeostasis, chronic inflammation, adverse remodeling and fibrosis. The longevity gene SIRT6 regulates anti-aging and anti-inflammatory properties that protect against several cardiovascular risk factors. However, the role of SRT6 in cardiac repair, and its role in macrophages remain unknown. Therefore, we aimed to determine the role of MQ SRT6 in acute myocardial infarction (MI).

Methods and results: First, we aimed to determine whether SIRT6 is involved in cardiac repair after MI. We induced MI in 12-week old SIRT6-overexpressing (SIRT6-OE) mouse and their wild-type (WT) litter mates as controls. Thirty days after MI, SIRT6-OE mice developed higher LV fractional shortening (46%, p<0.05) and smaller LV mass (25%, p=0.12), as compared with WT controls. Then, to determine whether SIRT6 influences cardiac MQ phenotype after MI, we induced MI in 12-week old SIRT6-OE mouse and their WT litter-mates and analyzed cardiac MQ phenotype by flow cytometry using the markers: CD68 vascular cell adhesion molecule (VCAM), macrophage 1 (M1), and macrophage 2 (M2). At day 4 after MI, the M2/M1 ratio was 4 fold higher in the cardiac MQs of SIRT6-OE mice, compared with WT controls (p=0.11). Subsequently, to assess the role of SIRT6 in MQ, we obtained peritoneal MQs from SIRT6-OE and WT mice and cultured them to homogeneity. Quantification of SIRT6 by immunofluorescence on cryosections showed that SIRT6 level was greater by 1.7 fold (p=0.06) in SIRT6-OE cardiac MQs compared with WT. Furthermore, we found reduced expression of the pro-fibrotic genes TGF-β (p=0.14), MMP9 (p=0.05) and MMP12 (p=0.02) in MQs extracted from SIRT6-OE mice, compared with WT mice. Conclusions: Over expression of the longevity gene SIRT62 improves cardiac remodeling and function after MI. SIRT6 regulates MQ activation and promotes anti-inflammatory and anti-fibrotic properties. Our preliminary results suggest that targeting macrophage SRT6 could be a novel therapeutic strategy for acute MI.

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Transplantation of cardiac progenitor cells with three-dimensional scaffold onto the surface of expected infarction area and confined it inside of the pericardial space by using parietal pericardium (pericardial grafting method). Finally, we compared the graftability of this method with that of conventional pericardial transplantation. Pericardial grafting of CPC-scaffold is a useful method to improve graft area 4 weeks after transplantation. By using CPCs expressing red fluorescence-labeled avidin, scaffolds were globally detected in the graft area and elongation of fibrotic length at 4 weeks after Tx, indicating attenuated ventricular remodeling after MI.

Conclusion: HiPSC-derived CPSs potentially ameliorate cardiac dysfunction of human-size intact heart.

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Human amniotic fluid stem cell secretome protects cardiomyocytes against doxorubicin toxicity

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Introduction: Anthracyclines are the mainstay of treatment for several tumor types, including breast cancer and lymphomas, but in a substantial proportion of patients. No truly effective way to prevent or treat anthracycline cardiotoxicity currently exists. In recent years, it has been demonstrated that soluble factors secreted by human amniotic fluid stem cells (hAFS) can exert cardioprotective effects. We sought to determine whether the secretome of hAFS could antagonize the toxicity of doxorubicin, the prototype of anthracyclines, on cardiomyocytes.

Methods: c-kit positive hAFS were isolated from amniotic fluid collected during second trimester diagnostic amniocenteses that had proved negative for disease. Cells were cultured in serum-free medium for 24 hours in normoxia (20% O2) or hypoxia (1% O2). The rat cardiomyoblast cell line, H9c2, and primary mouse neonatal cardiomyocytes (nCM) were pre-treated for 3 hours with hAFS-conditioned media (hAFS-CM) before being exposed to pro-senescent (0.1 μM) and pro-apoptotic (1 μM) concentrations of doxorubicin for 3 and 18 hours, respectively. Cell senescence and apoptosis, two main features of doxorubicin cardiotoxicity, were evaluated by staining for senescence associated (SA) β-galactosidase and apoptosis by Hoechst staining, respectively. The expression of a selected intracellular signaling pathways was investigated by immunofluorescence and/or western blot. Experiments with specific kinase inhibitors were then performed.

Results: Both senescence and apoptosis caused by doxorubicin were significantly counteracted by hAFS-CM, the effect being more intense with hAFS-CM obtained in hypoxic conditions. Positivity for SA-β-galactosidase was decreased by 39.5% and 51% by normoxic and hypoxic hAFS-CM, respectively. A reduction in apoptosis by 30% and 50%, respectively, was also observed. The capability of hypoxic hAFS-CM to prevent doxorubicin-triggered senescence and apoptosis was confirmed in nCM (47% and 43% inhibition, respectively). Protection by hAFS-CM was associated with phosphorylation of Akt and Erk1/2. Consistently, pre-treatment with LY294002 – which blocks phosphatidylinositol 3-kinase and thereby Akt signaling - and the Erk1/2 inhibitor, PD98059, significantly attenuated hAFS-CM antagonism of doxorubicin-induced senescence and apoptosis.

Conclusions: Our results provide unprecedented evidence that paracrine factors secreted by hAFS protect cardiomyocytes against doxorubicin toxicity, raising new prospects for therapy of chemotherapy-related cardiac disease.

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Transplantation of cardiac progenitor cells with three-dimensional thick scaffold into the pericardial space improves cardiac function and graftability after myocardial infarction in mice

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Transplantation of cardiac progenitor cell (CPC) for patients with ischemic heart disease has been examined enthusiastically. However, optimal method of CPC transplantation is still elusive because of low graftability and unclear treatment effect in clinical studies. We used clonally expanded stem cell antigen 1-positive CPCs from adult mice and produced a three-dimensional thick scaffold (CPC-scaffold), in which CPCs were cultivated up to 2 months with self-assembling peptide RADA16 as a scaffold. Addition of IGF-1 and specially modified self-assembling peptide with the active motif of RGD sequence, improved three-dimensional network of CPCs in the scaffold. After making myocardial infarction (MI) with left coronary artery ligation in mice, we transplanted CPC-scaffold onto the surface of expected infarction area and confined it inside of the pericardial space by using parietal pericardium (pericardial grafting method). Fibrosis formation was significantly improved in Tx group (24.8±7.6% vs 39.7±8.7%, p<0.01, n=5). Ejection fraction evaluated by left ventriclectomy significantly improved in Tx group (25.3±6.2% vs 39.8±4.2%, p<0.01, n=5). Spectacle tracking echocardiogram showed significant improvement of systolic function of left ventricle (fractional shortening: 22.6±5.0 vs 39.7±8.7%, p<0.01, n=5). CTS transplantation suppressed CM hypertrophy in the border region and capillary density in the border region significantly elevated indicating angiogenic effect of CPCs in Tx group (13.4±.4 vs 17.3±6.8%, p<0.01, n=5). CTS transplantation significantly improved in infarcted and border regions (anterior: 10.8±4.1 vs 20.6±3.5%, p<0.01, n=5), anterior-lateral: 13±6.5% vs 24.8±7.6%, p<0.01, n=5). CTS transplantation suppressed CM hypertrophy in the border region and elongation of fibrotic length at 4 weeks after Tx, indicating attenuated ventricular remodeling after MI.

Conclusion: HiPSC-derived CPSs potentially ameliorate cardiac dysfunction of human-size intact heart.

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A model of anthracycline-induced cardiotoxicity using induced pluripotent stem cell-derived cardiomyocytes

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Purpose: Doxorubicin (DOX), an effective chemotherapeutic drug, is limited in its clinical applications due to cumulative dose-dependent cardiotoxicity. The mechanisms of anthracycline-induced cardiotoxicity (ACT) are still not fully understood. The ability to generate human induced pluripotent stem cells (hiPSCs) provides a unique opportunity for modeling heart disease. We aimed to investigate the effects of DOX on iPSC-derived cardiomyocytes (iPSC-CMs) to establish a human in vitro model of ACT for understanding the underlying pathomechanisms.

Methods and results: iPSCs from healthy human individuals were directly differentiated in vitro into pure cardiomyocytes (95%) for two month and exposed to 0.1, 0.5, 1, 5, and 10 μM DOX for 24h. We investigated the cell survival of DOX-treated iPSC-CMs by MTT and WST-1 assay and found a dose-dependent decreasing expression of the calcium ion channels RYR2, SERCA, and NCX in DOX-treated iPSC-CMs. Furthermore, a higher percentage of iPSC-CMs treated with DOX showed abnormal sarcomeric α-actinin distribution in comparison to untreated cells, suggesting disorganized myofilament structure. Since titin (TTN) serves as a template for sarcomeric assembly, we analyzed its isoform expression and degradation as a function of DOX treatment. We found no changes in cardiac TTN isoforms, but a decreased overall TTN expression on mRNA level after DOX-treatment. In addition, the TTN degradation pattern altered dose-dependently in DOX-treated iPSC-CMs, shown by western blots, suggesting TTN degradation as early event in ACT. Because TTN is susceptible to calcium-dependent protease degradation, we hypothesized that TTN degradation is dependent on diastolic calcium concentration. We found a dose-dependent decreasing expression of the calcium ion channels RYR2, SERCA, and NCX in DOX-treated iPSC-CMs. These results are in line with a significantly increase in diastolic calcium after DOX-treatment in iPSC-CMs using Fluor-4. Furthermore, we found that DOX leads to an increased generation of reactive oxygen species (ROS) in iPSC-CMs, which could be explained by a DOX-dependent differential expression of NADPH-oxidase subunits that we showed in iPSC-CMs.

Conclusion: We demonstrate that DOX-treated hiPSC-CMs recapitulate the abnormalities that were found in individuals with ACT. We show evidence for a DOX-dependent downregulation of iPS-CMs and ROS-production in iPSC-CMs leading to sarcomeric disassembly and calcium-dependent titin degradation. HiPSC-CMs should therefore be used as an in vitro model of ACT to investigate the influence of the genetic background on ACT for the development of therapeutic and preventive strategies on a patient-specific level.
Physiologically trained cardiac adipose tissue derived progenitor cells within fibrin scaffolds to improve cardiac function

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Purpose: Cardiac tissue engineering aims to develop biostructures capable of re-establishing physiological organization and function of the infarcted myocardium. Cardiac cells are subjected to mechanical and electrical forces, which regulate gene expression and function. Therefore, in vitro electromechanical stimulation could benefit further integration of therapeutic cells into the myocardium. Our goals were: 1) study the viability of a tissue engineered construct with cardiac adipose tissue-derived progenitor cells (cardiactATDCPs); and 2) examine the effect of electromechanically stimulated cardiactATDCPs within a myocardial infarction (MI) model in mice.

Methods: CardiactATDCPs were electromechanically stimulated, harvested and labelled to generate the 3D fibrin construct. The electromechanical stimulation protocol was designed to mimic the physiological heart environment: 2ms pulses of 50mV/cm at 1Hz and 10% stretching during 7 days. Cell viability was evaluated through a Life & Death assay. The cellular construct was implanted in the murine heart and animals were sacrificed at 3 weeks post-implantation. 40 animals were randomly distributed: without cells (control MI, fibrin MI) and with stimulated or non-stimulated cardiactATDCPs (treated MI and sham). Echocardiography, gene and protein analysis were also carried out.

Results: In vitro electromechanical stimulation on cardiactATDCPs showed increased expression of cardiac transcription factors, structural genes and calcium handling related genes. After 3 weeks of in vivo culture in the fibrin construct, cells exhibited high viability and remained labelled. Cell treatment resulted in functional improvement of left ventricular ejection fraction (LVEF) relative to post-infarction values; indeed, stimulated cardiactATDCPs produced a 4.7% average increment compared to non-stimulated cells, as revealed by echocardiography. On the contrary, control MI and fibrin MI presented a decrement in LVEF (4.1% and 3% reduction, respectively). Finally, histology showed cell proliferation and main cardiac markers expression of implanted cardiactATDCPs, but also scarce migration to the heart was noticed.

Conclusions: The electromechanical stimulation protocol designed enhances cardiac properties of therapeutic cells at genetic and protein level. Furthermore, the construct used in our study confers a suitable environment for cell viability, proliferation, cardiac maturation and migration to infarcted myocardium. All together, electromechanical stimulation of therapeutic cells previous implantation could be a valuable tool for cardiac regeneration approaches.

STEM CELLS AND CELL THERAPY II

P3555 | BENCH

Post MI environment switches resident and transplanted mesenchymal stromal cells toward a pro-inflammatory phenotype and impairs their reparative properties via toll like receptor 4

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Background and purpose: Mesenchymal stromal cells (MSCs) are a promising source of stem cells for cardiovascular repair. However, much is known about the effect of myocardial infarction (MI) and subsequent left ventricular (LV) dysfunction on MSC phenotype and function. We aimed to test the hypothesis that the post-MI inflammatory environment could modulate the MSC reparative properties of resident and transplanted cells.

Methods and results: To test this hypothesis, we used mouse cardiac MSCs (cMSCs) and subcutaneous fat MSCs (SC MSCs) 28 days after MI or sham operation (LVEF: 27.9±3.8 vs. 54.9±3.8). To determine the MSC paracrine characteristics, we measured the levels of secreted cytokines in culture medium of the different MSCs, and found that MI significantly switched cMSCs toward a pro-inflammatory phenotype accompanied by increased secretion of inflammatory cytokines: IL-1, IL-6 and TNF-α (p<0.05), as well as monocyte recruitment factors: RANTES, MCP-1 and MIP-1 (p<0.0001). On the other hand, SC MSC phenotype and cytokine profile were less affected by MI. Next, to assess their therapeutic properties, we injected cMSCs and SC MSCs obtained from either MI or sham operated mice into the hearts of recipient mice subjected to MI. Surprisingly, regardless of their source, MSCs failed to improve cardiac remodeling and function. Then, to determine if toll-like receptor 4 (TLR4) is the mediator of MSC pro-inflammatory polarization which impairs their therapeutic properties, we activated cMSCs from TLR4−/− and wild-type (WT) mice and measured the levels of secreted cytokines. Notably, we found significantly less inflammatory cytokine secretion from the TLR4−/− cMSCs, compared with the WT cMSCs. Next, to evaluate whether lack of TLR4 could improve the therapeutic properties of MSCs, we subjected mice to MI, and treated them with cMSC transplantation from either TLR4−/− or WT mice. Significantly, cMSCs from TLR4−/− were the most effective in the prevention of LV remodeling after MI by inducing the smallest change in LV diastolic diameter and volume, compared with WT cMSCs (24 fold and 2.5 fold decrease, p<0.04) and saline treatment group (2.9 fold and 3 fold decrease, p>0.05).

Conclusions: We show, for the first time, that post MI environment “re-educates” resident and transplanted MSCs toward a pro-inflammatory phenotype via TLR4. We propose that inhibition of TLR4 in MSCs could diminish the negative effects of inflammation and improve the outcome of cell therapy after MI.

P3554 | BENCH

Allogeneic cardio-reparative cell therapy for acute myocardial infarction. Preliminary results of the CAREMI clinical trial


Purpose: We designed a “First-In-Man” clinical trial to evaluate the safety and efficacy data (by MRI) will be available during the conference.

Methods and results: To test this hypothesis, we used mouse cardiac MSCs (cMSCs) and subcutaneous fat MSCs (SC MSCs) 28 days after MI or sham operation (LVEF: 27.9±3.8 vs. 54.9±3.8). To determine the MSC paracrine characteristics, we measured the levels of secreted cytokines in culture medium of the different MSCs, and found that MI significantly switched cMSCs toward a pro-inflammatory phenotype accompanied by increased secretion of inflammatory cytokines: IL-1, IL-6 and TNF-α (p<0.05), as well as monocyte recruitment factors: RANTES, MCP-1 and MIP-1 (p<0.0001). On the other hand, SC MSC phenotype and cytokine profile were less affected by MI. Next, to assess their therapeutic properties, we injected cMSCs and SC MSCs obtained from either MI or sham operated mice into the hearts of recipient mice subjected to MI. Surprisingly, regardless of their source, MSCs failed to improve cardiac remodeling and function. Then, to determine if toll-like receptor 4 (TLR4) is the mediator of MSC pro-inflammatory polarization which impairs their therapeutic properties, we activated cMSCs from TLR4−/− and wild-type (WT) mice and measured the levels of secreted cytokines. Notably, we found significantly less inflammatory cytokine secretion from the TLR4−/− cMSCs, compared with the WT cMSCs. Next, to evaluate whether lack of TLR4 could improve the therapeutic properties of MSCs, we subjected mice to MI, and treated them with cMSC transplantation from either TLR4−/− or WT mice. Significantly, cMSCs from TLR4−/− were the most effective in the prevention of LV remodeling after MI by inducing the smallest change in LV diastolic diameter and volume, compared with WT cMSCs (24 fold and 2.5 fold decrease, p<0.04) and saline treatment group (2.9 fold and 3 fold decrease, p>0.05).

Conclusions: We show, for the first time, that post MI environment “re-educates” resident and transplanted MSCs toward a pro-inflammatory phenotype via TLR4. We propose that inhibition of TLR4 in MSCs could diminish the negative effects of inflammation and improve the outcome of cell therapy after MI.

P3556 | BENCH

Improvement in ADMA and oxidative stress after stem cell therapy in patients with critical limb ischemia

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Background: Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, acts as an inhibitor of angiogenesis, and is associated with an increased risk of cardiovascular mortality. Administration of stem cells is known to affect eNOS activity (24h, 1 week, 3 and 6 months) and 6-month efficacy data (by MRI) will be available during the conference.

Purpose: The aim of our study was to analyze ADMA concentration and changes in oxidative stress in responders to bone-marrow mononuclear cells (BM-MNCs) application for advanced critical limb ischemia (CLI).

Methods: Sixty one patients (age 64±11 years, M:F 54:7) with advanced CLI (Rutherford category 5.6) not eligible for revascularization were treated with intramuscular (n=30) or intraarterial (n=31) application of 40ml of BM-MNCs concentrate. Patients with limb salvage at 6-month follow-up were considered as responders to cell therapy. The concentration of ADMA and oxidative stress markers were analyzed before, 3 months, and 6 months after BM-MNCs delivery.

Results: The amputation-free survival 3 months and 6 months after cells delivery was 51/61 (84%), and 46/61 (75%), respectively. In responders to cell therapy, the concentration of ADMA and oxidative stress markers were analyzed before, 3 months, and 6 months after BM-MNCs delivery.
there was significant decrease in ADMA concentration after 6 months (1.66±0.67 to 0.97±0.65 μmol/l, p=0.0004), accompanied by decrease in TNF-α (2.13±0.30 to 1.81±0.46 pg/ml, p=0.0002), increase in reduced glutathione (6.8±3.0 to 0.97±0.65 μmol/l, p=0.0004), accompanied by decrease in TNF-α concentration at 6-month follow-up (p=0.009, n=−0.45), and with decrease in TNF-α concentration after 6 months (p=0.008).

Conclusion: Administration of BM-MNCs significantly correlated with decrease in ADMA concentration at 3-month follow-up (p=0.006, n=−0.08), and with decrease in TNF-α concentration at 6-month follow-up (p=0.009, n=−0.51). There was no correlation with number of applied CD34+ cells, or with dosage of administered atorvastatin.

Acknowledgement/Funding: This study was sponsored with a grant from Euro- pean Regional Development Funding (ITMS code: 2624020020).
Purpose: To assess the endogenous cardiac capacity for CM replenishment after incremental amounts of pure CM death.

Methods: Transgenic mice mutated to express a Tamoxifen (TAM)-inducible membrane-estrogen-receptor linked Cre recombinase (mER-Cre-mER) under the myh6 promoter were crossed with transgenic mice mutated in the Rosa 26 (R26) locus to generate a "cre erasable" stop sequence in front of the Diphtheria toxin A gene (R26-stop-DTA). Using double transgenic myh6-mER-Cre-mER/R26-stop-YFP mice, we demonstrated that the TAM injection and then at 7, 14, 21 and 28 days to assess cardiac function Results All mice from the group with 4 TAM injections (corresponding to at least 50% CM loss) died showing multiple areas of myocardial damage and extensive myocardial fibrosis. On the other hand, all animals from the groups with 2 or 3 TAM injections (corresponding to a cumulative total loss of 25 to 35% of CMs, respectively) survived and showed a significant LV dysfunction with LV dilation and reduced EF from 7 to 14 days. Cardiac performance started to improve at 21 days and was completely normalized at 28 days. Importantly, in response to pure CM loss, the myocardium compensates up to 20% of newly formed BRdU positive mononucleated CMs in 1 month.

Conclusions: Taken together these data demonstrate for the first time that the heart has an intrinsic robust and functionally productive regenerative capacity to respond to myocardial loss, and one of its CM content in just one month. This data strongly suggest that the heart has significant endogenous potential to repopulate its CM content that needs to be better analyzed and understood to design new effective protocols of myocardial regeneration for cardiovascular diseases.

P3561 | BENCH c-kit/CtCreERT2 knock-in allele minimally tags c-kit positive resident endogenous cardiac stem cells and its cardiomyocyte progeny in the adult life

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Introduction: Recently, we have demonstrated that resident tissue-specific c-kit-positive cardiac stem cells (ESC) efficiently recombine and are essential agent for myocardial regeneration in adult rodents. However, the first mouse model for c-kit positive genetic fate mapping using a Cre knock-in the c-kit Eox1 strain concluded that the c-kit+ cells minimally produce cardiomyocytes (CMs) either during development as well as in healthy or damaged adult hearts. Purpose: We addressed whether a tamoxifen (TAM)-inducible Cre knock-in the c-kit Eox1 strain efficiently recombine c-kit+ ESCs in the adult myocardium for reliable cell fate mapping.

Methods: Heterozygous c-kitCreERT2 (T2+)/mice were crossed with the global diphtheria toxin A receptor reporter mouse (R26mT/mG) that express in the ROSA (R26) locus a membrane-targeted tandem Tomato dimer (mT) prior to Cre expression and membrane-targeted green fluorescent protein (mG or GFP) after Cre recombination.

Results: CtCreERT2 Knock-in in the c-kit Eox1 strain produces a null c-kit+ allele with mice that are hemizygous c-kit hypomorphs. Indeed, c-kitCreERT2(T2+)/mice knock-in downregulates c-kit expression in all c-kit expressing cells of the body. When double mutant c-kitCreERT2(T2+)/R26mT/mG+ mice were treated with standard TAM diet for 3 months, ~80% of total c-kit+ bone marrow cells were recombined to express eGFP. The same high level of recombination was shown in c-kit+ cells of the skin, spleen, lung and testis. When we isolated c-kit+ HSCs, only a fraction of them, about 15%, were recombined by TAM. Thus, the c-kitCreERT2(T2+)/mice, exactly like the recently reported c-kitCreERT2/NER+ mouse, correctly labels the known c-kit expressing cells even though at an expected different rate proportionally to c-kit expression. Importantly, TAM labeled ~80% of all c-kit+ cardiac cells. However, these recombined c-kit+ cardiac cells were all lineage-committed cells as they were all either CD45+ or CD31+ cells. When gating the low expressing c-kit (c-kit-low) CD45neg/CD31neg cells, that are marked for true ECSCs, only ~8% of them were recombined to express GFP. Consequently, only rare GFP+ CMs were detected. Finally, the c-kitCreERT2(T2+)/null allele reduced clonogenicity and sphere formation of eSCSCs when compared to WT c-kit+/− controls.

Conclusions: Cre recombination in c-kitCreERT2(T2+)/mice is dependent on c-kit expression. Cells that express high levels of c-kit are efficiently recombined. However, true c-kit-low eSCSCs are only minimally recombined. Thus, using this fate map strategy, it is impossible to appropriately quantify the cardiac cell progeny, and CMs in particular, of c-kit+ eSCSCs in vivo.
Background: Pulmonary arterial hypertension (PAH) is a group of diseases characterized by elevated pulmonary arterial resistance, muscularization of the pulmonary arteries, and right ventricle hypertrophy of the vascular walls of pulmonary arteries in MCT-induced PAH rats. We hypothesized that combined therapy with shock wave (SW) and autologous bone marrow-derived mesenchymal stem cells (BMMSCs) is superior to either alone for alleviating left ventricular (LV) dysfunction.

Methods and results: Male mini-pigs (n=30) equally divided into group 1 (sham control), group 2 [acute myocardial infarction (AMI)] by left coronary artery ligation], group 3 (AMI-SW), group 4 (AMI-BMMSC), and group 5 (AMI-SW-BMMSC) were sacrificed by day 60 and the hearts were collected for studies. Baseline LV injection fraction [LVIF (%)] and LV chamber size did not differ among the five groups (p>0.05). By day 60, LVEF was highest in group 1 and lowest in group 2, significantly higher in group 5 than in those in groups 3 and 4, and significantly lower than those in groups 3 and 5 (p<0.001). Protein expression levels of VEGF, CXCR4, and SDF-1 were significantly increased progressively from groups 1 to 5 (all p<0.05). Small vessel number and protein expressions of CD31 and eNOS were highest in groups 1 and 5, lowest in group 2, and significantly higher in group 5 than those in group 3 (p<0.001). Cellular and protein levels of NOX, VEGFR, and NF-κB were significantly upregulated in group 5 compared to vehicle, with no additive effect by combined therapy. Importantly, only when cells were delivered together in the recipient heart, we observed a reduction in the infarct scar (p<0.05 vs vehicle). Both cell types and their combination were able to protect cardiomyocytes (CM) from apoptosis, recruit endogenous CSCs, with no additive effect given from the combined therapy. EdU incorporation showed that CSCs stimulate CM proliferation while SVPs promote endothelial cell proliferation compared to vehicle. Interestingly, only CSC-SVP therapy induced the proliferation of arterial smooth muscle cells. Conclusions: In vivo CSCs and SVPs cooperate to improve the healing of infarcted hearts in a complementary fashion. These data suggest that combinatorial cell approaches may improve cell therapy efficacy, opening novel opportunities for cardiac repair.

P3565 | BENCH

Human cardiac stem cells and saphenous vein-derived pericytes show a molecular interaction involving DPP-4/SDF-1 turnover and additive promote the healing of mouse infarcted hearts

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Background: Intramyocardial transplantation of c-Kit+ Cardiac Stem Cells (CSCs) and Saphenous Vein-derived Pericytes (SVPs) in single therapy promotes the recovery of left ventricular function in a mouse model of myocardial infarction (MI).

Purpose: To investigate if the simultaneous transplantation of CSCs and SVPs adds further benefits compared with the single therapies.

Methods: We isolated CSCs from discarded specimens of transplanted hearts and SVPs from vein leftovers of CABG patients. Cell surface phenotype, secretome, molecular interactions and paracrine effects were investigated in vitro. To assess the regenerative ability, CSCs, SVPs or CSCs+SVPs (300,000 cells of each type/heart - n=6 mice per group) were delivered in the peri-infarct of a mouse MI-model. Sham (n=3) and Vehicle-injected mice (n=6) were used as control. Mice were given 5-ethyl-2-deoxouridine - EdU (i.p., 300μg) every 2 days over the recovery period and sacrificed 14 days post-MI.

Results: In vitro, SVPs and CSCs exhibit a similar mesenchymal phenotype (CD44/90/105) and secrete similar paracrine factors (HGF, VEGF, FGF, SDF), as well as some pro-inflammatory cytokines like TNFα and IL-1β. In vivo, CSCs-SVPs combination did improve SDF-1α production (n=4, p<0.05 vs SVPs alone), IL-1β inhibition (n=4, p<0.05 vs single cultures). We first show that SDF-1 modulation occurs post-transcriptionally and possibly involves DPP-4 (dipeptidyl peptidase-4), an enzymatic activity. Soluble DPP-4 levels are reduced in co-cultures vs CSC-single cultures (n=4, p<0.05, with DPP-4 mRNA being downregulated in CSCs exposed to SVP-conditioned media (n=4, p<0.05 vs control).

Cell transplantation similarly improved cardiac function at 14 days post-MI compared to vehicle, with no additive effect by combined therapy. Importantly, only when cells were delivered together in the recipient heart, we observed a reduction of the infarct scar (p<0.05 vs vehicle). Both cell types and their combination were able to protect cardiomyocytes (CM) from apoptosis, recruit endogenous CSCs, with no additive effect given from the combined therapy. EdU incorporation showed that CSCs stimulate CM proliferation while SVPs promote endothelial cell proliferation compared to vehicle. Interestingly, only CSC-SVP therapy induced the proliferation of arterial smooth muscle cells.

Conclusion: In vivo CSCs and SVPs cooperate to improve the healing of infarcted hearts in a complementary fashion. These data suggest that combinatorial cell approaches may improve cell therapy efficacy, opening novel opportunities for cardiac repair.
amplitude than action potential alone after application of dofetilide (29.4% vs. 1.3%; p < 0.0084).

Conclusions: We have developed a highly versatile novel methodology for the simultaneous quantitative analysis of contraction kinetics, force generation, calcium cycling, and electrophysiology in human cardiomyocytes. This novel approach has led to novel application in the study of cardiac disease, drug discovery and drug cardiotoxicity screening.

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MITRAL VALVE DISEASE

P3569 | BEDSIDE
Echocardiographic and clinical long-term outcome of real world patients undergoing percutaneous edge-to-edge mitral valve repair
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Background: There is no data on long-term echocardiographic follow-up regarding the durability of mitral regurgitation (MR) in real-world patients undergoing percutaneous edge-to-edge mitral valve repair (pMVR).

Methods and results: From August 2009 to April 2011, 137 consecutive patients with severe MR were treated with pMVR in two high volume university centers. Mitral regurgitation could be successfully reduced to grade ≤2 in 84.7% of patients (116/137 patients). In 2014 we scheduled all patients for clinical and echocardiographic follow-up. Long-term follow-up (up to 5 years) revealed MR ≤1 in 91.7% (124/137 patients), excluding dead patients and those who underwent conventional MVR. In the remaining patients (73/137 patients, excluding dead patients), echocardiographic follow-up showed a good long-term durability of the intra-procedurally achieved reduction of MR in survivors. Furthermore, the majority of survivors presented with NYHA functional class ≤ II (64.2%). In survivors with available long-term echocardiographic follow-up (>3 years after pMVR, 53/73 patients, median echocardiographic follow-up of 47 months), MR grade ≤2 was present in 86.8% of patients (46/53 patients). More detailed echocardiographic parameters will be presented at the congress.

Conclusions: Patients undergoing pMVR between 2009 and 2011 long-term echocardiographic follow-up showed a good long-term durability of the intra-procedurally achieved reduction of MR in survivors. Furthermore, the majority of survivors presented with NYHA functional grade ≤ II. Hence, pMVR represents an alternative non-surgical approach reducing symptoms and the grade of MR sustainable in selected real world patients with severe symptomatic MR.

P3567 | BEDSIDE
Influence of ischemic and nonischemic cardiomyopathy on mortality and regurgitation after MitraClip results from the Dresdner MitraClip-registry
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Aims and background: Severe mitral regurgitation (MR) is the second most common valvular heart disease after aortic stenosis. The MitraClip is an interventional percutaneous method of repair of the mitral valve that mimics the surgical edge-to-edge Alfieri technique through mechanical coaptation of the mitral leaflets in high surgical risk patients. The purpose of this registry is to compare the safety, clinical efficacy, and in-hospital and short-term survival outcomes of MitraClip implantation in patients with severe MR of ischemic or nonischemic etiology.

Methods and results: From July 2012 to January 2015, a total of 140 patients were included in the Dresdner MitraClip Registry. In presence of a positive vote from ethics commission, all patients gave informed consent to the procedure and authorized data collection. Severity of MR was examined using 3D-Echo (phillips). Decision upon MitraClip procedure was made in the interdisciplinary heart team independently. Patients follow up was 3 and 6 months after successful procedure with transthoracal and transesophageal echo (TTE, TEE) and clinical examination.

Baseline characteristics showed a mean age of 78 years (57–97 years), with an adjusted in-hospital mortality of 12.1% (6.5% in the ischemic and 17.6% in the nonischemic cardiomyopathy group). Of all patients, 64 (46%) suffered from ischemic cardiomyopathy (ICM), with a mean left ventricular ejection fraction (LVEF) of 30.8% and elevated Euro-2-score of 21%. Patients with dilative cardiomyopathy (DCM) and degenerative mitral regurgitation (DMR) had a mean LVEF of 52% and 40% and Euro-2-score in the two groups were 15 and 13%. Implantation of the MitraClip was successful in 96% of patients. Procedural complication rate was low with 0.7% for stroke and myocardial infarction and the 6 month mortality rate was 23% for patients with ischemic cardiomyopathy (vs. 14.9% in patients with DCM and 5.8% in patients with DMR, respectively).

Conclusion: Percutaneous mitral valve repair with the MitraClip system is feasible in patients with ischemic or nonischemic cardiomyopathy with similar procedural results. Mortality was two times higher in patients with ICM, especially in those with severely reduced LVEF < 30%. Preoperative risk assessment with transthoracal measured ejection fraction and log EuroScore helps to identify patients with high mortality in this community of surgical high risk patients.

P3571 | BEDSIDE
New cutoffs are needed for the assessment of functional mitral regurgitation severity using three-dimensional echocardiography
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Background: Two-dimensional echocardiography (2DE) and 2D PISA method have limitations for the assessment of the functional mitral regurgitation (FMR) severity because of the dynamic changes in size and shape of both effective regurgitant orifice (EROA) and PISA during the cardiac systole. The assessment of MR severity using three-dimensional echocardiography (3DE), which determines the true volume of the PISA, enables itself as a more accurate method for measuring the EROA and the regurgitant volume (RVol).

Purpose: To assess the agreement between the severities of the FMR determined using 2DE and 3DE PISA analysis.

Methods: 25 pts (age 58±13 years, 18 males) with mild, moderate and severe FMR underwent 2DE using a commercially available system (Acuson SC2000, Siemens, CA). A 3D color full-volume of the MR jet was separately recorded at baseline 30–40 cm/sec, encompassing the PISA throughout the regurgitant period. The severity of FMR was firstly assessed according to current guidelines cutoff value for 2D PISA, EROA and RVol. 3D PISA volume was measured offline at each frame of the MR flow, using dedicated software package (ePISA PISA, SC2000, Siemens, CA). Peak and mean 3D PISA during the cardiac systole, EROA and RVol were also measured. The severity of the FMR was then classified as mild, moderate and severe, using the same current guideline cutoffs for comparability.

Results: 2D EROA showed good correlation with both peak and mean 3D EROA (r=0.90 and r=0.80, p<0.001), whereas 2D RVol showed lower correlation with peak and mean RVol (r=0.84 and r=0.64, p<0.001). According to the standard 2DE analysis, 44% of the patients had mild, 25% moderate, and 31% severe FMR. Using 3D peak PISA and same cutoffs, 6% of the patients had mild, 19% moderate, and 75% severe FMR, with a low inter-rater agreement with the 2DE analysis (k=0.26, CI 0.03–0.52). Using 3D mean PISA, 63% of the patients had mild, 29% moderate and 8% severe FMR, with a moderate inter-rater agreement with the 2DE analysis (k=0.60, CI 0.26–0.92).

Conclusions: 3D PISA analysis reclassifies the severity of the MR when using current cut-offs for FMR, and varies greatly with the method used (mean or peak
Mitral valve disease / Aortic valve intervention

PISA. Our data suggest that specific cut-offs should be further established for the 3D assessment of FMR severity, both for peak and mean 3D PISA.

P3572 | BEDSIDE
Comparing the clinical characteristics and long-term outcomes of patients undergoing MitraClip with degenerative versus functional mitral regurgitation
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Background: Percutaneous edge-to-edge mitral valve repair by using the mitracle system is a new treatment option for severe mitral regurgitation (MR) in patients whose condition is inoperable or who are at high conventional operative risk. MR has two different etiologies; degenerative MR (DMR) and functional MR (FMR). The clinical presentations and prognosis after the mitracle implantation in DMR and FMR patients still remain unclear.

Purpose: We aimed to clarify the difference in the characteristics and long-term outcomes of patients undergone mitracle between DMR and FMR.

Method and result: In a total of 206 consecutive patients after the mitracle implantation, 87 patients (42%) had DMR, whereas 119 patients (58%) had FMR. Male gender was more common in FMR. Patients with DMR were older than those with FMR. The prevalence of hypertension, diabetes mellitus, and chronic kidney disease was comparable between the two groups. Baseline MR severity and New York Heart Association (NYHA) class was similar between the two groups. N-terminal pro-B-type natriuretic peptide (NT-pro BNP) was higher and LVEF was lower in patients with FMR. Logistic euro SCORE was comparable between the two groups. Six months and 12 months after the procedure, MR severity and NYHA class similarly improved in patients with DMR and FMR. However, NT-pro BNP was still higher in FMR patients at 6 months and 12 months after the mitracle implantation. Kaplan-Meier curves and the log-rank test revealed that the all-cause mortality was comparable between patients with DMR and FMR.

Conclusion: Despite the various differences of clinical characteristics, the improvements of MR severity and heart failure symptom, and the long-term survivals after the mitracle implantation were comparable between DMR and FMR.

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P3573 | BEDSIDE
Transfemoral closure of mitral paravalvular leak in the presence of metallic aortic valve
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Background: The Use that retrograde femoral access to close Mitral Paravu- lar Leakage (MPVL) in patients with the combination of aortic and mitral metallic prostheses has considered contraindicated.

Purpose: The aim of this study was to assess the safety and feasibility of Percu- taneous Closure of MPVL in patients with double aortic and metallic prostheses.

Methods: Consecutive patients with double prosthesis (DP) who underwent percutaneous MPVL closure in our institution were included. Anterograde and ret- rograde approach consisting of crossing the wire across the aortic prosthesis in order to accept and pass the paravalvular mitral leak were used. Arterious ve- nous loop (AVL) were also performed in all cases but one. The devices used in all interventions were Amplatz Vascular Plug III. Immediate and mid-term follow-up results were analyzed.

Results: From February 2009 to December 2014, 56 patients underwent MPVL in our institution. Twenty five patients (44.6%) had double prosthetic mitral and aortic valve (DP). Mean age was 69±11. 40% were male. The mean clinical fol- low up was 416.5±323.1 days Retrograde approach with AVL was performed in 17 patients (48%). All procedures were hemodinamically well tolerated. Technical success rates were 86%, (2 patients needed two procedures). One patient had device embolization that was percutaneously captured and a second device was successfully implanted in the same procedure and 1 patient needed emergency surgery due to disc perforation. At follow-up 50% of the patients presented sig- nificant NYHA functional class improvement. Seven patients (28%) died during follow-up due to persistent cardiac failure.

Conclusions: Percutaneous Closure of MPVL in patients with double aortic and mitral prostheses can be done safely considering few tips are taking into consider- ation during the procedure.

P3574 | BENCH
Non invasive ultrasonic chordal cutting
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Objective: Chordal cutting targeting leaflet tethering has been described to im- prove the efficacy of annuloplasty during ischemic mitral regurgitation surgery. Histopspy is a novel ultrasound based technique for tissue fragmentation through the cavitation generated at the focus of a very intense ultrasonic pulse. In this study we investigate the feasibility of using histotripsy for chordal cutting to avoid cardiology bypass and invasive surgery in infected heart.

Methods: Experiments were performed in vitro in explanted sheep heart (N=5) and in vivo in sheep beating heart (N=3, 40±24 kg). In vitro, the mitral valve basal chordae was removed, fixed on a holder in a water tank. The ultrasound pulses were emitted from the therapeutic device (1-MHz focused transducer, pulses of 8μs duration, peak negative pressure of 17 MPa, repetition frequency of 100Hz) placed on a distance of 64 μm from the target. The ultrasound transducer was applied on the thorax cavity was filled out with water. We analysed MV compa- tion and chordae by real time 3D echocardiography before and after chordal cutting. The animals were sacrificed at the end of the procedure, for postmortem anatomical exploration to confirm the section of the basal chordae and the in- tegrity of the remaining marginal chordae.

Results: In vitro, all the basal chordae were completely cut. The mean procedure time was 6 (±3) minutes. The thickness of the chordae was the main criteria affecting the duration of procedure. In the sheep, central basal chordae on basal leaflet were completely cut. The mean procedure time was 19 (±3) minutes. By echography, the sectioned chordae was visible and no mitral valve prolapse was found. All the postmortem anatomical exploration of hearts confirmed the section of the basal chordae. No additional lesions were objectified.

Conclusions: Non invasive ultrasonic histotripsy succeed to cut mitral valve basal chordae in vitro and in vivo in beating heart. Future investigation will be needed to test this noninvasive technique on its ability to decrease ischemic or functional MR secondary to leaflet tethering. If positive, this will open the door of completely noninvasive technique for MV repair especially in case of functional MR.

AORTIC VALVE INTERVENTION

P3575 | BEDSIDE
Blood culture-negative infective endocarditis due to Tropheryma whipplei - biomarker suggest intestinal barrier dysfunction and systemic immune activation
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Background and aims: Blood culture-negative infective endocarditis (IE) is associated with a high mortality and morbidity. However, initial diagnosis is fre- quently challenging in these patients and a special diagnostic workup is neces- sary to identify causing microorganisms. Recent data suggest that Tropheryma whipplei, the infectious agent of Whipple’s disease, is the most commonly found pathogen associated with culture-negative IE. The pathogenesis of IE due to in- tracellular microorganisms is still a matter of debate. Since chronic inflammation may promote endothelial damage and therefore IE, the aim of the present study was to evaluate gut derived microbial translocation as a chronic immune stimulus in the pathogenesis of Tropheryma whipplei-induced IE (TWIE). We hypothesized that TWIE patients have systemic immune activation, bacterial derived Lipopolysaccharide (LPS), endotoxin core antibodies (Endo- CB), LPS binding protein (LBP) and soluble CD14 (sCD14) were determined in the serum of TWIE patients (n=6) at time of diagnosis and after antimicrobial treatment and compared to healthy (n=15) and disease controls (n=13).

Results: The diagnosis of TWIE was based on the analysis of cardiac valve tis- sue after valve replacement surgery by molecular techniques and/or histological methods and the absence of gastrointestinal symptoms. We found significantly increased levels of LBP and sCD14 in TWIE patients as compared to healthy controls (LBP = 0.0161, sCD14 = 0.0019). Values of sCD14, that not differed from patients with intestinal barrier dysfunction (p=0.3356), remained still high in TWIE patients (n=6) at time of diagnosis and after antimicrobial therapy induction (p=0.0222), indicating sustained immune response. Low levels of LPS (p=0.04) in the context of high EndoCAb titres (p=0.0015) illustrate a long lasting exposure to endotoxin and prolonged immune activation.

Conclusion: An increased gut derived microbial translocation may promote chronic systemic inflammation favouring endothelial damage and therefore the
Profile and outcome of patients with left-sided infective endocarditis with surgical indication who did not undergo surgery

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Introduction: In most of the series, around 60% of patients with left-sided infection had undergone surgery during their hospitalization, with mortality remaining 40%, some have an uncomplicated clinical course and do not have surgical indication and others should be operated but intervention is not performed for different reasons. This last group has not been systematically studied.

Objectives: To describe the main features of non-operated left-sided infective endocarditis patients despite having surgical indication, and to look for their predictors of bad prognosis.

Methods: Multipurpose registry including all definite episodes of left-sided infective endocarditis admitted in three tertiary care hospitals from 1996 to 2014. We considered as surgical indications heart failure, uncontrolled infection and prevention of embolisms. We described the profile of patients with surgical indication who did not undergo surgery and performed a multivariable logistic regression analysis to determine their predicting factors of mortality.

Results: Among 1,101 patients with left-sided infective endocarditis, 273 had surgical indication but were not operated (25%). Mean age was 67±14 years, 60% were male. Comorbidities were frequent: 27% chronic anemia, 20% chronic renal failure, 27% diabetes and 14% cancer. Staphylococcus aureus was the most frequent microorganism (30%), followed by coagulase-negative Staphylococci (18%) and enterococci (15%). On echocardiogram, vegetations were detected in 88% of the patients, perianimal complications in 23% and moderate or severe valve insufficiency in 63%. Clinical course was complicated with heart failure in 68%, renal failure in 61%, stroke in 16%, septic shock in 31%. In hospital mortality was extremely high (53%). Staphylococcal aureus infection (OR 3.8; 95% CI 2–7.4; p < 0.001), referral from other centers (OR 2.0; 95% CI 1.1–3.6; p < 0.021), Streptococcus viridans (OR 0.2; 95% CI 0.1–0.6; p < 0.001), renal failure (OR 2.3; 95% CI 1.3–4.3; p < 0.006) and septic shock (OR 3.1; 95% CI 1.1–8.6; p < 0.028) were the independent risk factors for heart mortality in these patients.

Conclusions: One quarter of patients with left-sided infective endocarditis with surgical indications did not undergo surgery in our series and had a dismal short-term prognosis. Staphylococcus aureus, referral patients, renal failure and septic shock increased their mortality whereas Streptococcus viridans protected them.

Impact of a per procedure electrophysiological study during transcatheter aortic valve implantation

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Conduction disorders are a frequent complication after transcatheter aortic valve implantation.
implantation (TAVI). Many studies describe the predictors of permanent pacemaker implantation after TAVI. We wanted to know if the per procedure exploration of atrioventricular conduction during TAVI could have an impact on conduction disturbances.

Methods: This is a prospective, single-center study. We included all patients undergoing TAVI in the cardiovascular surgery service for 1 year from February 2013 and the follow-up ended in March 2014. We performed during the TAVI procedure in the catheterization room an electrophysiological study (EPS) before any intervention, after the balloon valvuloplasty and immediately after the valve implantation. The primary endpoint was the permanent pacemaker implantation (PPM).

Results: 95 patients were included, 85 were pacemaker-free and an EPS was achieved in 58 patients. The mean follow-up was 117 days. Twenty nine patients (34%) had PPM implantation after the procedure. Patients requiring a PPM implantation significantly longer (p=0.071) to those other patients. The median 210±53.3 vs 166.12±29.1 ms (p=0.003). They also had at baseline a longer AH: 143.8±48 vs 107.4±23 ms (p=0.0023), and HV: 56.05±8 ms vs 44.95±6.8 (p=0.0001). If the indication for PPM was high degree atrioventricular block, patients were more dependent on stimulation than other PPM indications at follow up.

Conclusions: These results suggest that measurement of PR interval, AH and HV at baseline represent simple ways to identify patients at risk of conduction disturbances requiring PPM implantation after TAVI.

P3581 | BEDSIDE Evaluation of conventional surgery risk scores and the TAVI-SCORE to predict 1-year mortality after transcatheter aortic valve implantation with a self-expandable prosthesis C.M. Van De Heyning1, V.M. Collas1, T.E. Philipsen2, I.E. Rodrigues2, C.J. Vrints1, J.M. Bosmans1, 1 University of Antwerp Hospital (Edegem), Department of Cardiology, Antwerp, Belgium; 2 University of Antwerp Hospital (Edegem), Department of Cardiac Surgery, Antwerp, Belgium

Background: Several recent studies concluded that conventional surgery risk scores are not adequately predicted 1-year mortality after transcatheter aortic valve implantation (TAVI). Recently the TAVI-SCORE re-tested for this purpose and showed superior predictive ability in comparison with surgery scores. However, this tool has been validated in patients treated with a balloon-expandable transcatheter aortic valve implantation (TAVI) and high surgical risk according to the Heart Team assessment. The primary endpoint was the permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI). Many studies describe predictive factors of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI). The predictors of permanent pacemaker implantation after TAVI are not well established. True predictors of atrioventricular block (AVB) after TAVI still need to be assessed.

Purpose: To evaluate the ability of conventional surgery risk scores and the TAVI-SCORE to predict high vs. low mortality risk at 1-year in patients after TAVI with a CoreValve prosthesis.

Methods: 225 consecutive patients (80±4.7 years, 54.7% female) with severe symptomatic aortic stenosis and a high surgical risk according to the Heart Team underwent TAVI using a CoreValve system. Demographic, clinical, biochemical, echocardiographic and angiographic data were collected. Logistic EUROSCORE I, II, STS-score and TAVI-SCORE differences between groups (alive vs. dead at 1 year) were compared with the Student T-test, Mann Whitney U-test, Chi Square or Fisher’s Exact test as appropriate.

Results: The cumulative survival rate at high vs. low scores was assessed with the Kaplan-Meier method.

Results: 1-year cumulative survival was 84%. Patients who survived at 1 year had lower STS-scores than patients who died (median [Q1-Q3]: 4.61% (3.33–7.38) vs. 6.03% (3.66–10.54), p=0.03), but there was no statistically significant difference between the most recent cardiac logistic EUROSCORE I (15.25% vs. 16.05%, p=0.7), EU- ROSCORE II (5.04% vs. 5.63%, p=0.4) or the nominal variables used to calculate the TAVI-SCORE. Kaplan-Meier analysis showed significantly better cumulative 1-year survival in patients with STS-score <10% compared with >10% (84.1% vs. 66.4%, p=0.01) but when stratified by logistic EUROSCORE I >20% vs. ≤20% (81.1% vs. 82.0%, p=0.9) and EUROSCORE II ≤8% vs. >8% (81.3% vs. 81.8%, p=0.9). Furthermore, Kaplan-Meier analysis showed no significant difference in survival between patients with a TAVI-SCORE <3 vs TAVI-SCORE ≥3 (82.2% vs. 77.1%, p=0.46).

Conclusions: A high STS-score was predictive of worse 1-year survival after TAVI in contrast with logistic EUROSCORE I and EUROSCORE II. The newly developed TAVI-SCORE did not discriminate high vs. low mortality risk at 1 year in our cohort of patients treated with a CoreValve system.

P3582 | BEDSIDE Impact of mitral regurgitation in mortality of patients undergoing transcatheter aortic valve implantation M. Drakopoulou, K. Toutouzas, N. Anousakis-Vlachochristou, G. Latsios, A. Synetos, A. Mastrokostopoulos, S. Brili, S. Sideris, E. Tsiamis, D. Tousoulis. 1 University of Antwerp Hospital (Edegem), Department of Cardiology, Antwerp, Belgium; 2 University of Antwerp Hospital (Edegem), Department of Cardiac Surgery, Antwerp, Belgium

Introduction: Among patients undergoing transcatheter aortic valve implantation (TAVI) for the treatment of symptomatic severe aortic stenosis, it is currently under investigation whether the presence of mitral regurgitation (MR) has a significant impact on mortality.

Methods: We evaluated the contribution of MR in all-cause mortality of patients undergoing TAVI. Clinical and echocardiographic data from patients that prospectively underwent TAVI in our center were retrospectively examined. Patients were divided in two groups: with none/mild and with moderate/severe MR before the procedure. After clinical follow-up, statistical analysis of all-cause mortality events was performed with the Kaplan-Meier method and results were further evaluated for with Cox proportional hazard analysis.

Results: We included 119 patients in the analysis. Seventy six patients (63.9%) were classified to none/mild and 43 (36.1%) to moderate/severe MR. The median follow-up time was 23 months (mean 22±13 months). During follow-up period the cumulative probability for all-cause mortality was significantly different between two groups (14.5% for none/mild versus 34.9% for moderate/severe MR, p=0.006). Independent predictors of mortality were moderate/severe MR [HR: 2.78, 95% CI (1.09, 7.03), p=0.032] and low stroke volume index [HR: 5.1, 95% CI (2.19, 12.05), p=0.001]. Results were independent to low ejection fraction (EF <40%) [HR: 1.03, 95% CI (0.36, 2.93), p=0.957].

Conclusion: Patients with symptomatic severe aortic stenosis and moderate/severe MR before TAVI had increased mid-term risk for mortality in comparison to patients with none/mild MR, irrespective to EF. Low flow state contributed to mortality independent to MR grade.

P3583 | BEDSIDE Post-operative first degree atrio-ventricular block as a new predictor of complete atrio-ventricular block or sudden death after balloon-expandable transcatheter aortic valve implantation G. Viart, F. Anselme, E. Durand, A. Savoure, C. Tron, N. Auquier, N. Bouhazm, H. Eltchaninoff. University Hospital of Rouen, Cardiology, Rouen, France

Background: Many studies have described predictive factors of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI). The predictors of permanent pacemaker implantation after TAVI are not yet well established in this setting. True predictors of atrioventricular block (AVB) after TAVI still need to be assessed.

Purpose: We aimed to evaluate the true predictors of AVB following TAVI, using clinical follow-up and pacemakers’ memories.

Methods: Between January 2011 and November 2013, 213 consecutive patients without previous PPI underwent TAVI with a SAPIEN XT balloon-expandable valve using femoral approach, at our institution. All patients underwent continuous cardiac rhythm monitoring at least 24 hours after TAVI. Electrocardiogram (ECG) was performed the following 2 days after TAVI, and 1 month later. Medical clinical follow-up was 13 months, and 8 months for pacemaker interrogation. Multivariate analysis was performed including the most relevant ECG criteria.

Results: Complete AVB occurred in 4 patients (1.9%) during TAVI, in 7 patients (3.3%) the days after, and in 11 patients (5.2%) after discharge. Sudden death occurred in 8 patients (3.7%) during the follow-up period. Pacemaker was implanted in 26 patients. Twenty of them (77%) recorded complete AVB episodes or ≥2° ventricular pacing, despite the use of a minimizing ventricular pacing algorithm. As shown in the Table below, complete AVB or sudden death occurred significantly more often in the patients with preexisting right bundle branch block (RBBB), in those with new persistent (≥48H) left bundle branch block (LLBB) after TAVI, and those with first degree AVB after TAVI.

Results of the multivariate analysis

<table>
<thead>
<tr>
<th>Predictors</th>
<th>No complete AVB and no sudden death (%)</th>
<th>Complete AVB or sudden death (%)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preexisting RBBB</td>
<td>15 (8)</td>
<td>13 (43)</td>
<td>6.62 (1.66–26.32)</td>
</tr>
<tr>
<td>New persistent LLBB</td>
<td>14 (8)</td>
<td>8 (33)</td>
<td>10.1 (2.46–46.67)</td>
</tr>
<tr>
<td>LLBB after TAVI</td>
<td>34 (18)</td>
<td>55 (27)</td>
<td>2.29 (1.08–11.24)</td>
</tr>
</tbody>
</table>

AVB, atrio-ventricular block; LLBB, left bundle branch block; RBBB, right bundle branch block; TAVI, transcatheter aortic valve implantation.

Conclusions: Our findings confirmed preexisting RBBB and new persistent LLBB as predictors of AVB following TAVI. We also demonstrated here for the first time, first degree AVB was an independent predictive factor of severe conduction disorders after TAVI. This has important implication for selecting the appropriate patients for PPI following TAVI.

P3584 | BEDSIDE Impact of diabetes mellitus and hemoglobin a1c on patient outcomes following transcatheter aortic valve implantation E. Chorin, A. Finkelstein, S. Banai, L. Barak, G. Keren, A. Steinvil. Tel Aviv Medical center, Cardiology, Tel Aviv, Israel

Background: Transcatheter aortic valve implantation (TAVI) is an alternative to surgery for patients with symptomatic severe aortic stenosis who are inoperable or in a high operative risk. The incidence and prognostic impact of diabetes mel-
P3585 | BEDSIDE
Significance of aortic regurgitation pre transcatheter aortic valve implantation

Aim: The significance of aortic regurgitation (AR) pre transcatheter aortic valve implantation (TAVI) implantation is unknown. The present study aimed to assess the clinical repercussion of AR in patients undergoing TAVI.

Population and methods: Retrospective analysis of 150 patients (mean age 81±7 years old, 43% male), from a tertiary centre prospective registry of 185 consecutive TAVI procedures, between November 2008 and November 2014. The indication for TAVI was, aortic stenosis in 145 pts, degenerated biologic prosthetic valve in 3 pts and homograft dysfunction in 2 pts. AR was found in 122 (75%) pts and was moderate to severe in 33 (22%). We evaluated the clinical differences at the presentation and at a median follow up of 22 IQ [2–38] months, stratified by the presence of moderate to severe AR, using the following tests: Qui2, t-student and Mann- Whitney.

Results: Patients with moderate to severe AR presented more frequently with a NYHA functional class IV (21% vs 8.5%, p<0.04) and with a higher median NT-ProBNP (5190 IQ [1041–11457]pg/ml vs 1765 [795–3632] pg/ml, p=0.02). During the follow up, they showed a greater decrease of NT-ProBNP (3295 IQ [965–6661] pg/ml vs 2490 [1304–4724] pg/ml, p=0.04). The presence of AR was not associated with 30-day and 1-year mortality. Seven pts with moderate to severe AR developed moderate to severe leak. There was no difference between those pts and overall population in what concerns to functional class, NYHA functional class, NYHA functional class (p>0.03) and a more significant functional improvement (>2 NYHA stages) during the follow up (p=0.04).

Conclusions: Patients with moderate to severe aortic regurgitation have a worse baseline clinical status and improve more significantly after transcatheter aortic valve implantation. The presence of AR was associated with higher incidence of moderate to severe leak without significant clinical repercussion.

P3587 | BENCH
Effect of statins on tissue factor expression and calcification in human aortic valve interstitial cells
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Background and introduction: It has been shown that in aortic stenosis (AS) tissue factor (TF) - dependent coagulation pathway may play a significant role in the process of fibrosis and valves calcification. The valvular interstitial cells (VICS) activation and their transformation into osteoblastic phenotype seems to be the crucial step in AS development. Statis, which are very effective in atherosclerosis treatment, have been found to be generally ineffective in delaying the AS progression.

Purpose: The objective of this study was to evaluate the effects of statins on TF expression and calcification process in proinflammatory stimulated VICS.

Methods: Primary cultures of VICS derived from collagenase-digested stenotic aortic valves were stimulated with lipopolysaccharides (LPS, 200 ng/mL), peptideidoglycan (PGN, 200 ng/mL), peptidolipidoglycan (PGN, 10μg/mL) or TNFα (10 ng/mL) for 8 h to induce inflammation response. Some of stimulated VICS were pretreated with atorvastatin (0.1–10μM) or rosuvastatin (0.01–1μM) for 24 h with or without the addition of 1mM mevalonic acid (crucial in a protein prenylation pathway). The relative mRNA expression of TF was measured by real-time PCR. Calcification was determined by alizarin red S measurement, after 14 days of cells culture in osteogenic medium.

Results: The relative TF mRNA expression by VICS was significantly increased by LPS, PGN and TNFα stimulation (9.6-fold, 8.8-fold and 12.7-fold, respectively, p<0.01). Prolinflammatory stimulators also increased calcification process (8.4-fold, 7.4-fold and 10.4-fold, respectively, p<0.01). Preincubation with 1 and 10 μM atorvastatin for 24 h reduced the TF expression for all stimulators by average 24% and 89%, respectively (all p<0.01) as well as calcification process (8% and 82%, respectively, p<0.01). Similar effects were observed with 1 and 1 μM rosuvastatin (TF mRNA reduction by 31% and 91%, respectively, and calcification by 42% and 92%, respectively, p<0.01). The lowest atorvastatin (0.1 μM) and rosuvastatin (0.01 μM) concentrations had no effects on TF mRNA expression and calcification severity. Addition of mevalonic acid totally abolished the reduction of TF mRNA expression and calcification induced by atorvastatin and rosuvastatin.

Conclusion: This in vitro study highlights a potential role of statins in reduction of TF expression and calcification in VICS. Although, lack of effect of statins in clinical observation may suggest that early initiation of treatment is required to reveal clinical benefit.

AORTIC VALVE DISEASE

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Background: We aim to explore progression of mild to moderate AS in ESRD controls among these patients, the cohort was divided into 3 groups according to HbA1C levels (<5.7, 5.7–6.4, >6.5). HR for HbA1C levels (5.7, 5.7–6.4, 6.5). Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

Conclusions: History of DM does not significantly effect rates of complications compared with HBA1C levels among these patients, the cohort was divided into 3 groups according to HbA1C levels (<5.7, 5.7–6.4, >6.5). HR for HbA1C levels (5.7, 5.7–6.4, 6.5). Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

Purpose: The aim of our study was to evaluate the clinical characteristics and the impact of DM status on the updated valve academic research consortium-2 (VARC-2) defined outcomes of TAVI, as well as to stratify patients outcomes according to their initial HBA1c levels.

Methods: In the present study, 566 consecutive patients who underwent TAVI at our institutions were enrolled and stratified according to DM status. All-cause mortality at 30 days or in hospital and at follow-up was the primary end point, whereas periprocedural complications, rates of myocardial infarction, stroke, and reinterventions at follow-up were the secondary ones.

Results: In all, 586 patients were enrolled: 348 (59%) without DM and 238 (41%) with DM. Thirty-day mortality was not significantly higher in patients with DM compared with patients without diabetes (3.3% vs. 2.9%, p=0.974). Bleedings, vascular complications, post procedural acute kidney injury, and periprocedural strokes were not significantly different in the two groups. In a subanalysis of DM patients, complications were not significantly higher in patients with orally treated DM compared to insulin-treated DM. At 1-year follow-up, patients with DM had a non-significantly higher mortality rate (17.6% vs 12.3%, p=0.114) if compared with patients without diabetes. In order to define the prognostic power of HbA1C levels (<5.7, 5.7–6.4, >6.5). Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

Conclusions: History of DM does not significantly effect rates of complications in patients who underwent TAVI, however a less controlled disease as manifested by elevated HbA1C may be associated with increased mortality.

P3585 | BEDSIDE
Rapid progression of mild to moderate aortic stenosis in patients with end stage renal disease
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Methods: A total of 32 patients (23 males, 73±9.6 years) of ESRD on hemodialysis (mean duration: 7.1±5.6 years) with mild to moderate AS were enrolled. Propensity score matching was done to select age, sex and initial AS severity matched control (n=32). Comprehensive TTE was performed at baseline and during follow up. Severity of AS was accessed by peak systolic pressure gradient (PSPG), mean systolic pressure gradient (MSPG), and aortic valve area (AVA) calculated by continuity equations according to current guideline.

Results: Mean follow up duration was 32.7±24.3 months. Change of AVA and MSCP per month were significantly higher in ESRD (p<0.05) compared with control group (13 (40.6%) vs. 5 (27.8%), p<0.01). Significantly more patients progressed from mild/moderate to severe in ESRD compared to control group (13 (40.6%) vs. 5 (27.8%), p<0.01). During follow up, cardiovascular event including admission due to heart failure, aortic valve intervention or death occurred in 13 ESRD patients. From multivariate analysis including baseline MSPG, MSPG acceleration rate, left ventricle mass index, E/E′, parathyroid hormone (PTH), E/E′ (p=0.04) and PTH (p<0.04) were significantly associated poor clinical outcomes.

Conclusion: AS in ESRD progress in more accelerated manner compared to those without, even in mild to moderate AS. More frequent follow up than current guideline may benefit this group of patients in terms of determining timing of intervention.
late. Repeated HBR before and after TAVR did not show any significant predictive
Conclusion: HV interval, programmed with a diagnostic atrio-ventricular conduction preserva-
all implanted for early AVB. There was no AVB recorded in PPM for prolonged
18 (19,7%) for documented AVB, 8 for prolonged HV interval and 3 for sick si-
respectively. In total, 29 (34%) PPM were implanted before discharge of which
sion was performed to assess if HVB could well predict early (from day 1 to day
5) or late (from day 5 to day 30) AVB occurrence. Results: 86 patients aged of 85±8.2 years old, with a Euroscore of 15.3±3.9 and of whom 50 (79%) were female were recruited. Corevalve was predominantly used (59 (66%), HV1, HV2 and HV3 were 56±19ms, 70±13ms and 63±14ms respectively. In total, 29 (34%) PPM were implanted before discharge of which 18 (19,7%) for documented AVB, 8 for prolonged HV interval 3 for sick sii-
us syndrome. 12 patients (13,9%) showed AVB during follow-up after discharge, all implanted for early AVB. There was no AVB recorded in PPM for prolonged HV interval, programmed with a diagnostic atrio-ventricular conduction preserva-
tion algorithm. HV1 and HV2 were neither associated with early AVB occurrence (p=0.79 and p=0.34 respectively) nor with late AVB occurrence either (p=0.54, p=0.50 and p=0.91 respectively).
Conclusion: High degree AVB is a common finding after TAVR and can occur late. Repeated HBR before and after TAVR did not show any significant predictive value for early and delayed AVB.

P3589  |  BEDSIDE
Increased levels of NT-proBNP are associated with reduced exercise capacity and peak oxygen consumption in asymptomatic patients with chronic atric regurgitation
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Background: In patients with chronic, haemodynamically significant atric regurgitation (AR), a long period of remodelling usually precedes the development of symptoms or left ventricular dysfunction. The value of ergospirometric testing in patients with asymptomatic AR is not established.
Purpose: We aimed to investigate if peak oxygen consumption (VO2peak) were reduced in patients with AR, and whether exercise test parameters were associated with the size of the valvular regurgitation and indices of left ventricular (LV) dimension and function, including N-terminal pro-B-type natriuretic peptide (NT-proBNP).
Methods: 66 asymptomatic patients aged 44±14 years with moderate or se-
vere, chronic AR and no indication for atric valve replacement were evaluated by cardiac magnetic resonance imaging and exercise testing with measurement of VO2peak. Determinants of VO2peak were assessed by uni- and multivariate analysis.
Results: The average LV end diastolic volume was 244±62 ml and the aortic re-
gurgitant fraction 34±13%. VO2peak was 35.8±8.9 ml/min/m2, corresponding to 107±26% of the age, gender and weight adjusted expected value. As in healthy individuals, a relatively large LV end diastolic volume and a low resting heart rate were associated with a high exercise capacity and a high VO2peak. The atric regurgitant fraction was not predictive of VO2peak. Higher levels of NT-proBNP were independently associated with poorer exercise capacity and VO2peak (Fig-
ure).
Conclusion: Our results indicate that in symptomatic patients with moderate or severe AR and moderately dilated left ventricles, exercise capacity is preserved and remodelling is primarily adaptive. An increased level of NT-proBNP is asso-
ciated with a reduced VO2peak, possibly heralding the onset of adverse remod-
eling.
Acknowledgement/Funding: This work was supported by the South-East Nor-
way regional health authority and the Norwegian ExtraFoundation for Health and Rehabilitation

P3590  |  BENCH
Bisphosphonates inhibit calcification of atric valve in an experimental model of atric valve stenosis
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Background: Local delivery of bisphosphonates has been recently proven to in-
hbit calcification of the arterial wall in an experimental model of atherosclerosis. The aim of the present study was to evaluate the anticalcific effect of bisphosphonates on the atric valve in an experimental model of atric stenosis.
Methods: Twenty four New Zealand rabbits were placed on vitamin D enriched atherogenic diet for 3 weeks. At that time a cardiac ultrasound was performed to assess the aortic stenosis and atric calcification of the atric valve by measuring atric valve area (AVA). Subsequently eight animals were treated with local delivery of a mixture containing 50 μg zoledronate that was delivered on the cusps of the atric valve, by a dedicated balloon catheter. A placebo mixture was ad-
ministered with the same technique on another eight animals, while eight animals were left without intervention and were used as controls. At 28 days all animals were sacrificed. All atric valves were fixed in 10% neutralized buffered formalin solution for 24 hours. The cusps were embedded in paraffin wares. Serial sections 4 μm thick were obtained and routinely stained with eosin –hematoxylin and von Kossa stain for calcium deposits. The stained slides were digitized using a light microscope. The files were processed for histrnorphometric analysis using Image Pro Plus, version 5.1. The calculated areas were expressed as the per-
centage to the total area. Statistical analyses were carried out with the Statistical Package for the Social Sciences release 13.0.
Results: At baseline, all animals developed atric valve stenosis with severe cal-
cification. No differences regarding AVA were recorded between both groups. (21.37±1.76 vs 21.98±3.12, p=0.53). In all animals the local delivery of zole-
dronate and placebo mixtures was successful and uncomplicated. A total of 72 cusps were histologically examined. The cusps treated with zoledronate had significantly lower expression of calcium content compared to the cusps of the placebo group (16.40±0.90 vs 26.92±1.80% of the area, p<0.0001). Similarly the cusps treated with zoledronate had significantly lower expression of calcium con-
tent compared to the cusps of the placebo group (16.40±0.90 vs 26.22±1.69% of the area, p<0.0001). No differences were observed between the cusps of the placebo group and the controls. (26.92±1.60 vs 26.22±1.69, p=0.23)
Conclusion: Local delivery of bisphosphonates on the atric valve can inhibit calcification in an experimental model of atric stenosis.

P3591  |  BEDSIDE
Screening of GATA family reveals genetic variants in GATA5 gene in individuals with bicuspid atric valve
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Background: Bicuspid atric valve (BAV) is one of the most common heart dis-
ces, with prevalence between 1–2% in the general population. It has a pro-
posed genetic etiology and mutations have been described in several genes, as GATA5 gene, potentially involved in the development of BAV, as evidenced by the null mutant mouse.
Purpose: The aim of this study was to analyze the genetic variation of several members of GATA family in a series of patients with BAV and tricuspid atric valve (TAV) to find variants associated with this defect.
Methods: We prospectively recruited a total of 275 individuals, 122 patients with BAV (mean age 52.7±15.8 years, 77.9% male) and 153 with tricuspid atric valve (TAV) (mean age 72.1±9.4 years, 56.2% male), diagnosed by transthoracic eco-
cardiography. DNA was obtained from peripheral blood and stored in the Biobank of our center. Exons and flanking introns of GATA4, GATA5 and GATA6 genes were analyzed by Sanger sequencing. Polyphen2 and SIFT programs were used to predict the pathogenic potential effect of the non synonymous variants found.
Results: We identified 7 polymorphisms in GATA4, 7 in GATA5 and 4 in GATA6 genes. Out of them, only rs41058603 (p.Asp203Asn) in GATA5 resulted significantly associated with the presence of BAV (OR=2.2; 95% CI [1.23–3.97]; p=0.004). Interestingly, a non-synonymous variant in the contiguous amino acid was found (p.Arg202Gln). The mutated amino acid lies within one of the zinc fingers of the protein and is highly conserved in different species. Computer analyses consider this change as potentially pathogenic. Moreover, another two variants not pre-
viously described, but synonymous, each in an individual with TAV (p.H274= in GATA5 and p.Asn458= in GATA6) were identified.
Conclusion: A new GATA5 potentially pathogenic variant and a common poly-
morphism appear to contribute to the development of BAV. Our results support the involvement of this gene in the presence of BAV.
P3592 | BENCH
Pulmonary hypertension in patients undergoing transcatheter aortic valve replacement: incidence, clinical impact and evolution
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Background: A certain degree of pulmonary hypertension (PHy) is very common in patients undergoing Transcatheter Aortic Valve Replacement (TAVR) and a severe PHy is known to negatively affect the outcome. However, a clear understanding of the incidence, the clinical impact and the evolution of the different grades of PHy in the setting of TAVR is lacking.

Methods and results: 990 consecutive patients included in the CoreValve Italian Registry were included in 8 high volume centers and divided as follows: group 1, sPAP <40 mm Hg (none/mild PHy: 376 patients, 38%); group 2, sPAP 40 to 55 mm Hg (mild to-moderate PH: 485 patients, 49%); and group 3, sPAP ≥55 mm Hg (severe PH: 129 patients, 13%). Patients were followed up for 1 year. As compared to patients in group 1, patients in group 2 and 3 had a higher one-year overall mortality: [HR 1.5 (1.2–3.1), p=0.01, and HR 2.3 (1.9–2.9), p=0.001, respectively]. At 1 year, the systolic pulmonary pressure (SPP) decreased of at least 10 mmHg in 25% and 35% of the patients in group 2 and 3, respectively.

Conclusion: Moderate to severe PHy is associated with higher 1 year all cause mortality after TAVR. The persistence at 1 month post TAVR of severe PHy independently predicts mortality.

P3593 | BENCH
Baseline Mitral Regurgitation in Transcatheter Aortic Valve Replacement Patients: Does it Impact 1 Year Mortality?

Background: The prevalence of concomitant moderate to severe Mitral Regurgitation (MR) in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) ranges from 13% to 48%. In patients undergoing TAVR, the MR is often left untreated.

Purpose: As percutaneous devices and methods to treat significant MR in high risk patients have been approved, the impact of MR in patients undergoing TAVR needs to be revisited.

Methods: Data was retrospectively analyzed from an existing database. The study cohort (total N=588) was divided into 2 groups based on the degree of baseline mitral regurgitation: Group 1 ≥Moderate MR (n=71), and Group 2 < moderate MR (n=517). The two groups were compared in regards to baseline clinical, echo and procedural characteristics. In hospital, 30 days and 1 year outcomes were assessed. Univariate and multivariate Cox regression analyses were performed to test the independent effects. Kaplan-Meier assessment was completed for 1 year follow-up (Figure).

Results: Patients with ≥Moderate MR had a higher mortality rate vs. patients with less than moderate MR during the initial 30 days follow-up after TAVR (unadjusted, log-rank p=0.01). The mortality rates at 1 year follow-up were similar (HR=0.42 [0.11–1.61]). The only multivariate predictor of mortality at 1 year was baseline pulmonary artery systolic pressure. Among Group 1 62.5% and 77.7% of the patients had improved to below moderate MR at 30 days and 1 year, respectively.

Conclusions: The presence of pre-TAVR moderate to severe MR is not associated with an increase of mortality within one year of TAVR. Baseline concomitant MR in TAVR patients may not be a causal pathway for mortality within one year and may be left untreated.

P3594 | BEDSIDE
Association of myocardial fibrosis and clinical outcomes in aortic stenosis patients treated by transcatheter aortic valve replacement
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Background: Previous studies have suggested that myocardial fibrosis detection by cardiac magnetic resonance (CMR) was a predictor of worse clinical outcomes in aortic stenosis (AS) patients.

Purpose: To evaluate the association of left ventricular (LV) myocardial fibrosis and longterm clinical outcomes in a population of AS patients treated by Transcatheter Aortic Valve Replacement (TAVR).

Methods: 50 AS patients (50% males, age 85±6 years) treated by TAVR underwent a Late-Gadolinium Enhancement (LGE) study on a 1.5 Tesla CMR scanner prior to the intervention. Patients were followed prospectively and we performed a “landmark analysis” with a landmark set at 30 days for all-cause mortality and hospitalisation for heart failure.

Results: During a mean follow-up of 3.7 years, 12 (24%) patients died and 14 (28%) patients had one or more episodes of heart failure (HF). Before TAVR, LGE was identified in 35 (73%) patients. The extent of LGE was 6.7±7.8% of LV. The percentage of LV myocardial fibrosis by LGE was significantly associated with hospitalisation for HF (OR=1.1 per each 1% increase, 95% CI [1.002–1.21], p=0.045) and the combined incidence of all cause death and HF events (OR=1.1, 95% CI [1.004–1.22], p=0.041) by univariate logistic regression. In a stepwise multivariate logistic regression model, LGE extent was the only independent predictor of all cause death and heart failure events (OR=1.13, 95% CI 1.002 to 1.29, p=0.045). Patients without LGE had significantly better survival rates compared to patients with LGE (Figure).

Conclusion: Pre-intervention LGE extent in candidates to TAVR is an independent predictor of longterm subsequent worse clinical outcomes. These findings should be further tested with other independent predictors in larger groups of patients.

Acknowledgement/Funding: None

MYOCARDITIS

P3595 | BENCH
The myocard derived suppressor cell- determined innate immunity is decisive for the chronic course of viral myocarditis
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Background: The prevention of chronic enteroviral myocarditis in mice was found to be dependent on an effective innate immunity comprising natural killer cells (NK). Myocard derived suppressor cells (MDSC) are known to suppress the efficacy of the innate and adaptive immune response in viral infections. Previously, we found that coxsackievirus B3 (CVB3)-infected A.BY/SnJ mice differ from C57BL/6 mice with regard to chronic myocarditis, maturation profile, function and activation of NK cells. This study aimed to investigate the interplay between MDSC and NK cells in vivo and in vitro in enteroviral infection.

Materials and results: In vitro experiments of CVB3-infected co-cultured RAW (NK) cells and MDSC we observed a significant decrease of CD107a and granzyme B expression on NK cells, suggesting a reduction of NK degranulation by MDSC and, as a consequence a disturbed cytotoxic NK cell function. In vivo, we found significantly higher cell numbers of MDSC in spleens and hearts of CVB3-infected A.BY/SnJ mice compared to resistant C57BL/6 mice. Regarding the underlying mechanisms of MDSC attraction to the infected heart we identified S100 proteins. In ABY/SnJ mice the levels of cardiac S100A8 and S100A9 mRNA as well as the number of S100A8 and S100A9 protein expressing MDSC were significantly higher than in C57BL/6 mice resistant for chronic myocarditis. Depletion of MDSC by anti-Ly6G antibodies in CVB3-infected mice resulted in a downregulation of S100 proteins. In ABY/SnJ mice the heart which was accompanied by a significant decrease of the cardiac inflammation represented by CD3+T lymphocytes and Mac3+ macrophages as well as a reduced viral load in susceptible ABY/SnJ mice during acute disease.

Conclusions: In this study we demonstrate that MDSC influence the cytotoxic activity as well as the immune regulatory function of NK cells in enteroviral infect-
uction. In the murine model of CVB3 myocarditis MDSC were found to contribute to the suppression of NK cell function early in infection, thus leading to a severe acute CVB3 myocarditis and chronic inflammatory heart disease in ABY/SNj mice compared to C57Bl/6 mice. These findings might help to develop new therapeutic immune regulatory strategies for the prevention of chronic myocarditis and, thus of dilated cardiomyopathy at later stages of the disease.

P3596 | BENCH
NOD2 knock down induces cardiobiological effects in murine Coxsackievirus B3-induced myocarditis
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Introduction: The cytoplasmatic pattern recognition receptor, nucleotide binding oligomerization domain 2 (NOD2), belongs to the innate immune system and is among others responsible for the recognition of ssRNA.

Hypothesis: So far, the role of NOD2 in viral myocarditis has not been unraveled. In this study, we examined whether or not NOD2 regulates cardiac inflammatory signaling in CVB3-induced myocarditis.

Conclusion: NOD2 knock down (−/−) and C57Bl6/wild type (WT) mice, acute myocarditis was induced by intraperitoneal injection of 5×105 p.f.u. of CVB3 (Nancy strain). Seven days after infection, left ventricular (LV) function was evaluated by conductance catheter measurements. Cardiac fibrosis, inflammation, and apoptosis were determined via immunohistochemistry and real-time PCR. NOD2 was knocked down in LV cardiomyocytes by small interference (si) RNA. Subsequently, the cells were infected with CVB3 at a MOI 2 and 14 hours (h) and 24 h later collected for the analysis of CVB3 copy number, and mRNA expression or caspase 3/7 activity, respectively.

Results: NOD2−/− CVB3 mice exhibited an improved LV function compared to WT CVB3 mice. Cardiac infiltration of CD4+, CD8+, CD11b- and CD68-positive cells was less pronounced in NOD2−/− CVB3 versus WT CVB3 mice. Concomitantly, NOD2−/− CVB3 mice displayed 3.9-fold, 2.9-fold, 5.3-fold, 8.0-fold, 1.4-fold, and 2.3-fold (P < 0.05) lower LV mRNA expression of TNF-α, IL-1β, INF-γ, INF-β, RIPK2 and NLRP3 compared to WT CVB3 mice, respectively, and lower TLR4 and MyD88 mRNA expression. Furthermore, cardiac fibrosis in CVB3-infected NOD2−/− mice was less pronounced versus the infected WT group, as indicated by a 1.7-, 1.8- and 1.6-fold (P < 0.05) reduced LV mRNA expression of Col1α1, Col3α1 and TGF-β, respectively, and a decreased Col I to Col III ratio. In addition, cardiac viral load and apoptosis were 12.5-fold and 19-fold (P < 0.05) lower in NOD2−/− CVB3 versus WT CVB3 mice, respectively. In line with the in vivo data, NOD2 knockdown in HL-1 cells was associated with a decreased inflammatory response, a 1.4-fold (P < 0.05) lower CVB3 copy number, 1.2-fold (P < 0.05) reduced caspase 3/7 activity and 3.4-fold (P < 0.005) reduced TLR4 protein expression and underlying signalling.

Conclusion: NOD2 knock down improves left ventricular function and attenuates pathophysiological key mechanisms in acute CVB3-induced myocarditis mice. Modulation of NOD2 might represent a promising therapeutic strategy to treat viral myocarditis.

P3597 | BENDISE
Pentaglobin treatment in viral myocarditis - An update
B. Maisch1, S. Pankuweit1, H. Haake1, N. Schlotmann1, R. Funck2. 1 University Marburg, Germany; 2 Philipps University, Marburg, Germany

Background: Treatment of viral heart disease is a matter controversy. Patients and methods: We updated our treatment registry of 162 consecutive pts with biopsy proven viral myocarditis (24 cases, 98% treated within 24 h) related to 14 different pathogens (CMV, EBV, HHV6, HSV-1, HSV-2, influenza A and B, parvovirus A-B19, Coxsackievirus A-B3, hepatitis B and C, leptospirosis, malaria, and varicella-zoster). For the treatment we used Pentaglobin® (n = 161) and 1 patient was treated with IVIG. In the follow up we observed a significant improvement of NYHA class and mortality in patients treated with Pentaglobin®. However, currently no prospective randomized studies are available in contrast to studies from the 90s. Therefore, we updated our treatment regimen with a 10/100 g/day dosage of Pentaglobin®.

Results: After 141 patients were improved by at least one NYHA class also increased exercise capacity. Mean LVEF increased from 48.7 to 61.2%, (P < 0.005) independent from the respective virus. In 53 of the 75 (71%) rebiopsied pts inflammation had resolved. In all rebiopsied ADV-positive pts the inflammation had resolved and ADV-DNA had reached subthreshold levels. In Parvo B 19 myocarditis inflammation had resolved in 36 of the rebiopsied 46 pts (78%). Parvo B19 DNA viral load was substantially diminished in only in 22 out of 46 pts (48%). In patients in whom both virus and inflammation were eliminated enddiastolic LV dimension had decreased and EF had improved (p < 0.001).

Conclusion: Treatment with Pentaglobin is highly effective in resolving myocardial inflammation independent of the underlying viral etiology. Virus eradication was most effective for adenoviruses less effective for Parvo B19 infection.

Acknowledgement/Funding: Cardiac Promotions Society Marburg

P3598 | BEDSIDE
Treatment of viral myocarditis - An update
B. Maisch1, S. Pankuweit1, H. Haake1, N. Schlotmann1, R. Funck2. 1 University Marburg, Germany; 2 Philipps University, Marburg, Germany

Background: Treatment of viral heart disease is a matter controversy. Patients and methods: We updated our treatment registry of 162 consecutive pts with biopsy proven viral myocarditis (24 cases, 98% treated within 24 h) related to 14 different pathogens (CMV, EBV, HHV6, HSV-1, HSV-2, influenza A and B, parvovirus A-B19, Coxsackievirus A-B3, hepatitis B and C, leptospirosis, malaria, and varicella-zoster). For the treatment we used Pentaglobin® (n = 161) and 1 patient was treated with IVIG. In the follow up we observed a significant improvement of NYHA class and mortality in patients treated with Pentaglobin®. However, currently no prospective randomized studies are available in contrast to studies from the 90s. Therefore, we updated our treatment regimen with a 10/100 g/day dosage of Pentaglobin®.

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Conclusion: Treatment with Pentaglobin is highly effective in resolving myocardial inflammation independent of the underlying viral etiology. Virus eradication was most effective for adenoviruses less effective for Parvo B19 infection.

Acknowledgement/Funding: Cardiac Promotions Society Marburg

Our results suggest that myocarditis rather than post-infarction inflammation trig-
TLR3, TLR4, TLR7, TLR8; and CK had a good diagnostic accuracy in identifying a LGE mass greater than \( \rho = 0.78 \), with a sensitivity of 79.31%, specificity of 89.66%, positive predictive value of 88.46%, negative predictive value of 81.25%, and an overall diagnostic accuracy of 84.5%.

Conclusions: In acute myocarditis pts the highest value of TnI and CK have a good correlation with the LGE mass (AUC=0.92 and AUC=0.75, respectively), allowing an easy, adequate and low cost quantification of myocardial necrosis, that can therefore have a potential prognostic value.

P3602

Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis

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Introduction: Short and mid-term prognosis of acute myocarditis is still a matter of debate. Some reports suggested a better outcome in fulminant myocarditis (FM) than in non-fulminant acute myocarditis (NFAM), which seems contradictory with the dramatic presentation of FM.

Aims: To describe the outcome and changes over time in left ventricular ejection fraction (LVEF) in patients (pts) with FM compared with those with NFAM.

Methods: Between January 1, 2002 and May 31, 2014, acute myocarditis was diagnosed on the basis of clinical presentation (variable combinations of recent onset of chest pain, heart failure, arrhythmias, ECG changes, with increased troponin) in 102 pts. Clinical diagnosis was corroborated by normal coronary angiography (n=44) and/or endomyocardial biopsy (n=22), and/or cardiac magnetic resonance findings (n=78). Severe low-output state requiring inotropes was observed in 32 pts, which were classified as FM. Short (in-hospital) and mid-term transplant-free survival, need for mechanical circulatory support (MCS), baseline LVEF and its changes over time were compared in pts with FM vs. NFAM (n=70).

Results: Mean age was similar (28±16 vs. 33±15 years, p=0.12), while female gender was more represented (50% vs. 13%, p<0.001) and baseline LVEF improved significantly between admission and discharge in both groups, but the magnitude of change was greater in FM than in NFAM group (+34% [23–42%] vs. 0 [0–6%], p<0.0001). The proportion of pts with LVEF <55% was greater in FM vs. NFAM both at discharge (43% vs. 12%, relative-risk [RR] 2.88, 95% CI 1.6–6.5, p=0.001) and at the last follow-up (29% vs. 5%, RR 3.47, 95% CI 1.8–6.6, p=0.005).

Conclusions: Pts with FM are at higher risk for death or HTx than those with NFAM, and may benefit from an aggressive approach including short-term MCS.
In HTx-free FM pts, a significant and greater improvement of LVEF is observed, but follow-up values remain lower than in pts with NFAM. However, after discharge overall prognosis appears good both in FM and in NFAM pts.

P3604 | BEDSIDE
Short and long-term outcome of acute myocarditis: what can we expect?
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Introduction: Myocarditis is a relatively common inflammatory disease that affects the myocardium. Current data suggest a good overall prognosis for patients with myocarditis. The aim of this study is to evaluate baseline and long-term outcome of patients diagnosed with acute myocarditis in our tertiary referral center.

Methods: Retrospective analysis of 91 consecutive patients hospitalized with acute myocarditis between June 2006 and June 2014. Clinical features, complications, baseline and follow-up echocardiograms and cardiac magnetic resonance imaging were reviewed.

Results: The mean age of 33±10 years and 75 (82%) patients were men. Hypertension and dyslipidemia were present only in a few pts (17% and 15%, respectively). A viral proctorium was found in 76% of patients and chest pain was the commonest symptom (93%). All patients presented elevated levels of troponin I (mean peak level of 27±36ng/ml). Mean BNP, C-reactive protein values at admission were 204±571 pg/ml and 36±94 mg/dl, respectively. ST segment elevation (58%) was the most frequent ECG changes. Coronary angiography performed in 38 (42%) patients was normal in all of them. Left ventricular (LV) systolic dysfunction (ejection fraction <55%) was present at admission in 23 patients (25%). Myocardial oedema was present in 62% and late gadolinium enhancement in 96%, predominantly subepicardial (63%), with an inferior-lateral location in most cases (35%). Using 4 or more myocardial segments (58%). In hospital complications occurred in 5 patients (5%) and included cardiac shock (n=2); atrial fibrillation (n=2) and sustained ventricular tachycardia (n=1). There were no in-hospital deaths. After a mean follow-up of 36 months, residual LV dysfunction was reported in 3% without cases of heart failure. Recurrences occurred in 9% of cases. No other cardiac re-hospitalizations or deaths were recorded. In a multi-variation analysis, the presence of oedema in T2 weight imaging on admission was the only determinant of normalization of LV systolic function (p=0.042).

Conclusion: In this cohort, most of patients with acute myocarditis were male, at 3rd decade of life, without cardiovascular risk factors. Despite the favorable outcome, some patients do not fully recover LV function and others had recurrence of myocarditis. Myocardial oedema as defined by CMR was the only predictor of LV systolic function recovery.

P3605 | BENCH
Identification of potential pathogenetic epitopes in various cardiac pathologies
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Purpose: Heart diseases are the leading causes of death worldwide. Dilated cardiomyopathy (DCM) and critical congenital heart disease (CCHD) can be caused by various factors. The immune system is believed to play 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) was performed against 26,364 different 15-mer peptides derived from 166 proteins associated with cardiovascular diseases. The sera used was obtained from 10 DCM, 10 myocarditis, and ICM patients and compared against that from 10 healthy, age-matched controls. A/JIOa mice (n=8) were immunised on days 0, 7, 14 with peptide sequences of 15 patients (median age, 61 years) who undergone RFCA for paroxysmal or persistent AF and before and at least 3 months after successful RFCA for AF at the same laboratory. We retrospectively reviewed the changes of LAVI and defect size of ASD before and after RFCA for AF.

Results: In all patients, sinus rhythm was restored during observation period (mean, 5.2±1.3 months) after RFCA for AF. Compared to the baseline value, LAVI was significantly decreased after RFCA for AF (45.8±12.3 mm vs. 39.5±12.9 mm, p<0.001). Maximum ASD diameter was also significantly decreased after RFCA for AF (32.7±9 mm vs. 20.5±7.4 mm, p<0.001). Interestingly, in 3 patients with large ASD (maximum diameter >30mm) before RFCA, the maximum diameter showed decrease of more than 6mm after RFCA.

Conclusion: Sinus rhythm restoration can cause shrinkage of defect size as well as atrial reverse remodeling in ASD patients with AF. RFCA for AF prior to transcatheter closure is a feasible strategy not only for sinus rhythm restoration but also for defect size reduction especially in patients with large ASD.

P3606 | BENCH
The role of TWEAK and FN14 in autoimmune myocarditis
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Background: Dilated cardiomyopathy (DCM) is a myocardial disease characterised by progressive depression of myocardial contractile function and ventricular dilation. DCM can be caused by an inflammation of the myocardium triggered by autoimmune reactions. Our group developed a mouse model of experimental autoimmune myocarditis. Immunisation of A/J mice with cardiac troponin I (cTnI) induces severe inflammation and subsequently fibrosis in the myocardium. Little is known about the role of the innate immune system in the pathogenesis of this autoimmune disorder. However, it was already observed that the cytokine tumor necrosis factor-like weak inducer of apoptosis (TWEAK) and its receptor FN14 induce inflammation and fibrosis in the myocardium. We thought to evaluate the in-hospital and long-term outcome of patients diagnosed with autoimmune myocarditis in our tertiary referral center.

Methods: Retrospective analysis of 91 consecutive patients hospitalized with acute myocarditis between June 2006 and June 2014. Clinical features, complications, baseline and follow-up echocardiograms and cardiac magnetic resonance imaging were reviewed.

Results: The mean age of 33±10 years and 75 (82%) patients were men. Hypertension and dyslipidemia were present only in a few pts (17% and 15%, respectively). A viral proctorium was found in 76% of patients and chest pain was the commonest symptom (93%). All patients presented elevated levels of troponin I (mean peak level of 27±36ng/ml). Mean BNP, C-reactive protein values at admission were 204±571 pg/ml and 36±94 mg/dl, respectively. ST segment elevation (58%) was the most frequent ECG changes. Coronary angiography performed in 38 (42%) patients was normal in all of them. Left ventricular (LV) systolic dysfunction (ejection fraction <55%) was present at admission in 23 patients (25%). Myocardial oedema was present in 62% and late gadolinium enhancement in 96%, predominantly subepicardial (63%), with an inferior-lateral location in most cases (35%). Using 4 or more myocardial segments (58%). In hospital complications occurred in 5 patients (5%) and included cardiac shock (n=2); atrial fibrillation (n=2) and sustained ventricular tachycardia (n=1). There were no in-hospital deaths. After a mean follow-up of 36 months, residual LV dysfunction was reported in 3% without cases of heart failure. Recurrences occurred in 9% of cases. No other cardiac re-hospitalizations or deaths were recorded. In a multi-variation analysis, the presence of oedema in T2 weight imaging on admission was the only determinant of normalization of LV systolic function (p=0.042).

Conclusion: In this cohort, most of patients with acute myocarditis were male, at 3rd decade of life, without cardiovascular risk factors. Despite the favorable outcome, some patients do not fully recover LV function and others had recurrence of myocarditis. Myocardial oedema as defined by CMR was the only predictor of LV systolic function recovery.

P3607 | BEDSIDE
Shrinkage of defect size after the catheter ablation for atrial fibrillation in patients with unclosed atrial septal defect
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Background: In patients with atrial septal defect (ASD), the defect size directly influences the feasibility of transcatheter closure. It's common knowledge that atrial reverse remodeling occurs after successful radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF). However, it is unknown whether sinus rhythm restoration can cause atrial reverse remodeling and shrinkage of defect size in ASD patients.

Methods: From 811 patients with ASD in our hospital, we evaluated consecutive 15 patients (median age, 61 years) who undergone RFCA for paroxysmal or persistent AF prior to transcatheter ASD closure. Left atrial volume index (LAVI) and defect size of ASD were evaluated with echocardiography before and at least 3 months after successful RFCA for AF at the same laboratory. We retrospectively reviewed the changes of LAVI and defect size of ASD before and after RFCA for AF.

Results: In all patients, sinus rhythm was restored during observation period (mean, 5.2±1.3 months) after RFCA for AF. Compared to the baseline value, LAVI was significantly decreased after RFCA for AF (45.8±12.3 mm2 vs. 39.5±12.9 mm2, p<0.001). Maximum ASD diameter was also significantly decreased after RFCA for AF (32.7±9 mm vs. 20.5±7.4 mm, p<0.001). Interestingly, in 3 patients with large ASD (maximum diameter >30mm) before RFCA, the maximum diameter showed decrease of more than 6mm after RFCA.

Conclusion: Sinus rhythm restoration can cause shrinkage of defect size as well as atrial reverse remodeling in ASD patients with AF. RFCA for AF prior to transcatheter closure is a feasible strategy not only for sinus rhythm restoration but also for defect size reduction especially in patients with large ASD.
P3610 | BEDSIDE

Psychiatric disorders in adults with congenital heart disease (PsyConHeart): unmet needs and impact on quality of life

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Background: There are conflicting data regarding the prevalence of psychiatric disorders and the impact on quality of life in adults with congenital heart disease (ACHD), which is presumably based on methodological differences of the studies. We performed a nationwide study using routine healthcare data and aimed at understanding underrecognition and under treatment of psychiatric problems in ACHD patients.

Purpose: To assess psychiatric disorders and quality of life in ACHD, and to compare their prevalence during the last 12 months to that of the general population.

To determine specificity and sensitivity data for widely used screening instruments for depression.

Methods: A Structured Clinical Interview for DSM-IV (SCID) was applied to 150 ACHD patients. 12-month prevalence data of psychiatric disorders were compared to estimates of the general German population. The Beck Depression Inventory-2 (BDI-2), the depression subscale of our hospital (HADS-D) were related to psychiatric diagnosis. Quality of life (QoL) was measured with World Health Organization Quality of Life instrument (WHOQoL).

Results: In ACHD the prevalence of at least one psychiatric disorder was significantly higher than in the general population (48.0%; CI: 44.7–60.0 vs. 37.3%; CI: 35.2–39.6). In particular mood (30.7%; CI: 24.0–38.0 vs. 10.2%; CI: 9.0–11.5) and any anxiety disorder (28.0%; CI: 22.0–36.7 vs. 18.2%; CI: 16.4–20.1) were significantly raised. Psychiatric treatment was recommended in 62 (41.3%) patients. Prior to study 21 (42.2%) patients did not receive any treatment. Independent predictors of low QoL were major depression (p < 0.001), alcohol dependency (p = 0.004), nicotine dependency (p = 0.036), and NYHA class (p = 0.007). Accuracy of the HADS-D and BDI-2 as screening instruments for depression in ACHD was moderate (AUC 0.60–0.81), with low sensitivity dependent on the cut-off score used.

Conclusion: The 12-month prevalence of any psychiatric disorder, particularly of mood and anxiety disorders is significantly higher in ACHD patients compared to the general population. Widely used self-rating instruments such as HADS-D and BDI-2 rather underestimate this problem, therefore misleading clinicians. The results of our study point to unmet needs in the treatment of ACHD. Proper psychiatric and psychological assessments are recommended to optimize diagnostic procedures and comprehensive treatment plans in adults with ACHD.

P3611 | BEDSIDE

Atrial septal defect device closure in the elderly, symptomatic benefits except for arrhythmia

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Background: Although congenital, Atrial Septal Defect (ASD) is often diagnosed in adulthood. Untreated it can lead to right heart failure and arrhythmia. Transcatheter technique for closing the defect is nowadays available also for the elderly but reports on outcome in that population are rare.

Purpose: The purpose of this national study was to describe the clinical outcome of device closure of ASD of the secundum type in patients ≥65 years.

Methods: All patients ≥65 years of age who had an attempt of ASD closure by catheter during 1997–2014 were identified in the SWEDCON registry (n=171). Procedure data, comorbidity, functional class (NYHA), medication pre and post intervention were collected. A questionnaire was sent to all patients alive (n=135). Verification of data was done in patient records. Total follow up time was 5.2±3.3 years.

Results: The mean age at intervention was 72±5 years. (65.1–87.2) 72% were females. 56% had a history of hypertension. In 91.8% (n=157) the procedure was fulfilled. In 8.2% (n=14) the procedure was interrupted because of hemodynamic or anatomical reasons. There was no procedure related mortality. Major complication rate was low, 1.9% (1 stroke, 1 pulmonary embolism, 1 respiratory arrest). Minor complications were also infrequent in 4.3%, (1 stroke, 1 arrhythmia). During follow up 21 died, 1/3 of cardiovascular causes. Mean age at death was 79.2±5.8 years. NYHA class improved significantly after intervention, the proportion of patients in NYHA I increased from 39.1% to 67.3% (p<0.001) and the improvement seemed to persist at long-term follow up.

The prevalence of atrial fibrillation did not change, 57.4% before vs. 56.5% after. During follow up stroke/TIA occurred in 9 cases (6.1%). All patients but one had antiarthrombic therapy six months after the intervention. At follow up 81.8% still took antiarthrombic therapy. 62.5% of the patients reported improved working capacity and 39.5% of 78 patients who had had diuretics reported reduced doses of diuretics after intervention.

Conclusion: ASD device closure in the elderly provides symptomatic improve-
ment with a reasonable low complication rate. The prevalence of atrial fibrillation was not affected in the total cohort.

P3612 | BEDSIDE

Late outcomes in adults following anatomic repair of congenitally corrected transposition of the great arteries

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Introduction: There is limited data about long-term outcome of patients with transposition of the great arteries (TGA) repaired with the arterial switch procedure in adulthood. There is a paucity of data in adults regarding late sequelae. We sought to determine cardiac outcomes and prevalence of coronary stenosis in adults with TGA after ASO.

Methods and results: Retrospective cohort analysis of surgical survivors of ASO for TGA performed between 1980 and 1998 in a tertiary referral centre (n=68). Six patients were lost to follow up and the remaining 62 patients constitute the study population. Complex anatomy (ventricular septal defect or subpulmonary obstruction requiring repair) was present in 20 patients (32%) and 9 patients (12%) underwent palliative procedures before ASO. One late death (1.6%) was documented: sudden cardiac death during exercise in a 16-year-old. After a mean follow-up of 19.2±2.1 years, all the patients were in NYHA functional class I with a mean left ventricular ejection fraction of 63.2±6%. As for long-term complications, neo-aortic root dilatation (-40 mm) was present in 25 patients (40%), moderate to severe aortic regurgitation in 4 (6%), right ventricular outflow tract obstruction (RVOTO) at any level in 19 (31%) and arrhythmias in 9 (14%) patients with sustained ventricular tachycardia (1.6%). No acute coronary syndromes were documented during follow-up. In 34 patients (55%) who underwent a high-resolution computed tomographic scan at a mean of 19.2±2 years from ASO procedure that did not reveal any coronary obstruction. A total of 17 re-interventions (13 surgical and 4 percutaneous) were required in 11 patients (18%), the most frequent indication being RVOTO repair (8 re-interventions, 47%) and only one case (6%) of Bentall-Boscan procedure for severe aortic regurgitation and neo-aortic root dilatation. Complex anatomy (60% vs 31%, p=0.029) and age at time of ASO (27±54 days vs 90±134 days, p=0.036) were predictors of neo-aortic root dilatation.

Conclusions: Long term outcomes of patients with TGA who survive arterial switch repair are good in terms of mortality and complications. Coronary stenosis and coronary events in the long run are rare. Patients with complex anatomy and those older at time of ASO are more prone to develop neo-aortic root dilatation.

P3614 | BEDSIDE

Risk of cardiovascular events in children and young adults with congenital heart disease

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Introduction: Despite a significantly more positive overall prognosis for patients with congenital heart disease in the last decades, cardiovascular complications represent a significant source of morbidity and mortality in these patients. However, the excess risk of major cardiovascular events such as congestive heart failure, myocardial infarction or atrial fibrillation in children and young adults with congenital heart disease in Sweden has not been established.

Purpose: The aim of our study was to investigate the risk of developing congestive heart failure, myocardial infarction or atrial fibrillation in children and young adults with congenital heart disease in Sweden.

Methods: We used data from the Swedish patient and Cause of Death registries to identify all patients who were born between January 1970 and December 1993 with a diagnosis of congenital heart disease diagnosed at birth or subsequently, without previous congenital heart disease, atrial fibrillation or myocardial infarction. Follow-up and morbidity data were collected for all patients until December 31, 2015. Ten controls were matched for age, sex and county, were randomly selected from the general population for each patient (n=262,040).

Results: Altogether 26,204 children and young adults (51.4% men, 48.6% women) were diagnosed with congenital heart disease between 1970 and 1993. The mean age at diagnosis was 9.6 years, and 24,987 patients (95.4%) were still alive at the end of the study. Among all patients with congenital heart disease, 2.5% (n=661) developed congestive heart failure, a risk 53.1 times higher (95%, p<0.001, CI 44.1–64.1) compared to controls; a further 1.5% of patients (n=404) developed atrial fibrillation with a risk of 11.4 times higher (95%, p<0.001, CI 9.9–13.2) than controls. In addition, 0.7% of patients (n=184) developed myocardial infarction, a risk approximately 9.2 times higher (95%, p<0.001, CI 7.5–11.2) compared to controls.

Conclusion: In this large case-control study, the absolute and relative risk of developing congestive heart failure, atrial fibrillation and myocardial infarction was markedly increased in children and young adults with congenital heart disease compared to the general population. Despite the more positive prognosis for these patients, cardiovascular morbidity is very high compared to healthy controls.

P3615 | BEDSIDE

Outcome of adult survivors of congenital heart lesions after 25 years follow-up: estimates of the standardized mortality ratio

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Background: Comparison of mortality rate of adults with congenital heart disease (CHD) to that of the standard population has not been reported so far.

Methods: In a cohort of 3,345 adults with CHD followed up to 25 years, the standardized mortality ratios (SMR) were calculated using age at diagnosis and sex adjusted death rates. For mortality analysis, data provided by the National Death Index of Spain were used. One-sample log-rank test with online available software (http://biostatistics.mgh.harvard.edu/biostatistics/resources.htm) was used.

Results: Median age at first examination was 22 years (18–39) and median follow-up period was 10.8 years (1.6–31.9). There were 1,656 males, 1,348 females had a simple CHD (group I); 1,606 females, 1,348 patients had a complex CHD (group II); and 393 patients had CHD of great complexity (group III). A total of 328 patients had died (9.8%) at the end of the study. The SMR was calculated as 1.8 (95% CI 1.3–2.0, p=0.001) in male subjects and 1.8 (95% CI 1.2–2.1, p<0.001) in female subjects. For the patients group I, the SMR

<table>
<thead>
<tr>
<th>Main diagnosis</th>
<th>No. of cases</th>
<th>SMR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular septal defect</td>
<td>383</td>
<td>0.97</td>
<td>0.40–2.3</td>
<td>0.931</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>555</td>
<td>1.12</td>
<td>0.87–1.4</td>
<td>0.314</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>383</td>
<td>1.21</td>
<td>0.89–1.6</td>
<td>0.168</td>
</tr>
<tr>
<td>Subvalvular aortic stenosis</td>
<td>114</td>
<td>1.52</td>
<td>0.97–2.4</td>
<td>0.038</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>75</td>
<td>0.97</td>
<td>0.87–4.5</td>
<td>0.067</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>355</td>
<td>2.90</td>
<td>1.8–4.5</td>
<td>0&lt;0.001</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>325</td>
<td>3.20</td>
<td>1.9–4.8</td>
<td>0&lt;0.001</td>
</tr>
<tr>
<td>Transposition of the great arteries</td>
<td>124</td>
<td>8.02</td>
<td>4.4–14.4</td>
<td>0&lt;0.001</td>
</tr>
<tr>
<td>Eisenmenger syndrome</td>
<td>49</td>
<td>12.5</td>
<td>7.3–21</td>
<td>0&lt;0.001</td>
</tr>
<tr>
<td>Single ventricle physiology</td>
<td>100</td>
<td>14.5</td>
<td>9.0–24</td>
<td>0&lt;0.001</td>
</tr>
</tbody>
</table>

Despite a significantly more positive overall prognosis for patients with congenital heart disease in the last decades, cardiovascular complications represent a significant source of morbidity and mortality in these patients. However, the excess risk of major cardiovascular events such as congestive heart failure, myocardial infarction or atrial fibrillation in children and young adults with congenital heart disease has not been established.

Conclusion: The majority of patients required a second operation, largely in the Rastelli-Senning group. In the Senning-arterial group, late aortic valve insufficiency occurred in 50% of the patients. Conduction disease and atrial arrhythmias contribute to late morbidity in these patients. Nevertheless, the majority of patients are free of heart failure. Despite good short-term outcomes and survival following anatomic repair, careful long-term evaluation for structural and electrophysiologic abnormalities is required.
was not significantly different than that of the reference population (1.08; 95% CI 0.9–1.3; p=0.38). However, the SMR for the group II was 1.9 (95% CI 1.6–2.4; p<0.001) and for the group III I 0.2 (95% CI 7.8–13; p<0.001). The excess in mortality rate increased progressively with complexity of CHD (table).

Conclusions: The global excess of mortality, was 60% for males and 80% for females with important differences depending on complexity. These data may be used as a prognostic index in adult survivors with CHD.

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ACUTE PULMONARY EMBOLISM

P3616 | BEDSIDE

The influence of age on the prognostic value of the clinical prediction rules in patients with pulmonary embolism

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Introduction: Value of the Revised Geneva Score (RGS) and the Wells Score (WS) in prognostic stratification was tested in patients with acute pulmonary embolism (PE), especially in elderly. There is no data concerning younger patients.

Purpose: To investigate whether the initial assessment of clinical probability of PE has the same prognostic accuracy in terms of the long-term mortality among younger (<50 years old) and older (≥50 years old) patients with PE.

Methods: 238 consecutive patients with proven PE were retrospectively classified into three probability subgroups according to the simplified Geneva and Wells scores. Follow-up was conducted up 115 months.

Results: Younger patients accounted for the 19.7% of the study cohort. Overall the median age was 60 (17–88) years, 51% of patients had ≥70 years old. The total number of hospital deaths and deaths after follow-up. According to both probability rules younger patients significantly more likely than older were classified into the low-probability subgroups and less likely into the high-probability subgroups (p <0.05). In older patients long-term mortality rates differed significantly depending on the RGA and WS – determined PE probability subgroup (p=0.01; RGS; p=0.04 WS). Kaplan-Mayer curves for RGS differed markedly between the three probability categories, figure. WS well discriminated risk. Critical point of survival curves of patients at high and intermediate risk overlapped. On the contrary amongst younger patients, analysis of survival curves according to the initial probability of PE determined by the RGS and the WS failed to demonstrate their prognostic significance.

Conclusions: Initial RGS and WS assessed PE probability may have prognostic utility but only in older patients. In younger patients prognostic stratification according to the both scales was not confirmed.

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P3617 | BEDSIDE

Accuracy of a clinical-ultrasonic score for the diagnostic stratification of patients with suspected pulmonary embolism

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Introduction: International guidelines recommend the use of validated clinical scores to estimate the pre-test probability of pulmonary embolism (PE). Point-of-care ultrasonography proved to be accurate in the diagnosis of deep venous thrombosis (DVT) and of many pulmonary pathologies. The aim of this multicentric prospective study is to compare the diagnostic accuracy of a clinical-ultrasonic score (US-WS) with a clinical score as Wells score (WS).

Materials and methods: We calculated the traditional dichotomized WS (“PE likely” if < 4 points, “PE unlikely” if ≥ 4) in adult patients suspected of PE presenting to four hospitals. Lung and venous US were performed by a physician blinded to clinical data. US-WS differs from WS in the following items: “signs and symptoms of DVT”, replaced by “DVT at venous ultrasonography” and “alternative diagnosis less likely than PE” replaced by “alternative diagnosis less likely than PE after lung ultrasonography.” The latter item was positive (3 points) in presence of at least one subpleural infarct; in case of an alternative ultrasonographic diagnosis the item was considered negative (0 points). In case of a normal lung US examination, the item was considered positive or negative referring to what assigned to the same item of WS. Final diagnosis was obtained by multidetector CT pulmonary angiography or scintigraphy.

Results: Among the 249 enrolled patients PE was finally diagnosed in 60 (24.1%). Among the 143 patients (57.4%) with WS <4, PE was present in 25 (17.5%) cases. In the 106 patients (42.6%) with WS ≥4, PE was diagnosed in 35 (33%). Pulmonary and venous ultrasonography was performed in 7±3 minutes. US-WS was <4 in 187 patients (75.1%, p <0.05 vs WS), of which 18 (9.6%) had PE as final diagnosis. In the 62 patients with US-WS <4 (24.8%, p <0.05 vs WS), 42 (67.7%, p <0.05 vs WS) had PE as final diagnosis. US Wells score reallocated 74 patient (29.7%), moving 59 patients from PE likely to PE unlikely and 15 from PE unlikely to PE likely. US-WS sensitivity (70%, 95% CI 56.8–81.2) and specificity (89.4%, 95% CI 84.1–93.4) were superior to those of traditional Wells score (sensitivity 58.3%, 95% CI 44.9–70.9, specificity 62.4, 95% CI 55.1–69.4). The area under the curve of US-WS (88.4%, 95% CI 83.2–93.6), was significantly superior to that of WS (82.1%, 95% CI 53.5–70.7; p<0.01).

Conclusions: A clinical-ultrasonic score (US-Wells score), rapidly feasible at the bedside, increases the proportion of low-risk patients with a better global accuracy compared to traditional clinical score.

P3618 | BEDSIDE

Prognostic impact of cardiovascular risk in pulmonary embolism


Introduction: For a long time, venous thromboembolism (VTE) and atherosclerotic disease were believed to be completely distinct entities. More recent studies contradict this theory, suggesting that cardiovascular risk factors (CVRF) are linked to a greater risk of VTE. It is further claimed that patients with pulmonary embolism (PE) are at greater risk for cardiovascular events. This positive association is highly relevant in clinical practice, mainly in primary and secondary prevention of VTE.

Objective: Ascertain if there is a link between PESI (Pulmonary Embolism Severity Index) and cardiovascular risk (CVR), and the extent to which CVR and each CVRF individually affects PE’s six-month outcomes.

Methods: Retrospective, descriptive and correlation study extended to all patients (P) with PE hospitalized in our hospital, from January 2012 to November 2014. Basal clinical characteristics of the patients were analysed and stratification for CVR was carried out, computing the SCORE (Systematic Coronary Risk Evaluation Project) in two groups: low/mild CVR and high/very high CVR. PE was stratified, computing the PESI, in low risk (class I-II PESI) and high risk (class III-V PESI). Uni and multivariate analysis of 6 months recurrence, re-hospitalization and overall mortality was performed. The statistical methods used were Mann-Whitney’s U test, Fisher’s exact test and chi-squared test.

Results: Within a population of 130 hospitalized P due to PE, PESI score was applied to 125 P (65.6% female; 68.4±15.8 years). 22.4% had diabetes mellitus type 2; 63.2% hypertension and 32% dyslipidemia. 54.4% P were classified as low/mild CVR and 45.6% as high/very high CVR. Each individual CVRF was not associated with PE outcome. Individuals with high CVR tend to have a higher PESI (86% vs. 14%, p=0.001). Patients with lower CVR deceased less, regardless of PESI (22.2% vs. 50.0%, p=0.002). CVR stratification appears to be more closely related to death in hospital (7.4% vs. 19.3%, p=0.046) than at 6 months (13.8% vs. 20.9%, p=0.343). A lower 6 months re-hospitalization rate was also determined for individuals with low CVR (16.9% vs. 36.4%, p=0.025). A statistically significant difference in the recurrence rate was not found.

Conclusion: Whereas overall mortality was higher in the group with greater CVR, this analysis indicates SCORE can be an asset in stratifying PE risk; thus, prospective studies aimed at validating this application are required.
Background: Pulmonary embolism (PE) is a common and increasingly diag-
nosed disorder with high mortality and morbidity rates. However, population-
based information on its incidence and prognosis remains limited. We conducted a large epidemiology study collecting data on hospitalization for PE (from 2002 to 2012) in a population of about 13 million people in Northwestern Italy.

Methods: Patients were identified using the ICD-9-CM codes: 415.11, 415.19; gender and age specific incidence rate of PE during the study period were estimated using the resident population for each year of the study. Furthermore, time trends in the in-hospital PE-related mortality and case fatality rate were calculated. Results were adjusted for possible confounders.

Results: The overall crude incidence rate for the entire study period was 55.4 and 40.6 events per year per 100,000 inhabitants for women and men, respectively (p = 0.001). However, this difference completely disappeared when the incidence rate in the two genders was standardized according to age.

The mean case fatality rate was significantly higher in male patients compared to female patients (13.83 vs 12.95, p = 0.002). Incidence of PE significantly increased in both genders during the study period. In-hospital case fatality rate significantly decreased throughout the study period (p = 0.001) in women (from 15.6% to 10.2%) and in men (from 17.6% to 10.1%). The observed decrease of the in-hospital case fatality rate during the study period remained significant also after adjustment for possible confounders.

Conclusion: Time trends over an 11-year period show an increasing incidence of PE, but a significant reduction in mortality during hospitalization. Reduction in the case fatality rate remained significant after adjustment for these possible confounders.

P3620 | BEDSIDE
Low dose prolonged infusion of tissue type plasminogen activator therapy in massive pulmonary embolism
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Background: Pulmonary embolism (PE) has a high mortality but the in-hospital all-cause case fatality rates were lower in unstable patients who received bolytic therapy (TT) than those who did not. However TT is associated with major complications. The aim of the present study was to assess the efficacy and safety of low-dose (25mg) prolonged administration (in 6 hours) of tissue-type-plasminogen-activator (tPA) on in-hospital mortality and outcomes in patients with massive PE.

Methods: A total of 37 consecutive patients with massive PE were included in this study. The primary end-points consisted of in hospital all cause mortality, major complications, pulmonary hypertension and right ventricular dysfunction. Secondary end-points are all cause mortality, pulmonary hypertension and right ventricular dysfunction at 6 month.

Results: The mean age of the patients was 68.76±14.54. The mean pulmonary artery systolic pressure (PASP) (56.51±17.34 mmHg vs. 34.16±2.81 mmHg, p < 0.001), right/left ventricle (RV/LV) diameter (1.37±0.12 vs 0.96±0.12, p < 0.001) were significantly decreased after the TT. Tricuspid annular plane systolic excursion (1.43±0.33 cm vs 2.07±0.27 cm, p < 0.001), TTI index (0.47±0.08 vs. 0.55±0.07, p < 0.001), S’ (9.62±8 vs. 15.3±2.6) were significantly increased after TT (Table 1). No major bleeding was observed. None of the patients had stroke or transient ischemic attack. In hospital mortality was one and total mortality was three. Pulmonary hypertension was not developed during follow up.

Conclusion: Low dose prolonged infusion of tPA is an effective and safe therapy in patients with massive PE. This protocol is also effective in decreasing PASP and restoration of RV functions.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>On admission</th>
<th>Post TT</th>
<th>Pre-discharge</th>
<th>6 month*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PABS, mmHg</td>
<td>56.51±17.34</td>
<td>34.16±2.81</td>
<td>30.35±3.19</td>
<td>28.70±3.04</td>
</tr>
<tr>
<td>TPASE, cm</td>
<td>1.43±0.33</td>
<td>2.07±0.27</td>
<td>2.17±0.22</td>
<td>2.21±0.22</td>
</tr>
<tr>
<td>MR, cm</td>
<td>0.47±0.08</td>
<td>0.55±0.07</td>
<td>0.9±0.04</td>
<td>0.61±0.03</td>
</tr>
<tr>
<td>S’, cm/sec</td>
<td>0.96±0.28</td>
<td>1.53±0.26</td>
<td>1.61±0.22</td>
<td>1.69±0.24</td>
</tr>
<tr>
<td>RV/LV</td>
<td>1.37±0.12</td>
<td>0.99±0.12</td>
<td>0.84±0.10</td>
<td>0.67±0.10</td>
</tr>
</tbody>
</table>

Conclusion: Low dose prolonged infusion of tPA is an effective and safe therapy in patients with massive PE. This protocol is also effective in decreasing PASP and restoration of RV functions.

P3621 | BEDSIDE
Withholding anticoagulation after negative CTA is safe in patients with a likely clinical probability of PE
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Background: Withholding anticoagulation in patients with a likely probability of PE (CT-protocol alone) was safe. It could be debated whether patients with a likely probability and a prior episode of VTE should be referred for additional diagnostic testing.

Methods: Patient-level meta-analysis from 4 large prospective diagnostic management studies in which PE was ruled out based on the combination of an unlikely clinical probability (Wells score ≤ 4 points) and a normal D-dimer, or a normal CTPA. All patients were followed during 3 months for the occurrence of symptomatic VTE. The 3-month incidence of symptomatic VTE after exclusion of PE was pooled using a random-effects model for all patients, for those with a prior likely probability alone and from the latter cohort those with and without prior VTE separately.

Results: Data from 6,148 consecutive patients with suspected PE were pooled, with an overall PE prevalence of 25%. The failure rate in all 4,694 patients in whom PE was excluded was 1.2% (95% CI 0.5–2.6). In the 1,900 patients with a likely PE (Wells score ≤ 4 points) and negative CTPA alone, it was safe. It could be debated whether patients with a likely probability and a prior episode of VTE should be referred for additional diagnostic testing.

Conclusion: Withholding anticoagulation in patients with a likely probability of PE (CT-protocol alone) was safe. It could be debated whether patients with a likely probability and a prior episode of VTE should be referred for additional diagnostic testing.
P3623 | BEDSIDE
Homoarginine predicts mortality in treatment-naïve patients with pulmonary arterial hypertension
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Background: Pulmonary arterial hypertension (PAH) is a rare progressive disease with a 3-year mortality rate of 45% in incident patients, according to the French Registry. The prostacyclin, endothelin-1 (ET-1) and nitric oxide pathways are validated therapeutic targets, however the underlying pathomechanisms are not yet fully understood. In the present study, we investigated circulating markers (big ET-1, NT-proBNP and homoarginine), which are potentially involved in the pathophysiology of PAH.
Methods: 108 newly diagnosed, treatment-naïve incident PAH patients were recruited from 6 centres of the French Network on Pulmonary Hypertension, followed for 3 years. In longitudinal analyses we investigated the prognostic potential of these markers. Cross-sectional analysis was later used to study associations between prognostic relevant markers and clinical phenotypes.
Results: Among all enrolled patients (53±17 years; 56 females; mean±SD), 76 had idiopathic PAH. Kaplan-Meier survival analysis showed homoarginine median (1.38 μmol/L; p<0.01; Figure) and fully adjusted Cox proportional hazard models identified homoarginine as an independent predictor of mortality in this study (HR: 0.45, CI: 0.22–0.89). Plasma homoarginine was lower in 27 patients who died during the follow-up period, i.e. 1.26±0.48 vs. 1.64±0.69 μmol/L; p=0.01. In Pearson’s correlation analysis homoarginine correlated with 6-min walk distance (r=0.31), cardiac output (r=0.23), right atrial pressure (r=-0.21), big ET-1 (r=-0.31), and NT-proBNP (r=-0.21; p=0.05 for all).
Conclusion: Further experimental studies are necessary to elucidate the involvement of homoarginine in the pathophysiology of PAH.

P3624 | BEDSIDE
Survival based on the transpulmonary and diastolic pressure gradient in end-stage COPD post-capillary pulmonary hypertension
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Background: Pre-capillary pulmonary hypertension is an established complication of advanced COPD. Post-capillary pulmonary hypertension (pcPH), defined by a mean pulmonary artery pressure (mPAP) ≥25 mmHg and a pulmonary artery wedge pressure (PAWP) >15 mmHg, is less well-characterized in COPD. The transpulmonary gradient (TPG = mPAP-PAWP) <12 mmHg has previously been considered a marker of ‘passive pcPH’, while TPG >12 mmHg has been considered ‘reactive (out-of-proportion) pcPH’. The diastolic pressure gradient (DPG = mPAP-PAWP) >7 mmHg has recently been introduced for ‘isolated pcPH’ (icpPH), and DPG >7 mmHg for ‘combined pcPH’ (CpcPH).
Purpose: Although based on a strong pathophysiological reasoning, the role of the TPG and the DPG in predicting outcome remains uncertain. We have analysed the prognostic implications of a hemodynamic stratification based on the TPG and the DPG in COPD-pcPH.
Methods: 409 patients consecutive patients with end-stage COPD were assessed for lung transplantation including right heart catheterization during 1991-2010 (status follow-up January 2015) at Rigshospitalet, Copenhagen, Denmark. Fifty-two (13%) patients presented with pcPH. Patients were included in an analysis of post-transplant survival based on the TPG and the DPG. Furthermore, 35 (67%) had undergone transplantation and were subject to an analysis of post-transplant survival. Kaplan-Meier statistics with log-rank testing was utilized.
Results: Post-capillary PH patients were 56±6 years of age, presented with FEV1 22.9±7.4%, FVC 51.4±18.8%, TLC 118.0±21.7 and had preserved left ventricular systolic function (LVEF 62±9%). Hemodynamically pcPH patients presented with mPAP 32.4±6.2 mmHg, PAWP 18.4±2.5 mmHg, CO 5.8±1.4 l/min, PVR 2.6±1.5 WU. Survival analysis demonstrated a post-transplant survival benefit for patients with a TPG <12 mmHg vs >12 mmHg (p=0.012), but not for patients with a DPG <7 mmHg vs >7 mmHg (p=0.134). Post-transplant survival was unaffected by pre-transplant hemodynamic classification, TPG (p=0.23) or DPG (p=0.43).
Conclusions: The transpulmonary gradient (TPG), but not the diastolic pressure gradient (DPG), seems to be a valid pre-transplant prognostic tool in post-capillary pulmonary hypertension related to end-stage COPD. In contrast, neither the TPG nor the DPG grouping affects post-transplant survival.
classified as 390–459 and 100 to 199, ischaemic heart disease as 410–414 and I20 to I25, and cerebrovascular diseases, 430–438 and I60 to I69, respectively. The mortality rates were standardized by world standard age for each of the causes in general, presented by 100,000 inhabitants. The average focused on five points was calculated to reduce the oscillation of the coefficients mortality rate obtained. Later, joinpoint regression was performed to estimate mortality trends for each cause.

Results: During the study period there were 248,299 deaths, 51% of those in women. However all causes showed significant reductions in the mortality rate. For cardiovascular diseases, the mortality rate in the beginning was 256 deaths per 100,000 inhabitants and at the end, 145 deaths per 100,000 inhabitants, which represents a reduction of 2% (95% CI −2.4; −1.5) per year. The greatest reduction was observed in the 2005–08 period, 5.3% (95% CI −8.0; −2.5) per year. For ischemic heart disease, a reduction of 3.9% (95% CI −4.8; −1.6) per year. In relation to cerebrovascular disease, the mortality rate decreased from 91 to 14 deaths per 100,000 inhabitants, down 2.8% (95% CI −3.2; −2.4) per year; the largest reductions were 7% (95% CI −9.3; −4.6) per year in the 2005–08 period.

Conclusion: There was a progressive reduction in mortality from cardiovascular diseases, ishaemic heart disease and cerebrovascular diseases. However, despite this reduction, high rates of death from these diseases still exist.

P3627 | BEDSIDE
Stable prevalence of coronary heart disease according to electrocardiographic findings in Mauritius between 1987 and 2009
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Background: Mortality from cardiovascular disease is high in Mauritius. Also the type of two diabetes is high in Mauritius, and it has been increasing. It is unclear if the increase in glucose intolerance seen in Mauritius is paralleled with an increasing prevalence of CHD.

Methods: Five population-based surveys were performed in Mauritius between 1987 and 2009. Altogether 29,538 participated, and life-style related questionnaires with questions about previous cardiovascular disease (CVD), angina, stroke, myocardial infarction, anthropometry, biochemistry, and oral glucose tolerance tests were included. Four out of five surveys included 12-lead ECGs (n=18,073) in those aged 35 years or more. ECG changes were classified as “probable CHD” (anterior Q–waves) and “possible CHD” (ST depression/inversion or LBBB) according to Minnesota code. Prevalences were age and sex adjusted to the Mauritius population in 2009. Multivariable logistic regression was used to test associations between traditional risk-markers and CHD.

Results: Self-reported CVD did not increase in men between 1987 and 2009, 1.6% (1.2–2.1) and 1.7% (1.4–2.1), respectively, whereas between 1987 and 2009, 1.6% (1.2–2.1) and 1.7% (1.4–2.1), respectively, whereas the prevalence of possible CHD decreased, 23.7% (22.3–25.2) and 19.9% (18.7–21.0), respectively. Probable CHD was more common in men than in women, and increased with age, whereas possible CHD was more common in women, especially in those with an African ancestry. Probable CHD was more common in participants with self-reported cardiovascular disease, but not in those with hypertension, diabetes or prediabetes. Possible CHD was more common in those with CVD or hypertension, but not in those with diabetes or prediabetes. Diabetes, prediabetes, hypertension, total cholesterol, central obesity remained associated with CHD after adjustment for age, sex, ethnicity and survey year.

Conclusions: The prevalence of self-reported CVD or ECG-changes indicative of CHD did not increase in Mauritius between 1987 and 2009 despite a pronounced reduction, high rates of death from these diseases still exist.

P3628 | BEDSIDE
Analysis of drugs stored at home by elderly patients undergoing myocardial infarction
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Background: On the basis of evidence-based drug treatment improves prediction of cardiovascular morbidity and mortality in patients after myocardial infarction. Adherence is an important component of the effectiveness and safety of treatment. This research studied the drugs stored at home in older patients after myocardial infarction.

Methods: We examined 80 patients over the age of 65 years who had a myocardial infarction a year ago. Patients were visited at home and had a standardized interview. The number and composition of the packaging of the drugs that patients had at home were carefully evaluated.

Results: The average age of the patients was 71.7±4.7 years, 52.5% of men. There were 41.3% of subjects who had stable angina (mean NYHA functional class of 2.85). There were 51.3% of subjects who had chronic heart failure (mean NYHA functional class of 2.85) and there were 55% of subjects, who had arterial hypertension. The average number of the different packaging of the drugs per patient was 11.5±4.21. Cardiovascular drugs accounted for 65% of all drugs, 32.1±21.3% of the patients had 4 packs, 46.8% of the patients had 5 packs, and 27.9% of the patients had more than 6 packages. On average, 1.2 packing on the patient contained drugs that were not accepted (8% of all drugs). 54% of the drugs were prescribed by cardiologists, 20% by general practitioners, 10% by medical specialists and 16% of the drugs were acquired independently. 46% packages (0.08%) of the drugs at home were expired. 58% of patients and 37% of relatives of patients did not have knowledge and skills in relation to the pharmacological therapy.

Conclusion: One, one year after myocardial infarction, elderly patients keep at home 11.5 different drugs that they must take. New strategies are needed to support medication management at home. Education and training in relation to the pharmacological therapy are very important for the patients and their close relatives.

P3629 | BEDSIDE
Factors associated with grade-1 hypertension: a cross-sectional assessment and implications for hypertension care based on the Dietary Approaches to Stop Hypertension (DASH) approach in primary care
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Background and introduction: A Reference Framework for Hypertension Care was recently developed by Hong Kong government, and the Dietary Approaches to Stop Hypertension (DASH) regime was recommended for patients aged 40–70 years with grade 1 hypertension. However, few studies have been devoted to translating the Reference Framework into real primary care settings. Information on plausible determinants and dietary factors associated with grade 1 hypertension particularly in the Chinese population were scarce.

Purpose: To follow the Reference Framework to screen subjects with grade 1 hypertension in primary care settings, and explored factors associated with grade 1 hypertension (having systolic blood pressure [BP] of 140–159mmHg and/or diastolic BP of 90–99mmHg).

Methods: The study sample consisted of community dwellers (N=10,693) enrolled in a primary care programme in which participants overall had similar characteristics when compared to the Hong Kong population census. Invitation phone calls were given to a randomly selected subjects (N=2,673, [50% of total subjects aged 40–70 years]) in 2013. Physical examination was performed for anthropometric measurements on blood pressure (BP) and body mass index (BMI) according to a standardized protocol. Questionnaires were used to collect information on socio-demographics, lifestyles, and family medical history. Multiple logistic regression analysis was performed to explore factors associated with the presence of grade-1 hypertension.

Results: A total of 679 out of 2,673 subjects agreed to participate in the screening, and 320 subjects were grade-1 hypertensive (47.2%, [320/679]). Unhealthy diet regime (adjusted odds ratio [aOR]=2.19, 95% CI 1.04–4.62, BMI >27.5kgm² [aOR=1.87, 95% CI 1.53–2.27], irregular daily meals (aOR=1.47, 95% CI 1.11–1.95), cigarette consumption (aOR=1.59 for amount; aOR=1.83 for duration), alcohol drinks (aOR=1.87 for amount; aOR=1.65 for duration), and positive family history of hypertension (aOR=1.08) were independently associated significantly with the presence of grade-1 hypertension. The increase in the number of risk factors combined significantly correlated with higher predicted probability of grade 1 hypertension.

Conclusion(s): The finding that dietary-intake factors were associated with grade-1 hypertension echoes the incorporation of dietary-related interventional approach into the Reference Framework for hypertension management in the clinical class 2B. The association between aggregate risk factors and grade 1 hypertension should also be taken into consideration in long-term preventive strategy.

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P3630 | BEDSIDE  
Sub-specialization in cardiology care and outcome: should clinical services be redesigned, again?  
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Background: Inpatient management of cardiac patients by cardiologists results in reduced mortality and hospitalization. With increasing sub-specialization of the field due to growth in management complexity and use of technological innovations, the impact of sub-specialization on patient outcomes is unclear.  

Purpose: We sought to investigate whether management by subspeciality cardiologists impacts the outcomes of patients with subspecialty specific diseases and if so, whether this is due to clinical expertise or access to technological innovations in care.  

Methods: All patients admitted to a tertiary centre over nine years with a diagnosis of heart failure, acute coronary syndrome (ACS) or primary arrhythmia were reviewed. The outcomes of these patients managed by cardiologists subspecialized in their admission diagnosis (heart failure specialists, interventionalists, and electrophysiologists) was compared with those treated by general cardiologists.  

Results: Heart failure was diagnosed in 1,704 patients, ACS in 7,763 and arrhythmia in 4,398. There was no difference in length of stay (LOS) (p=0.26), mortality (p=0.27) and re-admissions in arrhythmia patients receiving subspecialty management (both p>0.05). However, no difference in mortality (p=0.14). ACS patients managed by interventionalists were more likely to undergo coronary intervention (p=0.025). Electrophysiologists more frequently referred patients for catheter ablation and pacemaker implantation than general cardiologists (p=0.05).  

Conclusions: The development of healthcare models which align cardiovascular disease with the subspecialist are likely to result in effective utilization of healthcare personnel and the appropriate selection of patients who would benefit from technological innovations in care.  

P3631 | BEDSIDE  
The weekend effect among patients presenting with acute coronary syndrome in the philippine general hospital  
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Background: Studies have shown that weekend and holiday admissions for patients with acute coronary syndrome (ACS) are associated with higher incidence of in-hospital mortality and major adverse cardiovascular events (MACE). This has been attributed to reduced staffing, fewer senior doctors, and the unavailability of certain diagnostic or therapeutic facilities and procedures. This has been referred to as the “weekend effect”. Local data on the “weekend effect” is lacking.  

Objectives: We aim to determine whether adults with ACS admitted on weekends had an increased risk for adverse outcomes, primarily in-hospital mortality.  

Design: Case-cohort study.  

Methods: We conducted a case-cohort study among the patients enrolled in the database of the prospective NLR Study of our General Hospital. (2013–2014). Cardiovascular diagnostic and admission data (weekend/holiday versus weekday admission) of all patients were collected. Outcomes of interest were in-hospital mortality, severe heart failure, and re-infarction. Simple and multiple logistic regression analyses were done to determine predictors of the outcomes of interest.  

Results: A total of 175 patients were included in this study, 59 were admitted on a weekend/holiday and 116 on a weekday. The mean age was 58.9±12.59, and mostly male (72.57%). Baseline characteristics did not differ between the two groups, except for a history of previous revascularization (0% vs 10%, p=0.010) and presence of both ischemia and infarct on ECG (57.6% vs 72.4%, p=0.048) in the weekday group. In-hospital mortality was significantly higher in the weekend group (27.1% vs 12.1%, p=0.0125). Multiple logistic regression identified a weekend admission and heart failure to be predictors of in-hospital mortality. Controlling other variables, a weekend/weekday hospital admission was found to be an independent predictor of in-hospital mortality (OR 7.69, 95% CI 1.78, 33.30; p=0.006).  

Conclusion: For patients with ACS, a weekend admission was independently associated with increased in-hospital mortality. This finding has important quality-of-care implications. There is a need to explore the factors that contribute to this “weekend effect” in our setting by a prospective study.  

P3632 | BEDSIDE  
Functional capacity recovery after myocardial infarction in patients with multivessel disease  

Background: Cardiac rehabilitation improves outcomes after Myocardial Infarction. We analyzed the functional capacity recovery in post ST segment elevation Myocardial Infarction patients with multivessel intervention (MVI) versus culprit- vessel intervention (CVI), after a cardiac rehabilitation program.  

Methods: We retrospectively compared functional capacity recovery in 282 patients (87.9% male) with ST segment elevation myocardial infarction and multivessel disease undergoing primary percutaneous coronary angioplasty and CVI (143 patients) versus MVI (139 patients), who were referred to a cardiac rehabilitation program between July 2006 and November 2013. The program included physical training, dietary and pharmacotherapy counseling and a specific smoking cessation follow-up when needed, lasting about 8–10 weeks. The functional capacity was assessed with a treadmill stress test before and after the program. Exercise capacity was reported in terms of estimated metabolic equivalents of task (METs).  

Results: Mean age was 58.1 years (SD=11.5), 56% were hypertensive, 27.3% diabetic, 65.2% dislipidaemic, 26.2% obese, 55.3% were current smokers and 12.4% had been previously diagnosed with coronary heart disease. The characteristics of the patients at baseline were similar in the two groups, unless the higher prevalence of diabetes mellitus in the CVI group. Significant increase of functional capacity after the rehabilitation program was observed in both groups: in the CVI group from 7.1 (SD=2.5) to 9.9 (SD=2.3) METs (p<0.001) and in the MVI group from 7.6 (SD=2.5) to 10.8 (SD=2.1) METs (p<0.001). Significant difference was observed in initial functional capacity (p=0.07) but a main difference was observed in the final workload capacity (p<0.001) between the two groups.  

Conclusions: Cardiac rehabilitation program is effective improving functional capacity in post myocardial infarction patients with multivessel disease. Patients with complete revascularization had a better recovery of functional capacity in comparison with partial revascularization.  

P3633 | BEDSIDE  
An exploratory study to determine if younger patients' with implantable cardioverter defibrillators have an improved quality of life following cardiac rehabilitation  
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Abstract: The quality of life and anxieties of young patients with implantable cardioverter defibrillators (ICD) are not clearly understood. A small number of studies have looked at both physical and psychological issues in this group however not by evaluating attendance and outcomes of ICD patients' participating in cardiac rehabilitation (CR).  

Purpose: The study aims to establish whether a CR programme offered to young ICD patients (less than 50 years of age) helps improve their quality of life and reduces stress and anxiety levels. A comparison was made to a group of young ICD patients who had not yet completed a CR programme.  

Methods: The sample size was twenty ICD patients with inherited cardiac conditions. Ages ranged from 23–49 years, mean age was 40 (± 7.83). The CR group (n=10) had enrolled on an eight week CR programme and completed a quality of life questionnaire and Hospital Anxiety and Depression Scale (HADS) at baseline and after the programme. The non-CR group (n=10) were asked to complete the same questionnaires. Retrospective questionnaire data was analysed pre and post CR using repeated measures and compared with prospective data collected from the non-CR group. Quality of life components included physical fitness, feelings, daily activities, social activities, pain, change in health, overall health, social support and quality of life.  

Results: In total five patients in the CR group completed the CR programme within the study timeframe and 80% of patients in the non-CR group returned the questionnaires. None of the CR group quality of life scores were found to be statistically significant following CR. There was a reduction between pre and post questionnaire median scores in components “quality of life” (12.5%), “daily activities” (25%), and “physical fitness” (25%). A reduction of 14.29% was observed in the CR group depression scores, however differences in both anxiety and depression scores were not found to be significant (p=0.680, p=0.06 respectively). Post CR scores and non-CR group quality of life scores were not significantly different.  

Conclusion: This exploratory study identified areas of quality of life where younger ICD patients experience problems and how CR may assist them in their initial recovery after ICD implant. A reduction was found in depression scores following CR, however it is not clear whether CR improves quality of life for this population. There may be scope for specific ICD follow up in the future as these patients currently have access to specialist advice from healthcare professionals within Cardiology.
ICD-10 defined angina or chest pain unplanned admissions in the 360 days pre or post first presentation at the CB-CDMP. Reduction in frequency and duration in days of these unplanned admissions was calculated as 63.5% (p<0.01) and 76.1% (p<0.01) respectively. Reduction in frequency of unplanned admissions was significantly associated with cardiac misconceptions (p=0.01).

Conclusion: Analysis of the impact of the CB-CDMP demonstrates a significant reduction in frequency and duration of patients’ unplanned admissions. The CB-CDMP has an important role to play in meeting national and local targets for reducing unplanned admissions.

P3636 | BEDSIDE
Seasonal difference in angina attacks in patients with vasospastic angina
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Background: Patients with stable angina due to coronary artery atherosclerosis often suffer angina attack when they are in cold weather. On the other hand, there is little information about seasonal difference in angina attacks in patients with vasospastic angina, although cold pressor test is used to provoke vasospasm. The present study evaluated seasonal difference in angina attacks in patients with vasospastic angina.

Methods: Between April 2012 and December 2014, acetylcholine provocation (ACH) test was performed in 269 patients. They were divided into 4 groups according to the season when ACH provocation test was performed: 1) spring (March to May, n=54); 2) summer (June to August, n=83); 3) autumn (September to November, n=68); and 4) winter (December to February, n=54).

Results: There were no significant differences in age, gender, and risk factors of coronary artery disease among the 4 groups. Positive ACh provocation test was observed more frequently in winter compared to spring, summer, and autumn (72.2% vs. 46.2% vs. 45.2% vs. 39.7%, p<0.001). Multivariate analysis showed winter as an independent predictor of positive ACh provocation test (odds ratio (95% CI) 2.74 (1.51–5.05)).

Conclusions: Angina attacks in not only patients with stable angina due to coronary artery atherosclerosis but also those with vasospastic angina may be observed more frequently in winter.

Acknowledgement/Funding: none

P3637 | BEDSIDE
Eastern European immigrants with ischemic heart disease in southern Europe: Cardiovascular profile and risk of events
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Introduction: Previous studies have suggested a higher cardiovascular risk of eastern Europeans as compared to southern population in Europe. Genetic factors but also environmental and dietetic contributors could be behind this epidemiological profile.

Objective: We aimed to describe the profile, clinical presentation, degree of coronary disease and in-hospital outcomes of immigrants from eastern Europe under-going coronary angiography, and compare them with patients in southern Europe.

Methods: All patients from Galicia treated in the last 5 years at all hospitals in Galicia, who underwent coronary angiography between 2008 and 2014 because of heart failure, stable angina or acute coronary syndrome (ACS) were included. Those presenting coronary artery disease (n=145) were compared with a cohort of patients in southern Europe consecutively admitted with the same syndromes within the same period (n=146).

Results: Mean age of immigrants from eastern Europe was 51±11 years and 83% were males. Clinical presentation was: STEMI 45%, NSTACS 39%, stable angina 12%, and heart failure 4%. Coronariography showed left main disease in 3%, three vessels in 15%, proximal LAD in 32%, and RCA in 33%. Angioplasty was performed in 88% and coronary artery bypass graft in 10%, with complete revascularization in 68% patients, and in-hospital mortality of 0%. Compared to non-selected patients, eastern Europeans were younger (51±11 vs 69±11 years, p<0.001), with less hypertension (48 vs 60%, p<0.001) and diabetes (19.4 vs 28.6%, p=0.079, albeHBa1c of 7 (IQR: 5.9–8.2) vs 6.1 (5.8–6.8), p=0.15), but higher smoking rate (62 vs 21%, p<0.001), family history of ACS (10 vs 4%, p=0.044), LDL-cholesterol (117±35 vs 107±38mg/dl, p=0.047), and triglycerides (190±94 vs 140±88mg/dl, p<0.001) despite similar rate of former diagnosis of coronary artery disease in the 4 groups. Positive ACh provocation test was more frequent (44 vs 32%, p=0.036), but no differences in extension and severity of coronary disease or revascularization technique (surgical or percutaneous) were found. Drug-eluting stents were implanted less frequently (33 vs 59%, p<0.001). No differences in in-hospital outcomes, remaining LVEF, or in-hospital mortality were found.

Conclusion: Immigrants from eastern Europe in our environment present similar coronary disease compared to unselected patients, but at a younger age. Underdiagnosed risk factors as hypertension or dislipidemia, family history, and three times higher smoking rate led to a higher proportion of STEMI. However, in-hospital outcomes were similar maybe due to their younger age. Long-term outcomes will be reported at the congress.
P3639 | BEDSIDE
Twelve weeks of successful smoking cessation therapy with varenicline improves spirometric lung age
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Purpose: Cigarette smoking makes an accelerated decline in forced expiratory volume in one second (FEV1), and a low FEV1 predicts morbidity and mortality from smoking-related illnesses including cardiovascular disease. There is extensive evidence that smoking cessation slows down the accelerated decline in FEV1 in the long term. However, the extent to which smoking cessation therapy can affect respiratory function in the short term is not well understood. Therefore, we evaluated the short-term effects of smoking cessation therapy on respiratory function.
Methods: Participants included 93 consecutive subjects who received 12 weeks of smoking cessation therapy. All subjects were treated with varenicline, and no changes were made to their medications during treatment. At first and last visits, physical examination and spirometry was performed. Spirometric lung ages were calculated by the formula using height and FEV1 developed by Morris and were compared to baseline values; patients who attained exhaled carbon monoxide-confirmed 4-week continuous abstinence, included 72 subjects, whereas the failure group, comprising those who did not achieve complete smoking cessation, included 21 subjects. The number of cigarettes consumed per day was reduced in all subjects in the failure group.
Results: Spirometric lung ages significantly improved from baseline to 12 weeks in the success group (61.5±20.0 vs. 59.3±19.4 mg/dL, respectively, p<0.01); however, spirometric lung ages significantly deteriorated in the failure group (62.8±20.1 vs. 65.7±21.9 mg/dL, respectively, p<0.01). The effect sizes (Cohen’s d) of spirometric lung age in the success and failure group were 0.35 and 0.84, respectively. The post-hoc statistical powers of spirometric lung age in the success and failure group were 0.84 and 0.95, respectively.
Conclusion: These findings suggest that successful smoking cessation therapy with varenicline improves spirometric lung age in the short term.

P3640 | BEDSIDE
A contemporary model of cardiovascular rehabilitation improves accessibility and uptake
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Background: While evidence suggests that cardiovascular rehabilitation (CR) is under-resourced. An alternative model of CR for cost effective secondary prevention (ACCES) was implemented and evaluated at a tertiary hospital in Western Australia.
Purpose: Through service redesign, ACCES aimed to increase the proportion of patients receiving four guideline-advocated components of CR: an initial assessment, individualised plan, education and follow-up.
Methods: A comparative group (historical) implementation study design evaluated effects on service accessibility and uptake. Patients from cardiology wards with a primary diagnosis of ACS discharged 1/4/2013-31/3/2014 (ACCES-group) were compared to controls discharged 1/4/2011-31/3/2012. Patients transferred directly to another hospital for continuing cardiology care, aged ≥80 years, or deceased within four weeks of discharge were excluded.
A participatory action research approach helped guide service redesign. Surveys were completed on both CR staff (n=44) and patients (76/86) occurred, supplemented with phone interviews (11/8) and focus groups (1/18) and feedback from CR staff (8), cardiologists (4), hospital management (4), associated external CR services (20) and general practitioners (18). CR, its components and associated processes of care were standardised.
Results: ACCES was associated with a significant increase in the provision of each of the four CR components (Table 1) and resulted in almost twice as many patients receiving all four components, culminating in follow-up, by 6 months post discharge.
Table 1. Uptake of CR components

<table>
<thead>
<tr>
<th>Component</th>
<th>Controls (n=999)</th>
<th>ACCES (n=982)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial assessment</td>
<td>723 (72.4)</td>
<td>835 (96.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Individualised CR plan</td>
<td>544 (54.5)</td>
<td>648 (75.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education</td>
<td>503 (50.5)</td>
<td>638 (74.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow-up</td>
<td>291 (29.1)</td>
<td>478 (55.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: ACCES compared with controls, engaged twice as many patients in CR, incorporating standards of care to improve in and post-hospital care. This increase in service utilisation was achieved with no additional staffing. These findings have important implications for the many CR programs with limited staff resources or relatively low levels of uptake.

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P3638 | BEDSIDE
Twelve weeks of successful smoking cessation therapy with varenicline improves spirometric lung age
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Background: Exercise training has been well documented to reduce cardiovascular event rates in patients with coronary artery disease (CAD) and is well established in cardiac rehabilitation programs. Studies comparing interval training and continuous training observed similar improvements in peak VO2. However, data are still lacking about the optimal exercise training extent. The aim of the study was to elucidate the impact of regular physical exercise on 5 days/week compared to 3 days/week for 4 weeks on aerobic exercise capacity (relative maximum oxygen uptake, VO2 max) and uptake of CR components.
Methods: A total of 100 patients with CAD (mean age 66±7.3 years, 84% men) were randomly assigned to 4-week exercise training on 5 days/week (Monday-Friday) or 3 days/week (Monday/Wednesday/Friday) with time for recovery at our institution (moderate continuous training, 70–75% of peak heart rate). Primary study endpoint was the change of aerobic exercise capacity (relative maximum oxygen uptake, VO2 max) assessed by bicycle ergospirometry at baseline and follow-up. At 4 weeks, individualised plan, education and follow-up.
Results: Spirometric lung ages significantly improved from baseline to 12 weeks in the success group (61.5±20.0 vs. 59.3±19.4 mg/dL, respectively, p<0.01); however, spirometric lung ages significantly deteriorated in the failure group (62.8±20.1 vs. 65.7±21.9 mg/dL, respectively, p<0.01). The effect sizes (Cohen’s d) of spirometric lung age in the success and failure group were 0.35 and 0.84, respectively. The post-hoc statistical powers of spirometric lung age in the success and failure group were 0.84 and 0.95, respectively.
Conclusion: These findings suggest that successful smoking cessation therapy with varenicline improves spirometric lung age in the short term.

P3641 | BEDSIDE
The role of the individual hospital in adherence to medical guidelines after acute myocardial infarction
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Background: Adherence to pharmacotherapy guidelines after acute myocardial infarction (AMI) is not satisfactory, and studies concerning causes are insufficient. National Danish registers were used to examine changes in individual hospitals and their characteristics in relation to location, size, and specialization.
Purpose: To examine initiation of both beta-blockers, statins, and acetylsalicylic acid depending on individual hospitals and their characteristics in relation to location, size, and specialization.
Methods: Patients in Denmark surviving >30 days after an AMI in 2009–2012 were identified. Information on medication use was obtained from a national register of prescriptions. Hospitals were analyzed individually and in groups depending on hospital characteristics: (a) location, determined by Danish main regions, (b) hospital size, according to AMI incidences, and (c) degree of specialization, determined by whether the hospital offers specialized cardiac functions. Multi-variable logistic regression model was used to analyze treatment initiation of all three recommended drugs.
Results: 68% (n=10,021) of the study population (n=14,726) initiated recommended treatment. The proportion varied among the individual hospitals, ranging from 45.3% to 76.8%. Moreover, when adjusted for patient characteristics, regression analysis also revealed significant differences between the individual hospitals (OR=0.80 [95% CI: 0.51; 1.24] to OR=0.71 [95% CI: 0.23; 3.60] compared to the largest hospital). When exploring hospital characteristics, initiation varied from 63% in the South Region to 75% in the North Region. The regression analysis confirmed regional differences with the largest difference between the reference region, South Region, and the North Region (OR=1.82 [95% CI: 1.58; 2.10]). In relation to hospital size, the initiation varied -5%. However, logistic regression analysis revealed differences: compared to the large hospitals, the small and medium-large hospitals performed significantly better. In regards to specialization, there was no difference in proportion, yet, the regression analysis showed that specialized hospitals performed worse (OR=0.91 [95% CI: 0.84;0.98]) than the non-specialized hospitals.
Conclusion: The analyses suggested that there are pronounced regional differences, while differences in size and specialization are present, yet less important. The relation between the individual hospitals’ characteristics and the hospitals’ outcomes in initiation remains unclear. The main factor determining initiation is therefore to be explored further. A policy to ensure guideline adherence in individual hospitals is likely to improve appropriate treatment.
P3642 | BEDSIDE
Comparison between moderate-high exercise and continuous exercise in a real-life cardiac rehabilitation setting - nine months follow-up
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It has been postulated that interval training is superior to the traditional continuous training in cardiac rehabilitation (CR). Yet, most of the studies included only heart failure patients with relatively small sample sizes and diverse training methodologies that are not always in concordance with real-life CR settings.

The purpose was to compare the outcomes between interval and continuous training in: functional capacity, cardiac risk factors, quality of life, LV systolic and diastolic functions, respiratory muscle symptoms and exercise over 6 months follow-up.

Methods: Following a 4-week adaptation to exercise period, eighty-four coronary artery disease patients were recruited and randomly assigned to an interval exercise group (IE) or a continuous exercise group (CE). Measurements were obtained at baseline, after 12 weeks of training, and at 9 months. Functional capacity was obtained by the oxygen consumption (VO2 max) exercise test. Participants attended the CR twice a week for 60 minutes. Exercise intensity relied on the VO2 peak and rating of perceived exertion (RPE).

Results: Both groups increased their VO2 peak significantly after training with no differences between them. Maximal load improved more notably in the IE group (11%) compared to the CE group (4.8%) (p<0.05). Both groups demonstrated reductions in weight, body mass index, and resting heart rate. Glycosylated Hb decreased significantly within the IE group only. Both groups improved QOL variables similarly but slightly. The calculated left ventricular ejection fraction (EF) was significantly increased over time among all patients. No cardiac events were registered during the intervention, and no differences between the groups were noticed in cardiac symptoms. At 9 months no differences were observed between the groups. However, regardless of group allocation, patients who had started in the IE group maintained the physiological adaptations while patients who had left the program demonstrated reduced cardiorespiratory performance. Patients maintaining physical activity, further improved their LVEF (p<0.05).

Conclusion: Interval training in a real-life CR setting can produce similar cardiorespiratory, weight, QOL, and LV diastolic and systolic function benefits as continuous training. Regardless of training methods it seems that a prolonged CR program and exercise is more effective in preserving the benefits.

P3643 | BEDSIDE
Short term inspiratory muscle training associated with combined aerobic and resistance training is beneficial in patients undergoing cABG surgery in phase II cardiac rehabilitation program
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Background: The inspiratory muscle training (IMT) program has been the subject of several studies in the clinical setting of phase I cardiac rehabilitation. However, the efficacy of short-term inspiratory muscle training associated with combined aerobic and resistance training results in improvement in inspiratory muscle strength and functional capacity in patients undergoing CABG surgery in phase II cardiac rehabilitation program is largely unexplored and deserves further investigation.

Purpose: To investigate the efficiency of short-term IMT associated with combined aerobic resistance training on respiratory muscle strength, functional capacity, quality of life in patients undergoing CABG surgery participated in a phase II cardiac rehabilitation program.

Methods: Twenty-four patients undergoing CABG surgery were randomly assigned to a 12-week IMT program associated combined aerobic and resistance training (IMT + AE + RT, n=12) or to combined aerobic and resistance training (AE + RT, n=12). Before and after intervention, the following measures were obtained: maximal inspiratory and expiratory pressures (PImax and PEMax), peak oxygen uptake (VO2peak), and quality of life scores. For statistical analysis, Student’s t test and Chi-square test were used (p<0.05).

Results: Compared to AE + RT, IMT program associated increased aerobic and resistance training resulted in significantly large increments in PImax (p<0.001), PEMax (p<0.001), VO2peak (p<0.001) and quality of life scores (p<0.001).

Conclusions: The present study demonstrated that the addition of short-term IMT program possibly potentiated the effects of combined aerobic and resistance training and could be a potentially strategy in patients undergoing CABG surgery in phase II cardiac rehabilitation program. The clinical significance of these findings should be addressed in larger randomized trials.

P3644 | BEDSIDE
Effects of inspiratory muscle training in patients with atrial fibrillation
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Background and purpose: It has been previously shown that the specific inspiratory muscle training resulted in increased functional capacity, inspiratory muscle strength, and endurance in patients with congestive heart failure. The aim of this study was to investigate the effects of inspiratory muscle training on pulmonary functions, functional capacity, quality of life and depression in patients with atrial fibrillation.

Methods: Thirty three patients with atrial fibrillation were participated to the study. Patients were randomly divided into two groups. Seventeen patients (training group) received inspiratory muscle training with Threshold IMT® device for three months. Training was applied for 7 days/week, twice-daily for 15 minutes with intensity at 30% of maximal inspiratory pressure (MIP). Sixteen patients were in control group and received standard medical treatment only. Patients were evaluated with spirometer for pulmonary functions; mouth pressure device for respiratory muscle strength; six-minute walk test for functional capacity; SF-36 and Minnesota Living with Heart Failure questionnaires for quality of life and Beck Depression Inventory for depression at the beginning and at the end of the study.

Results: After the training, there was a significant improvement in MIP (p<0.0001), maximal expiratory pressure (MEP) (p<0.0001), FEV1 (p=0.0001), FVC (p<0.0002), FEF25-75 (p=0.0001) and six-minute walk distance (p<0.0001). There was no significant changes in the control group.

Conclusion: In conclusion, inspiratory muscle training can improve pulmonary functions, respiratory muscle strength, functional capacity, quality of life and depression in patients with atrial fibrillation.

P3645 | BEDSIDE
Effects of home-based training with telemonitoring guidance in low to moderate risk patients entering cardiac rehabilitation
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Introduction: Home-based exercise training in cardiac rehabilitation (CR) has the potential to improve CR uptake and decrease costs of CR. In addition, patients are expected to develop self-management skills during home-based CR, which will help them maintain an active lifestyle. The FIT@Home study evaluates physical fitness and physical activity levels after home-based CR with telemonitoring guidance. In this interim analysis we discuss the long-term results of home-based CR on physical fitness.

Methods: This randomized controlled trial compared the long-term effects of a 12-week home-based (HB) training program with 12-week centre-based (CB) training program in low to moderate risk patients entering CR. The home-based group (n=45) received three supervised training sessions, before they started training with a heart rate monitor in their home environment. They received individual coaching by telephone based on objective training data uploaded on the Internet. The CB group (n=45) received regular exercise of similar duration and intensity under direct supervision of a physical therapist. Physical fitness was assessed by a cardiopulmonary exercise test at baseline, 12 weeks and 1 year.

Results: Preliminary short term results show that exercise adherence of the HB group (n=36) was similar to the supervised CB group (n=40) in the first 12 weeks (HB: training frequency of twice a week, intensity of 73.6% of HRmax). Patients in the HB and CB group showed a significant improvement in peakVO2 after 12 weeks training (14% and 11% respectively), without significant between-group differences (p=0.75). By February 2015, 34 patients (HB=17; CB=17) had completed the long term assessment of physical fitness. In both groups, physical fitness levels were maintained one year after the start of CR, without a significant difference between groups (p=0.52).

Conclusion: This study shows that HB training with telemonitoring guidance has short term effects on physical fitness as regular CB training in CR patients. Although data from only 34 patients were available, long term analysis indicate that both groups were able to maintain their physical fitness levels. This study demonstrates that home-based cardiac rehabilitation is an effective alternative compared to regular centre-based training for low to moderate cardiac risk patients.
P3646 | BEDSIDE
A multidimensional score: a way to predict the success of cardiac rehabilitation
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Background: To date, no comprehensive indicator of performance is available for the cardiologist to assess success of a cardiac rehabilitation program (CRP).

Purpose: In this study we propose a simple and handy score, “PERFSCORE” that allows to assess the achievement of therapeutic goals indicated by the guidelines.

Methods: We identified 6 indicators of performance referring to current guidelines: heart rate (HR) <70 beats/min, blood pressure (BP) <140/90 mmHg, smoking cessation or non-smoker (SMK), left ventricular ejection fraction (LVEF) >40%, LDLc <100 mg/dl or <70 mg/dl if diabetics, on treatment with at least 3 drugs among ACE inhibitors or ARBs, Betablockers, Statins and ASA.

To assess the relative contribution of each indicator in the definition of CR performance, we fitted a structural equation model employing “Stata 13” system.

Results: 839 consecutive patients (68% male, aged 69±11) included in our registry from 2009 and 2010, were analyzed. 49% had recent STEMI/NSTEMI and 51% hypertension and 51% diabetes. 21% were on beta-blockers, 78% ACE inhibitors or ARBs, 87% statins and 9% ASA. All pts were under antiplatelet therapy. A comprehensive indicator in the PERFScore were 0.57 for HR, 0.40 for BP, 0.87 for LVEF, 0.78 for SMK, 0.42 for LDL and 0.75 for drugs, multiplied by 1 if the target has been reached, otherwise by 0. The point range is 0–36: >24 unsatisfying CRP, 24–29 satisfying CRP and <29 optimal CRP.

Conclusion: We propose an easy algorithm to calculate the success of CRP that could help the cardiologist to achieve therapeutic goals.

P3648 | BENCH
Inspiriory muscle training and aerobic training present similar effects on blood pressure and cardiovascular autonomic control in hypertensive patients
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Background: Inspiratory muscle training (IMT) and Aerobic training (AT) lead to beneficial effects on the cardiovascular autonomic control, reducing sympathetic modulation and blood pressure levels in hypertensive patients. However, the effects of both interventions have never been compared in this population.

Aims: To date, no comprehensive indicator of performance is available for the cardiologist to assess success of a cardiac rehabilitation program (CRP).

Methods: Hypertensive patients were randomized to perform 12 wks IMT (7 days/wk, 30 min/day, at 30%PIMAX) or TA (treadmill, 2 days/wk, 60 min/day, at 70% HRmax). Ambulatory blood pressure monitoring, spectral analysis of blood pressure and heart rate variability and microneurography for assessment of muscle sympathetic nerve activity (MSNA) were performed.

Results: After 12 weeks of intervention, we observed reduction of SBP (IMT: 119±10.01 vs 112±1.5 mmHg, AT: 123±14.84 vs 118±7.77 mmHg) and DBP (IMT: 75±15.60 vs 70±10.80 mmHg, AT: 85.5±13.43 vs 81±13.11 mmHg). In addition, there was reduction of blood pressure variance (SD: IMT: 8.33±5.43 vs 5.33±2.05 mmHg; AT: 3.85±1.21 vs 4.42±1.39 mmHg) and reduced cardiac sympathetic modulation, (LF/eps: IMT: 2274.54±3390.88 vs 734.94±854.52 ms2 At: 2254.66±1424.63 vs 975.52±172.05 ms2) in both groups. Additionally, we observed reduction of MSNA after both interventions (IMT: 38±11.79 vs 25.07±13.28 spikes/min, AT: 27.80±7.07 vs 24.09±3.73 spikes/min). There was no statistical difference comparing the effects between groups.

Conclusions: Both interventions showed beneficial effects on patients with hypertension, by reducing blood pressure levels, cardiac sympathetic modulation and peripheral sympathetic activity. So, we believe the effects of IMT and AT are similar in hypertensive patients and both interventions may be used in the treatment of hypertension, reducing complications this population.

P3647 | BEDSIDE
Home-based walking training and adherence to medical therapy in patients undergoing coronary artery bypass grafting

Aim: To evaluate the effects of home-based walking training on adherence to medical therapy in patients who have undergone coronary artery bypass grafting.

Material: 112 patients (mean age 56.8±5.5 years) with coronary artery disease (CAD), who have undergone CABG, were examined. One month after CABG (after supervised outpatient program), patients were enrolled into three groups, comparable in demographic and clinical characteristics: Group 1 with supervised walking training (SCT) (n=35), Group 2 – home-based walking (HBWT) (n=36) and the comparison group (n=41). Subjects did 3 trains per week for 3 months. Patients were examined 1 month and one year after CABG.

Methods: Echocardiography (ECHOCO), bicycle ergometer (BE) and the asessment of the number of patients treated with ACE inhibitors/ARBs remained at the same level (73% and 75%, p=0.693). The number of patients treated with β-blockers (from 97% to 80%, p=0.001), antithrombotic therapy (from 97% to 82%, p=0.0005) decreased in Group 1 with SCT. The number of patients treated with ACE inhibitors/ARBs decreased from 77 to 66%, p=0.003. A more significant decrease in the number of patients treated with β-blockers (from 100% to 70%, p=0.0001), antithrombotic therapy (from 100% to 65%, p=0.00001) and statins (from 98 to 87%, p=0.00001) was significantly higher compared to the patients in the comparison group.

Results: One year after surgery the number of patients receiving β-blockers (from 97% to 80%, p=0.0005), antithrombotic therapy (from 100% to 68%, p=0.0004) and statins (from 97% to 82%, p=0.0005) decreased in Group 1 with SCT. The number of patients treated with ACE inhibitors/ARBs remained at the same level (73% and 75%, p=0.693). The number of patients treated with β-blockers (from 97% to 80%, p=0.001), antithrombotic therapy (97% to 82%, p=0.01) and statins (from 98 to 82%, p=0.001) also decreased significantly in Group 2 with HBWT. The number of patients treated with ACE inhibitors/ARBs decreased from 77 to 66%, p=0.003. A more significant decrease in the number of patients treated with β-blockers (from 100% to 70%, p=0.0001), antithrombotic therapy (from 100% to 65%, p=0.00001) and statins (from 98 to 87%, p=0.00001) was observed in the comparison group. The number of patients treated with ACE inhibitors/ARBs also tended to decrease (from 75% to 65%, p=0.07). Importantly, the number of patients in Group 1 and Group 2 taking statins (p=0.007 and p=0.02, respectively), antithrombotic therapy (p=0.003 and p=0.003, respectively) and β-blockers (p=0.01 and p=0.04, respectively) was significantly higher compared to the patients in the comparison group.

Conclusion: Home-based walking training has low effect on adherence to medical therapy, compared to supervised cycling programs. Thus, they are more effective compared to the results of patients without any physical training programs.
**CARDIOVASCULAR REHABILITATION: INTERVENTIONS AND OUTCOMES II**

**P3650 | BEDSIDE**

Impact of a cardiac rehabilitation programme on mortality and cardiovascular events after a percutaneous coronary intervention in patients with multivessel disease and incomplete revascularization

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**Background:** Multivessel coronary artery disease and incomplete revascularization is one of the most serious conditions in ischaemic heart disease. Although the benefits of postintervention programmes in patients with ischaemic heart disease after an acute event is recognized, it has never been studied in this subgroup of patients.

**Purpose:** Analyse the effect of a cardiac rehabilitation programme on long-term all-cause mortality and cardiovascular morbidity and mortality in patients with multivessel disease and incomplete percutaneous revascularization.

**Methods:** We performed a retrospective cohort study of 401 patients undergoing a percutaneous coronary intervention at our hospital between January 2006 and December 2010. We compared the course of individuals who followed a three-month cardiac rehabilitation programme (n=130) to patients not included in the programme (n=271), with a 2-year follow-up individual.

**Results:** Participation in these programmes is associated with a significant reduction in non-fatal acute myocardial infarction (RR 0.947; 95% CI 0.576–1.556; p=0.047) and restenosis of previously treated lesions (RR 0.831; 95% CI 0.429–1.611; p=0.583).

**Conclusions:** Cardiac remote telemetry is a useful diagnostic tool in cardiac rehabilitation program, especially in patients after surgery in whom paroxysmal atrial fibrillation is common disorder. Our response time to emergencies is immediate.

**P3652 | BEDSIDE**

Case management in patients after TAVI: are frailty and exercise capacity predictors for decision making process?

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**Purpose:** For a decade, transcatheter aortic valve implantation (TAVI) has become a promising treatment modality. Up to now, there are no sufficient data about postinterventional treatment pathways. Therefore, we aimed to evaluate predictors for referring pat. to cardiac or geriatric rehabilitation (CR/GR). Additionally, the effect of the intervention itself and of CR on exercise capacity is investigated.

**Methods:** Since 2010/2013, pat. with an elective TAVI are enrolled in the prospective multicentre registry. Postinterventionally, further pathways of patients are recorded. We documented sociodemographic, laboratory and echocardiographic parameters like LVEF, and comorbidities (e.g. stroke, renal failure). Functional testing (6-Minute-Walk-Test (6MWT), exercise stress test and Frailty-index including instrumental Activities of Daily Living (iADL)) were performed. The Frailty index is a comprehensive geriatric assessment tool exploring the presence of age-associated impairments. The physical function was measured by iADL and the physical performance test was performed during the 6MWT. The physical performance test was performed during the 6MWT.

**Results:** Of 1224 patients (80.6±5.1 years, 45.5% male) with EF 52.7±11.9% and NYHA III/IV 213 (96.4%) were enrolled. 212 (95.5%) underwent transfemoral and 10 (4.5%) transapical intervention. A pathologic Frailty-index (>3 points) emerged in 110 of 204 (53.9%) patients. After TAVI, 126 (58.8%) patients were referred to CR and 36 (16.2%) to GR. 32 (14.4%) patients were discharged home and 28 (12.6%) were either transferred into a hospital, died or couldn’t be figured out. CR, GR and home group differ in preinterventional frailty (Frailty-index >3 in 43.7%/45.1%; p<0.005) and in 6MWT (210.4/113.9/181.5m, p<0.001). Patients have a significant increase in 6MWT admission of CR compared to the preinterventional measurement (146.3±96.9 m 95% CI 24.2 - 68.5; p<0.001) and during CR (156.0±72.7m 95% CI 39.7– 72.4; p<0.001). Exercise capacity is significantly improved by +0.15±0.22W/kg (CR vs. 0±0.2; p<0.001) during CR.

**Conclusions:** The preliminary results of the TAVI registry provide information about the treatment pathways of patients after TAVI. More than two thirds of the patients are referred to rehabilitation for preventing nursing care. In this context, 6MWT and the Frailty-Index seem to be meaningful assessments for targeted assignment to aftercare. Furthermore, a benefit in exercise capacity for the GR patients results in the independence of long-term care.

**P3651 | BEDSIDE**

Importance of in-hospital remote telemetry in cardiac rehabilitation units. Our centre experience

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**Introduction:** Cardiac rehabilitation helps heart patients re-cover quickly and improve their overall physical and mental functioning. A critical component of every cardiac rehab pro-gran is the monitoring of the patient’s ECG signal during exercise. Cardiac remote telemetry is the transmission of cardiac signals from a patient to a distant receiving location with a goal of rhythm monitoring to ST segment monitoring and sophisticated arrhythmia detection and diagnosis under surveillance of trained personal.

**Purpose:** To investigate the usefulness of cardiac telemetry in patients’ admitted to our in-hospital cardiac rehabilitation center.

**Materials and methods:** Out of 2276 patients admitted for in-hospital cardiac rehabilitation, we studied two hundred eighty nine patients with previous CABG (53%) or PCI (47%), 62% males, aged from 26 to 83). Risk factors were noted, blood was sampled for analyses. Exercise test were performed on admission and after 21 days of in-hospital rehabilitation. According to the first test results patients were selected for rehabilitation: free walking, cycle and/or Nyllin steps. During the exercise patients were continuously monitor by using wireless cardiac remote system of 3 channels.Signals were transmitted to the central work station. The surveillance of the displayed signals was continuously assessed in real time by a personal trained in arrhythmia recognition supervised by a cardiologist.

**Results:** By using cardiac remote monitoring ST segment depression ranging (95% CI 0.09–0.20); p<0.001) during CR. CR patients have a significant increase in 6MWT admission of CR compared to the preinterventional measurement (146.3±96.9 m 95% CI 24.2 - 68.5; p<0.001) and during CR (156.0±72.7m 95% CI 39.7– 72.4; p<0.001). Exercise capacity is significantly improved by +0.15±0.22W/kg (CR vs. 0±0.2; p<0.001) during CR.

**Conclusions:** Our study shows that in patients with multivessel coronary artery disease and incomplete revascularization, a comprehensive cardiac rehabilitation program is associated with a significant reduction in cardiac mortality and in all-cause mortality rates.

**P3653 | BEDSIDE**

Cardiopulmonary exercise testing is predictive of return to work in cardiac patients after multicomponent rehabilitation

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**Introduction:** Return to work (RTW) is a pivotal goal of cardiac rehabilitation (CR) in patients after acute coronary syndrome or elective cardiac surgery. We therefore aimed to evaluate cardiopulmonary exercise testing (CPX) parameters as predictors for RTW at discharge after CR.

**Methods:** We analysed data from a prospectively collected registry of 498 working-age patients (51.5±8.9 years, 87.9% men) who had undergone inpatient CR between 06/2009 and 12/2011, predominantly after percutaneous coronary intervention (PCI, 62.6%), coronary bypass graft (CABG, 17.2%), or heart valve replacement (9.0%). Sociodemographic and clinical parameters, noninvasive cardiac diagnostic (2D echo, exercise electrocardiogram, 6MWT) and psychodiagnostic screening data, as well as CPX findings were compared with RTW data from the German statutory pension insurance program and analysed for prognostic capability.

**Results:** During a mean follow-up of 26.5±11.9 months, 373 (76.3%) patients returned to work, 116 (23.7%) did not, and 60 (12.3%) retired. Comorbidities (p=0.011) and physically heavy work (p=0.001) were negatively associated with RTW, whereas a higher exercise capacity at entry into CR (p=0.001) and elective PCI (p=0.02) increased the probability of RTW. After adjustment for covariates, maximum work load (in Watts) at CPX termination and the VE/VCO2 slope (p=0.011) were independent predictors for RTW. A higher work load increased (p=0.009) the probability of RTW, while a higher VE/VCO2-slope decreased (p=0.027) it. CPX even had prognostic value for retirement: the likelihood of retirement decreased with increasing anaerobic threshold (VO2AT) (p=0.016).

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Conclusion: CPX is a valid tool for assessing patients' ability to return to work. Therefore, it should be an essential part of functional assessment during CR for predicting participation in employment within two years after CR.

P3654 | BEDSIDE
Cardiac rehabilitation versus usual care increases physical capacity but not mental health after heart valve surgery: results of the randomized CopenHeartVR trial
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Background: Although survival after heart valve surgery has improved, physical and mental functioning might remain impaired. The aim of this randomized clinical trial was to assess the effect of comprehensive cardiac rehabilitation versus usual care for patients after heart valve surgery.

Methods and results: The CopenHeartVR trial was an investigator-initiated, randomized superiority trial. We randomized 147 patients after heart valve surgery 1:1 to 12 weeks of cardiac rehabilitation consisting of physical exercise and monthly psychological educational consultations (intervention) versus usual care without structured physical exercise or psycho-educational consultations (control). 76% were men, mean age 62 years, with aortic (62%), mitral (36%), or tricuspid/pulmonary valve surgery (2%). Cardiac rehabilitation compared with control had no beneficial effect on the primary outcome VO2 peak at 4 months (24.8 ml/kg/min versus 22.5 ml/kg/min, p=0.045), but did not affect the secondary outcome Short Form-36 mental component score at 6 months (53.7 versus 55.2 points, p=0.40) or the exploratory physical and mental outcomes. The number of self-reported non-serious adverse events (e.g., musculoskeletal injuries, heart-beat, chest pain) were 11/72 (15.3%) in the intervention group versus 3/75 (4.0%) in the control group (p=0.02).

Conclusions: Cardiac rehabilitation after heart valve surgery significantly improved VO2 peak at 4 months and inversely affected the risk of non-serious adverse events at 6 months compared with control, but does not seem to affect mental health and other measures of exercise capacity and self-reported outcomes.

P3655 | SPOTLIGHT
A web-based social-cognitive sexual counseling intervention for nurses: a pilot study
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Background and purpose: Nurses consider cardiac patients’ education and sexual counseling needs within their scope of responsibility, although infrequently addressed in practice, citing inadequate knowledge, skills and confidence to address sexual concerns. This study evaluated a web-based social-cognitive intervention for evidence-based sexual counseling by student nurses with cardiac patients.

Methods: A pre-/post-test survey design was used to pilot test the intervention with baccalaureate students (N=57) in two Midwestern United States. The website included multiple methods of delivery and social-cognitive approaches for user integration of content, embedded in a secure website. Testing included: a pre-test (T1), immediate post-test after intervention (T2), and at 4–6 weeks post-intervention (T3). Data were collected using the Survey of Sexuality Related Nursing Practices (SSRNPs)–cardiac version. Statistical analysis: t-tests, ANOVA.

Results: Participants were mostly women (84%), single (67%), White (83%), with a mean age of 26 years (R=21–48). From T1 to T3, the intervention significantly increased Sexual Counseling subscale (4.87 ± 1.37 to 6.53 ± 1.37, p=0.001), MET level (4.97±1.37 to 7.38±1.53, p=0.001), oxygen pulse (9.46±3.76 to 10.58±3.36, p=0.05), and VO2peak (39.42±8.40 to 36.58±7.82, p=0.05) as well as 6-MWT (meters) (433±58.95 to 494.33±74.77, p<0.001) after the 8-week rehabilitation program. After physicians’ assessment, 4 subjects out of 6 (who were originally on heart transplantation wait list) were grounded in social-cognitive theory and provided a feasible approach to enhance sexual counseling knowledge and practice.

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P3656 | BEDSIDE
Beneficial effect of cardiac rehabilitation on endothelial function in patients who received coronary revascularization
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Background: It is well known that cardiac rehabilitation including exercise training has cardioprotective effects on patients with ischemic heart disease. Endothelial dysfunction can increase the risk of a coronary event. In this study, we investigated whether the endothelial function measured by using flow-mediated dilatation (FMD) was improved after CR in patients who had received percutaneous coronary intervention (PCI).

Methods: Consecutively 119 patients (104 males, mean age: 54.9±1.5 years) who had treated with PCI were included. The patients were divided into 2 subgroups; 69 patients with acute coronary syndrome and 50 stable angina patients. All patients were examined on the second or third day after PCI, and 6 months follow-up (9.2% vs. 8.9%, p=0.61) between the patients with angina and ACS. However, FMD which was measured after 6 months CR was significantly improved on both groups (increase by 1.1% in angina; 95% CI: 0.1–2.0, p=0.03 vs. 1.1% in ACS group; 95% CI: 0.5–1.8, p=0.002). And also, peak oxygen uptake (V02max) was improved on both groups (increased by 2.1 ml/kg/min in angina; 95% CI: 0.8–3.4, p=0.003 vs. 2.6 in ACS group, 95% CI: 1.1–4.2, p<0.001).

Conclusions: FMD was improved after CR in patients with PCI, and this beneficial effect was noted equally on both groups. Our results support that improvement of endothelial function is one of the important effect of CR reducing cardiovascular risk in patients with coronary disease.

P3657 | BEDSIDE
Multidisciplinary rehabilitation program in patients with advanced heart failure after cardiac resynchronization therapy
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Introduction: Cardiac resynchronization therapy (CRT) has been proven to improve functional class and systolic function in heart failure patients (NYHA class III- ambulatory IV) and additional cardiac rehabilitation program with exercise training in this high risk group remains to be determined.

Objective: The objective of this program was to assess further improvement of exercise capacity of patients with advanced heart failure after CRT through multidisciplinary cardiac rehabilitation program.

Methods: Twelve patients (5 women and 7 men; mean age 48, ranged 18–70) who received CRT (mean duration of 2.2 months) further completed an 8-week multidisciplinary cardiac rehabilitation program with aerobic exercise training (including 3 sessions/week with a total of 24 sessions & 40 minutes/session on treadmill walking & cycling) plus specific counseling services on heart failure disease with emphasis on patients’ self-management. Cardiopulmonary exercise test (CPET) and six-minute hall walk (6-MWT) were assessed and compared at baseline (before implantation of CRT), after CRT and after rehabilitation respectively.

Results: There were statistically significantly further improvement on the duration (seconds) of the CPET (614±166 to 743.46±147, p<0.001), peak VO2 (ml/kg/min.) (17.44±4.76 to 20.11±5.36, p<0.001), MET level (4.97±1.37 to 7.33±1.53, p<0.001), oxygen pulse (9.46±3.76 to 10.58±3.36, p=0.05), VO2peak (39.42±8.40 to 36.58±7.82, p=0.05) as well as 6-MWT (meters) (433±58.95 to 494.33±74.77, p<0.001) after the 8-week rehabilitation program. After physicians’ assessment, 4 subjects out of 6 (who were originally on heart transplantation wait list) did not request heart transplantation waiting list due to the improvement of functional class to NYHA class II.

Conclusions: Well prescribed exercise training program specifically designed for heart failure patients who received evidence-based heart failure therapy is bene-
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ficial and safe. Additional multidisciplinary intervention further improved patients' well-being.

P3658 | BENCH
Loaded breathing exercise increases cardiovascular sympathetic modulation acutely in patients with essential hypertension
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Introduction: Inspiratory muscle training (IMT) reduces cardiac sympathetic modulation and blood pressure levels in hypertension. However, there are no reports about the acute effects of one single session of loaded breathing exercises (LBE) in this population.

Objectives: To compare the acute responses of the autonomic cardiovascular control components in patients with essential hypertension and healthy volunteers to a LBE session.

Methods: Hypertensive volunteers (GH) and healthy controls (GC) were recruited to perform a 30 min LBE session, at 30% of maximal inspiratory pressure (PI-MAX). Cardiac autonomic responses were monitored by oscilometric method and the autonomic modulation was evaluated by spectral analysis. The measurements were performed before and in the first hour after LBE sessions.

Results: One hour after the session, hypertensive volunteers showed increase of blood pressure variance (SD: 51.51±37 vs 47.89±37.33 mmHg, p<0.85; GH: 4.42±16.1 vs 6.11±44.1 mmHg, p=0.01), heart rate variance (SD: 51.88±17.15 vs 49.23±17.51, p=0.78; GH: 35.14±17.61 vs 41.42±27.20, p=0.05) and sympathetic peripheral modulation (LFBs: GC: 14.90±16.51 vs 9.71±9.32 mmHg2, p=0.46; GH: 16.00±25.08 vs 27.15±13.56 mmHg2, p=0.02) as well as increase of cardiac parasympathetic modulation (HFBs: GC: 108.99±81.28 vs 1110.61±1048.16, p=0.96; GH:667.75±547.43 vs 1079.52±1200.37, p=0.03). In addition, there was improvement of the baroreflex sensitivity (BRR): 56.5±4.4 vs 69.1±12.6, p=0.03 and changes in baroreceptor effectiveness index (EIB: 0.32 vs 0.27, p=0.01) after LBE, only in the hypertensive group.

Conclusion: Acute responses of the autonomic cardiovascular control components to a loaded breathing exercises session seem to be more evident in populations with impairment of such systems, as in hypertension. Considering the increase of sympathetic modulation is associated to increase of parasympathetic modulation, we believe that the beneficial effects observed after chronic IMT protocols, are obtained from the acute responses to single sessions of LBE.

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P3659 | BEDSIDE
Effect of long-term home based cardiac rehabilitation programme on recurrent anginal chest pain, readmission and mortality risk after coronary revascularization
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Background: We compared readmission and mortality risk between cardiac rehabilitation participants (CRP) and nonparticipants.

Methods: A total of n=197 patients (61.5±0.8 years) were randomized: group 1 – 91 pts; group 2 – 106 CRP performed a training and secondary prevention programmes over 12 months. Clinico-functional assessment and the Seattle Heart Failure programme over 12 months. The results of the programme showed significant improvement of long term estimative survival prognosis. Programmes improved long term estimative survival prognosis. Longer period follow-up managed to reduce risk of readmission during first year after intervention (2) Partially supervised rehabilitation programme improved long term estimative survival prognosis.

Conclusions: 1) Cardiovascular rehabilitation participation is associated with a markedly reduced risk of readmission during first year after. 2) Partially supervised rehabilitation programme improved long term estimative survival prognosis.

P3660 | BENCH
Implementation of Jacobson’s progressive relaxation in coronary bypass surgery patients before chest tube removal
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Introduction: The purpose of this study was to determine whether the use of a Jacobson progressive muscle relaxation, when used without opioid analgesia, decreases pain during chest tube removal (CTR) after coronary bypass surgery. Methods: A two-group quasi-experimental posttest design was used. A convenience sample of 100 subjects was divided into an experimental group (n=50), which received relaxation training 15 minutes before chest tube removal and a control group (n=50), who did not receive relaxation. All patients received 500mg of paracetamol 30 minutes before relaxation. Pain was assessed with verbal pain score (0–5). Analysis of variance was used to analyze the data.

Results: Significant decreases in pain were demonstrated as a result of implemented relaxation test: 2.63±0.725 vs 3.62±0.725, p<0.001. All experimental subjects stated that the relaxation technique was simple to perform.

Conclusion: This study supports the use of Jacobson progressive muscle relaxation for pain management during CTR among patients who have undergone coronary bypass surgery.

P3661 | BEDSIDE
Prognostic value of endothelial parameters changes during cardiac rehabilitation on recurrent chest pain in patients with coronary artery disease: 30 months follow up
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Purpose: To evaluate the effects of cardiac rehabilitation on circulating blood markers of endothelial function: nitric oxide (NOx), Advanced Oxidation Protein products (AOPP) and Xanthine Oxidase (XO), and their prognostic value on recurrent chest pain.

Methods: 47 patients (pts) (57.9±3.6 years, all men) were admitted to cardiac rehabilitation after myocardial infarction (MI). All pts underwent a supervised residential 3-weeks exercise training. At baseline and after 3 weeks in all pts values of NOx, AOPP and XO were determined. Clinical long-term follow-up (30 months) was performed. All medical therapy was documented, and for this analysis, we focused on recurrent anginal chest pain.

Results: After 30 months there were no cardiovascular (CV) hard endpoints (CV death, MI, stroke), however 24 pts (51%) had episodes of typical anginal chest pain (AP group) while 23 pts (49%) were without anginal chest pain (no-AP group). During rehabilitation NOx increase in both groups (p<0.0005, both). The mean NOx increase in no-AP group was higher than in AP group (13.7±10.5 vs 4.03±4.7, p=0.009). AOPP levels were decreased in both groups, with higher mean AOPP decrease in no-AP group (46.7±13.5 vs 2.5±13.5, p<0.0005). Also, XO levels decreased in both groups (p<0.0005, both), with higher mean XO decrease in no-AP group (120.9±72.19 vs 93.13±28.15, p<0.0005). A positive correlation was found between NOx increase and XO decrease in all pts (r=0.965, p<0.0005), between NOx increase and AOPP decrease in all pts (r=0.925, p<0.0005) and between AOPP and XO decrease in all pts (r=0.711, p=0.0005). Univariate logistic regression analyses showed that NOx increase (OR 0.836, CI 0.745–0.938, p=0.005) and XO decrease (OR 0.921, CI 0.872–0.973, p=0.003) during rehabilitation, significantly predict a 30 months period without anginal chest pain.

Conclusion: Residential cardiovascular rehabilitation, in patients with coronary artery disease, induced improvement in endothelial function. Patients who had a higher increase of NOx, and greater reduction in XO and AOPP values after 3 weeks of specialized cardiac rehabilitation, during 30 months of follow up, were without anginal chest pain and without any CV event.

IMPROVEMENT OF MEDICAL CARE IN CARDIOVASCULAR PATIENTS: SOCIAL AND ECONOMIC ISSUES

P3662 | BEDSIDE
Long-term healthcare costs after myocardial infarction in a clinical practice setting in Sweden: results from a contemporary nationwide registry study
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Background: Nationwide data on healthcare costs after myocardial infarction (MI) are not widely studied, in particular beyond first year after MI. The aim was to investigate long-term healthcare costs after MI in a clinical practice setting.

...
compared with hospital outpatient care visits or drugs (Figure 1).

P3664 | SPOTLIGHT
Weekend and out of hours admission to hospital with acute coronary syndrome confers poorer mortality and longer length of hospital stay
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Introduction - Acute Coronary Syndrome (ACS) is the most common cardiovascular diagnosis requiring hospital admission worldwide and in the UK. It is associated with substantial mortality and healthcare burden. Given the current five day working pattern in the UK, we hypothesise a significant variation in the outcomes of patients admitted with ACS during the standard working hours compared with out of hours and weekends.

Methods: Retrospective cohort study including all patients identified in the compulsory Swedish nationwide inpatient registry with an MI between 2006–2011 (NCT01984307). These data were linked to the cause of death- and the drug utilization registries. Cardiovascular (CV)-related hospitalizations, CV-related hospital outpatient care visits, and pharmaceuticals were assigned unit costs to calculate healthcare costs. Per-patient mean healthcare costs are reported (2014 Euros [€]) separately for first year after MI, and cumulatively for year 2 and onward over a maximum follow-up of 6 years. Results were stratified by median age (>74 or ≤74) and high risk (≥ one of diabetes mellitus, prior MI, coronary artery bypass graft surgery, peripheral arterial disease, stroke, heart failure, or chronic renal dysfunction).

Results: The study included 97 254 patients, with a total of 315 839 observation years. Mean healthcare costs were €12 460 first year after MI. The mean 5-year cumulative healthcare costs from year 2 onward were €6 389. High-risk patients had higher healthcare costs both in the first year after MI and in the long-term follow-up. CV-related hospitalizations contributed to the majority of these costs compared with hospital outpatient care visits or drugs (Figure 1).

Conclusion: This nationwide registry study shows that healthcare costs after MI are primarily driven by CV-related hospitalizations, and that risk stratification has a substantial impact on healthcare costs, in particular in a long-term perspective.

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patients from low SEP. This could be attributed to the implementation of universal health coverage. These results will be useful to evaluating public policies implemented during the last decade in Chile.

Acknowledgement/Funding: School of Public Health grant

P3667 | BEDSIDE
Trends in social inequalities in the prevalence of major cardiovascular disease among adults in Germany
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Background: Social gradients in cardiovascular disease (CVD) and risk factors have been reported in many countries, but little is known whether these social inequalities have increased or decreased in recent years.

Purpose: To investigate whether there are social inequalities in the prevalence of major CVD in the adult population in Germany and whether these inequalities have changed between 1998 and 2010.

Methods: Using data from two German National Health Interview and Examination Surveys conducted in 1997–1999 (GNHIES99, n=4170) and 2008–2011 (DEGS1, n=8530), we examined trends in the lifetime prevalence of major CVD (myocardial infarction, chronic ischemic heart disease, stroke or heart failure) according to socioeconomic status among adults aged 40–79 years in Germany. History of major CVD was assessed by structured computer-assisted physician interview. Socioeconomic status (SES) was classified as low, medium and high using an index based on information on education, occupational status and net equivalent income. Trends of social inequalities in CVD prevalence were examined in logistic regression models including interaction terms for survey*SES and adjusting for age, region, community size and behavioural risk factors (smoking, obesity, sports activities, alcohol intake).

Results: Between 1998 and 2010, age-standardised lifetime prevalence of major CVD decreased from 13.9% to 11.3% (p=0.03) among women but did not change significantly among men (16.0% and 17.5%, p=0.2). In 2010, prevalence of major CVD was significantly higher in low vs. high SES groups among women (17.0% vs. 5.2%) and men (24.1% vs. 12.8%). Adjusting for age, lower SES was associated with significantly higher odds of CVD among women (OR low vs. high SES 2.18 (95% CI 1.29–3.66); OR for Relative Index of Inequality score (RII) 2.61 (95% CI 1.49–4.58)) and men (OR low vs. high SES 2.02 (95% CI 1.35–3.02); OR for RII 2.11 (95% CI 1.34–3.3)). Among men, social inequalities have increased since 1998 (p for interaction survey*SES <0.05), with fully adjusted prevalences increasing by +3.2% among men with low and medium SES and decreasing by –4.6% among men with high SES. Among women, no significant change in social inequalities was found (p for interaction survey*SES < 0.1), with fully adjusted prevalences decreasing similarly by about –3% in all SES groups.

Conclusions: There is a significant social gradient in the prevalence of major CVD among women and men in Germany. Between 1998 and 2010, social inequalities in CVD prevalence remained stable among women and increased among men.

P3668 | BEDSIDE
Acute coronary syndrome perception: determinants and impact on medical care seeking
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Background: The interpretation of acute coronary syndrome (ACS) symptoms may influence the time to hospital admission. Long pre-hospital delay relates to lost opportunities for early risk stratification and management, leading to increased mortality and morbidity. We explored predictors of illness perception and its association with the delay in medical help seeking.

Methods: We assembled a cohort of all consecutive patients admitted to the Cardiology department of two tertiary hospitals of different regions with ACS diagnosis between September 2013 and January 2014. ACS perception was evaluated by personal interview in the first 48h of hospital admission with the question: “Did you consider the possibility of your symptoms being related to a cardiac problem?” Clinical data was obtained from medical patient’s records and by interview.

Results: 311 patients (mean age 63.3±13.2 years; 71% male) were included; 59.5% with non-ST segment elevation ACS and 40.5% with ST-segment elevation ACS. A large proportion of patients (40.5%) did not perceive symptoms as cardiac until the doctor’s information. Previous ACS diagnosis influenced the symptoms perception: 87.3% of those with ACS past history compared to 53.5% in others (OR 5.81; 95% CI: 2.51–13.46; adjusted for age, sex, hospital localization and ACS type). No association was found between ACS perception and ACS type, age, sex, academic degree and income.

Conclusion: Perception of ACS was significantly related to earlier arrival for medical help, with a median time to hospital admission of 157 (interquartile range (IQR):72–329) minutes compared to 303 (IQR:101–560 minutes) in non ACS perception group (p=0.021). The difference according to perception was pronounced in patients without previous ACS diagnosis (156 (69–321) minutes vs 201 (107–449) minutes, p=0.012) and non-significant in patients with previous ACS (170 (86–625) vs 207 (77–1577) minutes, p=0.570). After adjusting for age, sex, ACS past history, ACS type and hospital location, perception of ACS was significantly associated with 30% shorter pre hospital delay (p=0.036).

Conclusion: The illness perception of patients with acute coronary syndrome needs to be improved, independently of socio-demographic factors. Mistaken ACS symptom interpretation was significantly associated with delay in treatment seeking. These results reinforce the need for better health education, focusing on the alert signs for ACS to improve hospital admission time and treatment in this setting.

P3669 | BEDSIDE
ST-segment Elevation Myocardial Infarction and primary angioplasty: the predictors of patient delay
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Introduction: Primary angioplasty (PPCI), is the best treatment for ST-segment Elevation Myocardial Infarction (STEMI) when performed earlier in the course of the disease. Despite the campaigns to raise general population awareness for STEMI symptoms, the time between symptoms onset and first medical contact...
(“patient delay”) is still suboptimal. Therefore it is essential to understand the factors related to this delay in order to improve the performance of this healthcare intervention and patients’ outcomes.

Objective: To evaluate the factors associated with the “patient delay” in patients with STEMI.

Methods: We prospectively collected the data of 18 national interventional cardiology centers capable to perform PPCI in 24/7. A survey was done during one month for each four consecutive years (2011–2014) in order to characterize all patients admitted for STEMI with indication for PPCI (-12 hours after onset of symptoms). Demographic and clinical characteristics were analyzed descriptively. Independent predictors of “patient delay” above the median value were analyzed through univariate and multivariate logistic regression.

Results: 865 STEMI patients were included for analysis (mean age of 62±13 years; 22% female; and 18% had diabetes). The overall median of “patient delay” was 106 min and 432 patients have exceeded such time. Annual data regarding “patient delay” did not show statistical significant differences among years (118 min in 2011, 102 min in 2012, 91 min in 2013 and 106 in 2014 min; p=0.067). Age >75 years, female gender, the onset of symptoms during the night (midnight to 8 AM) and going to a primary healthcare facility before the first medical contact were found as independent predictors of increased “patient delay” in multivariate regression analysis. Patients from the North region, the contact through the emergency telephone number and the use of Emergency Medical Services were independently associated to a “low patient delay” time.

Conclusions: Our data shows that national “Patient delay” is still very high. Our findings suggest that the elderly population and women should be subject of specific programs and be taken as priority in the development of awareness programs. To highlight the need of knowledge that patients should not delay the call for aid, even if symptoms occur during the night. The contact should always be made through the emergency phone number.

P3670 | BEDSIDE
Gender differences in predictors of left ventricular myocardial relaxation in non-obese, healthy individuals
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Background: Previous studies indicate that individuals with metabolic syndrome (MetS) might be at risk for left ventricular (LV) diastolic dysfunction. However, little is known about which metabolic factors contribute to the development of LV dysfunction in individuals who are not obese or overweight and who do not have diabetes mellitus and/or cardiovascular diseases.

Methods: Participants without diabetes mellitus, systolic dysfunction, or other causes and features of the phenomenon of delayed hospital discharge (DHD) were subject of special analysis.

Conclusions: We found favorable time trends in rates of smoking and low physical activity, strongly marked just after the accession; however the rates of over-weight and unfavourable eating habits have not improved. The relationship between smoking and poverty and structure of the family have become stronger. Unhealthy lifestyle habits among Polish teenagers remain a major issue for public health in Poland.

P3672 | BEDSIDE
Delayed hospital discharge in an italian cardiology department: causes and features of the phenomenon
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The phenomenon of Delayed Hospital Discharge (DHD) is well known, but studies so far were performed in implemented emergency departments, surgical or internal medicine ward. This phenomenon is a source of inefficiency of the hospital care system and increase health care spending. From 06/02/13 to 12/02/14 we conducted a study to detect the patient delay in all DHD in ICCU and CW, comparing it to all hospitalizations; for all pts were evaluated several clinical variables and for pts with DHD also the number of days lost and the reason for the delay. For 3 weeks, from 24/3 to 13/04/14, we calculated the period prevalence (PP) of the phenomenon.

Results: The cumulative incidence (CI) of DHD is 12.6% with 290 DHD (233 ICCU and 57 CW) of 2306 total admissions. The (PP) was 7.4%. Because of DHD were lost 759 bed-days. The inappropriate bed occupation days (IBOD) due to the phenomenon of DHD are 8.3% of total hospitalization days. The phenomenon has different features in ICCU and in CW. In ICCU the CI of DHD is 24.9% and the PP 15.5% and in CW is respectively 4.2% and 3.3%. However the bed-days lost are similar (ICCU 364 and CW 395), because the IBOD in ICCU is shorter (1.56 vs 6.93 days). An analysis of the causes of the phenomenon reflects the difference between ICCU and CW. In ICCU 100% of the DHD is explained by an organization system due to the lack of non-acute beds (LNAB) to transfer the patients to univariate analysis are significantly associated with the DHD age >85 years, heart failure, disability, diversion, anaemia, recent stroke and/or surgery. At multivariate analysis (logistic regression) remain significant recent stroke and/or surgery, age -85 years, and heart failure with Odds Ratio, respectively, 20.5, 4.1, 5.3 and 1.9.

Conclusion: Even in our Cardiology Dept. (hub center with Cath Lab) the phenomenon of DHD is relevant and cause the loss of more than one bed per day throughout the year both in ICCU and in CW. In ICCU it is more evident with an IBOD 11% and is due to organizational reasons (LNAB), while in CW is largely attributable to clinical and social pieces, which make it difficult to discharge

P3671 | BEDSIDE
Trends in adolescents lifestyle in post-communist country following the accession to the European Union (EU)
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Introduction: Deep socioeconomic changes have been observed in Poland following accession the EU in 2004. The aim was to assess time trends in adolescents’ lifestyle habits in Poland from 2004.

Material and methods: We used the Polish data of the four Health Behaviour in School-aged Children surveys conducted in 2002–2014 on the sample of 7540 teenagers (3rd grade of lower secondary school; mean age 15.68±0.31; 48.0% boys; 63.2% urban inhabitants). The following cardiovascular risk factors were considered: excessive body mass, poor physical activity, every day meals of fast food and unbalanced and poor food choices. A series of multivariate logistic models were estimated, among others year-specific models and full model containing year of data collection as independent variable (with “repeated” contrast to check trend). All analyses were adjusted for age, gender, domicile, family structure and perceived family wealth.

Results: The proportions of teenagers with unhealthy lifestyle habits are presented in the Table. Time trends were similar in teenagers living in the city and in the countryside. Not living with both birth parents was related to smoking (OR 1.66 [95% CI 1.23–2.24] in 2002, 1.75 [1.30–2.35] in 2006, 1.97 [1.37–2.83] in 2010 and 2.38 [1.66–3.43] in 2014). Self-perceived poverty was related to the probability of smoking in 2014 (2.20 [1.15–4.21]) and in 2010 (2.25 [1.18–4.26]) but not in 2006 (1.58 [0.98–2.54]) nor in 2002 (1.26 [0.78–2.01]) and to low physical activity in 2002 only. The proportions of teenagers with at least three unhealthy habits was 5.9% in 2002, 7.1% in 2006, 9.0% in 2010, and 5.7% in 2014 (p<0.003).

Unhealthy lifestyle habits in teenagers

<table>
<thead>
<tr>
<th>Year</th>
<th>Every day smoking (%)</th>
<th>Low physical activity (%)</th>
<th>Poor food choices (%)</th>
<th>Overweight or obesity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>16.3</td>
<td>87.4</td>
<td>20.4</td>
<td>7.2</td>
</tr>
<tr>
<td>2006</td>
<td>12.3</td>
<td>84.8</td>
<td>31.5</td>
<td>9.5</td>
</tr>
<tr>
<td>2010</td>
<td>11.0</td>
<td>83.5</td>
<td>36.4</td>
<td>14.3</td>
</tr>
<tr>
<td>2014</td>
<td>9.8</td>
<td>82.2</td>
<td>32.5</td>
<td>12.6</td>
</tr>
</tbody>
</table>

Conclusions: We found favorable time trends in rates of smoking and low physical activity, strongly marked just after the accession; however the rates of over-weight and unfavourable eating habits have not improved. The relationship between smoking and poverty and structure of the family have become stronger. Unhealthy lifestyle habits among Polish teenagers remain a major issue for public health in Poland.

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P3673 | BEDSIDE
Cost effectiveness analysis of oral anticoagulant therapy with rivaroxaban for nonvalvular atrial fibrillation in a secondary hospital in Spain
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Background: Atrial fibrillation (AF) is the most prevalent arrhythmia. Prevalence in Spain is estimated in 4.4% of total population. It is widely associated with increased risk of stroke, cardiac failure and quality of life loss. Classic preventive treatment was dose-adjusted vitamin K antagonist (VKA) therapy (warfarin or acenocoumarol, International Normalized Ratio (INR) 2.0–3.0). ROCKET AF study (2011) showed that Rivaroxaban is an effective treatment for preventing stroke in AF patients. Purpose: To assess a cost effectiveness analysis of anticoagulant treatment with Rivaroxaban vs VKA in nonvalvular AF patients in a Secondary Hospital in Spain.

Methods: Retrospective analysis of all patients treated with Rivaroxaban or acenocoumarol with diagnosis of nonvalvular AF discharged from a secondary hospital during 2012 and 2013. Demographic and clinical variables as well as main costs of treatment, hospitalization, rehabilitation, INR determinations were included in an Excel database for analysis.

Results: 336 p were included in the study; 292 p were treated with acenocoumarol and 44p with Rivaroxaban. Mean age was 79±8.6 years, 53% women (180g) with a CHA2DS2VASc score of 3.7±1.3. There were no statistical differences between groups in age, gender, hypertension, diabetes, ejection fraction, CHA2DS2VASc score or mortality. Treatment with Rivaroxaban was dominated by standard therapy with VKA. We analysed a subgroup of patients treated with VKA with suboptimal mean time in therapeutic range (TTR) (<40%). For this patients Rivaroxaban proved to be cost effective but at an Incremental Cost Effectiveness Ratio (ICER) of 1053000€ for avoided ischemic stroke and 280017€ for haemorrhagic stroke. Rivaroxaban therapy did not showed gain of QALY’s versus standard anticoagulant therapy.

Conclusions: In our population novel oral anticoagulant therapy with Rivaroxaban did not seem to be cost effective. Further and wider studies are needed to take on the best therapeutic options at an optimal cost.

DELETERIOUS EFFECTS OF OBESITY AND DIABETES
P3674 | BEDSIDE
Obesity is associated with subclinical myocardial injury independently of a dysmetabolic state
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Background: Obesity is an independent risk factor of cardiovascular disease and is commonly associated with a dysmetabolic state. Circulating high sensitivity cardiac troponin I (hs-TnI) concentrations reflect cardiac mass and subclinical myocardial injury and are strongly predictive of subsequent risk of heart failure and premature death. It remains unclear whether obesity is associated with subclinical myocardial injury independently of a dysmetabolic state. Purpose: Assess the association between obesity and subclinical myocardial injury in subjects with and without a dysmetabolic state.

Methods: hs-TnI was measured in 4431 men and 5281 women aged >20 years participating in the prospective observational Nord-Trøndelag Health Study (HUNT) using the ARCHITECT STAT High-Sensitive Troponin assay. All patients were classified according to body mass index (BMI) and metabolic status.

<table>
<thead>
<tr>
<th>Levels of troponin I</th>
<th>BMI</th>
<th>Median hs-TnI (ng/L)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Eumetabolic (p&lt;0.001)</td>
<td>Dysmetabolic (p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>16.5–24.9</td>
<td>3748</td>
<td>2.70 (1.90–4.00) ng/L</td>
<td>4.80 (3.40–6.35) ng/L</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>3748</td>
<td>4.40 (3.10–6.90) ng/L</td>
<td>4.10 (2.90–5.90) ng/L</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>1239</td>
<td>3.30 (2.50–4.80) ng/L</td>
<td>4.30 (3.20–6.50) ng/L</td>
</tr>
<tr>
<td>35.0–39.9</td>
<td>254</td>
<td>3.50 (2.50–4.30) ng/L</td>
<td>4.30 (2.50–4.30) ng/L</td>
</tr>
<tr>
<td>≥40.0</td>
<td>56</td>
<td>4.14 (2.00–7.10) ng/L</td>
<td>4.00 (2.70–5.15) ng/L</td>
</tr>
</tbody>
</table>

*Comparing levels of hs-TnI in eumetabolic and dysmetabolic subjects across BMI strata (Mann Whitney U test); †Spearman rank correlation between BMI and levels of hs-TnI within groups.

Results: 7879 and 1627 subjects were classified as eumetabolic and dysmetabolic respectively and were included in the analyses. Median hs-TnI levels (IQR) were 3.10 (2.10–4.50) ng/L in the eumetabolic and 4.40 (3.10–6.60) ng/L in the dysmetabolic (p<0.001). The dysmetabolic subjects exhibited significantly higher levels of hs-TnI through all BMI strata, except in those with BMI ≥40 (see Table). In subsequent univariate analyses, hs-TnI was associated with increasing body mass index in the dysmetabolic group (p<0.001). No significant association was observed across BMI strata in the dysmetabolic group (p=0.058).

Conclusion: Obesity is associated with subclinical myocardial injury in the eumetabolic, but not in the dysmetabolic state.

P3675 | BEDSIDE
Impact of low serum levels of 1,5-anhydroglucitol on cardiovascular events in patients after low first-time elective percutaneous coronary coronary intervention

Background: Postprandial hyperglycemia plays an important role in the pathogenesis of coronary artery disease and cardiovascular events. Serum 1,5-anhydroglucitol (1,5-AG) levels are known to be a clinical marker of postprandial hyperglycemia. We examined whether serum 1,5-AG levels can predict cardiovascular events in patients after the first-time elective percutaneous coronary intervention (PCI).

Methods: We enrolled 278 consecutive patients after first-time elective PCI with drug-eluting stents. We selected the patients with a history of acute coronary syndrome, advanced chronic kidney disease (eGFR <30 mL/min/1.73 m²), or a prior history of subsequent diabetes mellitus (HbA1c ≥7%). The end points consisted of acute coronary syndrome, coronary revascularization, and hospitalization due to heart failure within a year. The subjects were divided into two groups (event group [EV, n=49] and non-event group [NEV, n=229]). We measured the levels of fasting blood glucose (FBS), hemoglobin A1c (HbA1c) and 1,5-AG just before PCI and at the follow-up angiography. We assessed the relationship between glycemic markers and cardiovascular events in patients after the first-time elective PCI.

Results: No significant differences in baseline clinical characteristics, including FBS, HbA1c, and 1,5-AG, were observed between the two groups. At follow-up, serum levels of 1,5-AG (14.2±6.9 μg/mL vs 16.5±7.3 μg/mL, P<0.05), but not HbA1c (6.1±0.7% vs 6.1±0.7%, P=0.86) at the follow-up were significantly lower in the EV group than in the NEV group. After adjusting for confounding factors including age, gender, creatinine, and C-reactive protein, 1,5-AG level was an independent risk factor for cardiovascular events (OR 0.95, P<0.04).

Conclusion: Low 1,5-AG levels were associated with cardiovascular events after first-time elective PCI. These data suggest that postprandial hyperglycemia and lower 1,5-AG are important risk factors for adverse clinical events after first-time elective PCI.

P3676 | BEDSIDE
Exercise intolerance in elderly asymptomatic type 2 diabetes: left ventricular dysfunction, diabetes control, therapy or insulin resistance?
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Background: LV dysfunction is associated with impaired exercise capacity adverse outcome in type 2 diabetes mellitus (T2DM). We hypothesized that the mechanism of this was through insulin resistance (IR), which is linked to waist circumference (WC). We tested the hypothesis that WC is associated with 6-minute walk distance (6MWD) independently and incrementally to clinical, biochemical, therapeutic and echo variables in T2DM without overt heart failure.
Methods: From a community-based population, we enrolled 284 asymptomatic T2DM pts (71±4y, 55% men). Associations were sought between 6MWD and WC, diabetes duration, HbA1c, heath questionnaire (EQ5D) and echo results including global longitudinal strain (GLS). Nested multivariable linear regression models were created to assess increment value of 6MWD.

Results: Tertiles of increasing WC were associated with worsening 6MWD (1st:475±959m; 2nd:470±966m; 3rd:404±117m; p<0.001), and worsening GLS (1st: −18.1±2.5; 2nd: −17.4±2.7; 3rd: −16.7±2.9; p=0.01). Reduced exercise capacity was significantly associated with age (r=−0.30, p<0.001), gender (r=−0.14, p=0.02), BMI (r=−0.42, p<0.001), diabetes duration (r=−0.29, p=0.001), insulin use (r=−0.27, p=0.001), WC (r=−0.38, p<0.001), WC was independently associated with 6MWD after adjusting for other variables including BMI (model R²=0.45). The association of clinical variables (age, sex, EQ5D and BMI) was not independent of 6MWD (R²=0.45), diabetes duration (p=0.90), insulin use (p=0.72), or HbA1c (p=0.03), but significantly increased by adding WC (p=0.05).

Conclusions: Clinical, biochemical, therapeutic and echo information appear inferior to simple measurement of WC as a predictor of exercise capacity in asymptomatic T2DM.

P3677 | BEDSIDE
Effects of renin-angiotensin-aldosterone system blockers on contrast-induced nephropathy and its association with NGAL levels in diabetic patients undergoing coronary angiography

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Introduction: Contrast-induced nephropathy (CIN) is a common cause of hospital-acquired acute kidney injury (AKI). NGAL represents non-invasive, troponin-like biomarker for the early prediction of AKI in various clinical situations. In the present study, we aimed to investigate effects of renin-angiotensin system blockers (RASB) on the development of CIN in diabetic patients after coronary angiography.

Methods and results: We prospectively enrolled consecutive 80 patients undergoing elective coronary angiography. Serum creatinine (SCr) and plasma NGAL levels were measured at baseline and after intervention (SCR at 72 hour and NGAL at 4 hour). CIN was defined as an increase in Scr of ≥25% or 0.5 mg/dl from baseline within 48–72h after angiography.

Patients were divided into two arms based on the use of RASB: RASB(+) group and RASB(-) group. Drugs not stopped before the procedure, RASB(-) group. Drugs stopped 24h before the procedure.

CIN was observed more in common in RASB(+) group than in RASB(-) group, but statistically not significant (0.195% vs. 4.0% [p=0.30]). The amount of contrast agent volume and preventive treatment were independent predictors of CIN in multivariate analysis (OR=0.2, 95% CI: 0.1-1.0, p=0.03). The amount of contrast agent volume and preventive treatment were independent predictors of CIN in multivariate analysis (OR=0.2, 95% CI: 0.1-1.0, p=0.03). The amount of contrast agent volume and preventive treatment were independent predictors of CIN in multivariate analysis (OR=0.2, 95% CI: 0.1-1.0, p=0.03).

PLasma NGAL levels were not elevated at 4 hour post-procedure in CIN(+) patients versus CIN(-) patients (4839±3374 pg/ml versus 4304±1814 pg/ml, p=0.68) (see table).

P3678 | BEDSIDE
Concordance of glucose based and HbA1c based diagnoses of diabetes in patients with established coronary atherosclerosis: a comparison between men and women

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Background and introduction: Concordance between glucose based and HbA1c based diagnoses of diabetes mellitus is an essential parameter in interventional cardiology. Purpose: The purpose of our study was to investigate their concordance in men and in women with stable coronary artery disease (CAD).

Methods: We measured fasting glucose as well as HbA1c and performed standard oral glucose tolerance tests in a consecutive series of 711 patients, 513 men and 198 women, who had angiographically proven coronary artery disease (CAD) but not previously diagnosed diabetes. Based on glucose values, diabetes was diagnosed with a fasting plasma glucose (FPG) ≥126 mg/dl or a postchallenge glucose ≥200 mg/dl 2 hours after the oral glucose load; based on HbA1c values diabetes was diagnosed with an HbA1c ≥5.5%

Results: Among men, 33 had diabetes based on fasting or postchallenge glucose values, of whom 26 also had diabetes according to HbA1c criteria. Of the 480 men who did not have diabetes based on glucose values, 446 also did not have diabetes according to HbA1c criteria; among women, 3 had diabetes based on glucose values, of whom 2 also had diabetes according to the HbA1c criterion. Of the 195 women who did not have diabetes based on glucose values, 185 also did not have diabetes according to HbA1c criteria. Concordance of glucose and HbA1c criteria was similar in men and women (92% and 94%; p=0.335). Applying glucose criteria as a standard, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the HbA1c criterion for men were 78.8%, 92.9%, 43.3%, and 98.5%, respectively. For women, sensitivity, specificity, PPV and NPV of the HbA1c criterion were 66.7%, 94.9%, 16.7%, and 99.5%, respectively.

Conclusion: We conclude that concordance of glucose and HbA1c criteria among patients with stable CAD is high and is similar in men and women with CAD. However, for both sexes the sensitivity of the HbA1c criterion is poor in this patient population.

P3680 | BEDSIDE
Role of interleukin-6 in the visual impairment of diabetic patients

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Background: Diabetic Retinopathy (DR) is a complication of diabetes mellitus leading to deterioration of vision. Inflammatory cytokines are key players in the pathophysiology of arteriosclerotic disease.

Purpose: To investigate the association of inflammatory status with visual acuity in subjects with diabetes mellitus.

Methods: We enrolled 100 consecutive subjects with diabetes mellitus. Patients were divided in those with DR (53 subjects, mean age 68±9) and those with no evidence of DR (NDR) (mean age 66±7). The diagnosis of DR was made by ophthalmologist. A BCVA less than 0.8 was considered as severely impaired. C reactive protein and interleukin-6 (IL-6) were measured as well established inflammatory markers.

Results: Although there were no significant differences in baseline characteristics, patients with DR compared to NDR patients had increased levels of IL-6 [2.24 (1.33–3.99)pg/ml vs. 1.51 (0.96–3.05)pg/ml, p=0.03] and worsed BCVA [0.8 (0.92–
During 2001–2002, 1514 men and 1528 women (8.9%) compared to those with a history of PDE5i use (5.2%; P=0.021). In a population of men with T2DM, on-demand use of PDE5is was compared to those without such a prescription. This reduction in risk remained statistically significant after adjusting for age, gender, BMI, smoking status and use of a statin (HR 0.62 (0.47–0.83), p=0.001). Among men with a history of AMI, the risk of death was significantly lower in the group of men who took PDE5is (2.6% (95% CI: 0.91–7.38)) compared to those without (6.4% (95% CI: 4.54–8.92)).

Results: Patients with DR have significantly impaired visual acuity which is associated with systemic inflammatory status. These findings highlight the significant role of inflammation in the progression of diabetic complications and provide therapeutic implications which merit further study.

### P3681 | BEDSIDE

**Metabolic syndrome and the contributory predictive role of inflammatory or renal markers on cardiovascular disease: 10 year (2001-2011) follow-up of the ATTICA Study**


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**Background and purpose:** To evaluate the influence of metabolic syndrome (MS) and the contributory predictive role of inflammatory or renal markers on cardiovascular disease (CVD) incidence.

**Methods:** 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD was defined according to WHO-ICD-10 criteria. MS was defined using three definitions, provided by the National Cholesterol Education Program Adult Treatment Panel III (revised NCEP ATP III definition), the International Diabetes Federation (IDF) or the Harmonized definition. Furthermore, the contributory predictive role of C-reactive protein (CRP), interleukin-6 (IL-6), uric acid and estimated glomerular filtration rate, in addition to MS presence, regarding CVD incidence, was evaluated.

**Results:** History of MS according to the revised NCEP ATP III definition was positively associated with CVD, after adjusting for potential confounding factors: age, sex, physical activity, smoking and eating habits, using the MedDietScore (OR: 1.83, 95% CI: 1.24–2.72). CRP and IL-6, and to a lesser extent uric acid, were independently associated with altered mortality.

**Conclusion:** The role of inflammatory and renal markers in the incidence of CVD seems to be significant and merits further study.

### P3683 | BEDSIDE

**Phosphodiesterase type-5 inhibitor use in type 2 diabetes is associated with a reduction in all cause mortality in patients with coronary artery disease**

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**Objectives:** Phosphodiesterase type 5 inhibitors (PDE5is) are cardioprotective in animal models of acute myocardial infarction (MI). We investigated whether on-demand PDE5i use (T2DM), with high attendant cardiovascular risk, was associated with altered mortality.

**Design:** Population based cohort study

**Setting:** The pseudonymised records of 5956 men (mean follow-up of 6.9 years) aged 40-89 years diagnosed with T2DM before January 2007 were identified from 42 GP practices in Cheshire, UK.

**Main outcome measures:** We used hazard ratios (HR) from Cox regression models to describe the association between PDE5i use and all cause mortality.

**Results:** A lower percentage of deaths (18% versus 25%) and mortality rates (26.7 (22.7–30.7) versus 37.0 (35.0–39.2) per 1000 person-years; P=0.001) as well as a significantly reduced risk of all-cause mortality from unadjusted Cox regressions [hazard ratio (HR) = 0.69 (95% confidence interval: 0.60, 0.79); P<0.0001], was observed among the 1.359 (22.8%) men prescribed a PDE5i, compared to those without such a prescription. This reduction in risk remained after adjusting for age, eGFR, smoking status, history of myocardial infarction, systolic blood pressure (per 5 mmHg), use of a statin, metformin, aspirin and beta-blockers (HR=0.83 (0.70–0.98); p=0.038) to an equaling a 17% reduction in risk of all-cause mortality.

**Conclusion:** The pattern of lower mortality (unadjusted HR=0.69, P<0.0001) was similar in those with a history of acute MI (25.7%, (49/191) versus 40.1% (337/840) deaths prior to 2007. The reported incidence of an acute myocardial infarction during 7 years follow-up was greater in those who were never prescribed PDE5i treatment (8.9%) compared to those with a history of PDE5i use (5.2%; P=0.001). In this sub-group, reduced risk of mortality remained after adjusting for age, smoking status and use of a statin (HR 0.62 (0.47–0.83), P=0.001).

**Conclusion:** Mobilization of endothelial progenitor cells after endovascular interventions in patients with type 2 diabetes mellitus

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**Aim:** To study mobilization of endothelial progenitor cells (EPC) in patients with type 2 diabetes mellitus (T2DM) after endovascular interventions on coronary and peripheral arteries.

**Methods:** We observed 50 patients (22 women), admitted for elective percutaneous coronary intervention (PCI) or endovascular revascularization of lower extremity, 27 patients with T2DM were included in group 1 (14 women, mean age 65±10 years), while 23 patients were included in group 2 (9 women, mean age 65±10 years). PCI was performed for stable angina. Endovascular revascularization of lower extremity was done for critical limb ischemia (CLI). In group 1 PCI was performed in 15 patients, endovascular limb revascularization in 12.
group 2 PCI was performed 12 patients, endovascular limb revascularization in 9. Levels of CD34 + VEGFR2 + CD45- cells and CD34 + CD133 + CD45- cells were determined by flow cytometry 1–2 days before endovascular intervention and 2–4 days after the surgery. Number of cells was expressed as a percentage of leukocytes.

Results: In non-diabetic patients levels of CD34 + VEGFR2 + CD45- cells has increased in 55.5% (0.009±0.004% and 0.014±0.004% before and after procedure, respectively; p<0.001), levels of CD34 + CD133 + CD45- cells has increased in 27.7% (0.01±0.010% and 0.02±0.007% before and after procedure, respectively; p=0.048). Levels of EPC in the peripheral blood of patients with T2DM before and after endovascular interventions did not significantly differ. We divided patients with T2DM into 2 subgroups: the 1st subgroup included 14 patients with HbA1c<7.5%; the 2nd subgroup included 13 patients with HbA1c≥7.5%. In the 1st subgroup the increase of CD34 + VEGFR2 + CD45- cells in 46.6% (p=0.01), and CD34 + CD133 + CD45- in 43.4% (p=0.006) were observed after endovascular intervention.

Conclusions: The study has shown that patients with T2DM had the alteration of EPC mobilization after endovascular interventions. In addition, the dynamics of EPC levels depended on the glycemic control. Thus, in the subgroup of patients with T2DM with good glycemic control (HbA1c<7.5%) the EPC levels were significantly higher after endovascular interventions.

P3686 | BEDSIDE

The optimal interval of screening to detect type2 diabetes for pre-diabetic patients with coronary artery disease

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Background: It has been recommended to adopt hemoglobin A1c (HbA1c) testing as one basis for identifying diabetes and pre-diabetes. We assessed the optimal interval of measuring HbA1c to detect new onset of type2 diabetes for pre-diabetic patients with coronary heart disease (CHD).

Methods: We retrospectively assessed a trend of HbA1c of 1049 Japanese pre-diabetic patients (5.7≤HbA1c<6.4%, age 65.9±10.9, male 860) who had undergone percutaneous coronary intervention or coronary artery bypass graft surgery from April 2001 to December 2013. Two groups were defined as the lower group (5.7≤HbA1c<5.9%) and the higher group (6.0≤HbA1c≤6.4%). We analyzed the number needed to diagnose (NND) by annual measuring of HbA1c for 632 patients as the lower group and 417 patients as the higher group. The optimal interval of screening was defined the estimated time for 10% of patients whose HbA1c rose up to 6.5% and over.

Results: The NND was 70.2 in the lower group and 5.63 in the higher group. The estimated optimal screening interval of HbA1c was 6 years in the lower group, whereas 6 months in the higher group.

Conclusion: Appropriate measurement of HbA1c is considered as a useful adjunct to prevent coronary disease in this challenging population. Metabolic follow-up is desirable in a potential high risk group (HbA1c 6.0≤HbA1c≤6.4%), whereas unnecessary investigation should be reconsidered in a relatively low risk group (5.7≤HbA1c≤5.9%) from the point of clinical benefits and cost-effectiveness.

P3687 | BEDSIDE

Comparisons of the outcomes of the two drug eluting stents in diabetic patients: abliminal biolimus-eluting biodegradable polymer stents and zotarolimus-eluting permanent polymer stents

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Background: Outcomes of treatment of small vessel lesion in diabetic patients are relatively unsuccessful with the first generation drug-eluting stents (DES). Second generation biodegradable polymer DES offer better for prognosis and might be favorable in diabetic patients compared with permanent polymer DES. We sought to compare the angiographic in-stent and in-segment late losses in patients with diabetes treated abluminal biolimus-eluting biodegradable polymer stents (BES) and zotarolimus-eluting permanent polymer stents (ZES).

Methods: This study is sub-study of OPTIMA-C study which compares abluminal biolimus-eluting biodegradable polymer stents and zotarolimus-eluting permanent polymer stents. 1200 patients were enrolled in prospective, double-randomized, open-label, multicenter trial. Among them, a total of 236 diabetic patients (1167 men, 64.8±9.6 years) who needed small vessel stenting were prospectively randomized into abluminal biolimus-eluting biodegradable polymer stent (Group I, n=117) or zotarolimus-eluting permanent polymer stent (Group II, n=119). Clinical outcomes of one year were investigated in both groups and all patients underwent follow-up coronary angiography (CAG).

Results: There was no difference between abluminal biolimus-eluting biodegradable polymer stent group and zotarolimus –eluting permanent polymer stent group in demographic data and baseline QCA data. In follow up CAG data, late loss of group I tends to lower than that of group II, however there was no statistical significance (0.17±0.33 mm vs 0.28±0.37mm). There was no in-stent restenosis and major adverse cardiac events (MACE) in both groups.

Conclusion: Both second generation DESs showed improved outcome in treating small vessel disease in diabetic patients. The safety and efficacy of abluminal biolimus-eluting biodegradable polymer stents were not inferior to those of zotarolimus-eluting permanent polymer stents. Although there was no statistical significance between the two groups, the late loss of abluminal biolimus-eluting biodegradable polymer stent tend to lower than that of zotarolimus-eluting permanent polymer stent in diabetic patients with stent diameter of less than 2.75 mm.
In terms of clinical performance, there was no significant difference in MACCE between the groups (Figure, panel A), although 2nd generation significantly reduced MI (Figure, panel B), and tended to reduce ST (Figure, panel C).

Conclusions: The use of 2nd generation DES was associated with similar efficacy profile and improvement in safety performance, with a marked reduction in MI occurrence.

P3691 | BEDSIDE
Serum vascular endothelial growth factor-C levels inversely associated with the risk of atherosclerotic cardiovascular events following drug-eluting stent implantation

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Background: Vascular endothelial growth factor-A (VEGF-A) is a central player in angiogenesis and is involved in the progression of atherosclerotic plaque. However, a previous report showed that circulating VEGF-A levels have only a minor impact on atherosclerosis. Vascular endothelial growth factor-C (VEGF-C), a homologue of VEGF-A, plays a key role in lymphangiogenesis. Recently, we demonstrated that VEGF-C is significantly associated with dyslipidemia and atherosclerosis. However, the relationship between VEGF-C levels and atherosclerotic cardiovascular events after drug-eluting stent (DES) implantation is unknown.

Methods and results: We performed a prospective cohort study involving a total of 443 patients (age, 71.7±9.0 [SD]; male, 73.8%; number of lesions, 1.6±0.8) who underwent successful DES implantation. Patients were recruited between January 2010 and October 2013, and were followed up over 3 years. The primary outcome was major adverse cardiac and cerebrovascular events (MACCE) defined as cardiovascular death and hospitalization due to acute coronary syndrome (ACS), stroke, and coronary vasularization. The median follow-up was 617 (interquartile range, 320–937) days. Pre-procedural serum levels of high-sensitivity C-reactive protein (hsCRP), VEGF-A, and VEGF-C were measured. During the follow-up period, MACCE developed in a total of 86 patients (19.9%). At baseline, there was no significant difference in the age, rate of male gender, and prevalence of risk factors, chronic kidney disease, and previous myocardial infarction and stroke between MACCE and non-MACCE groups. Serum levels of hsCRP and VEGF-A did not differ between the two groups. In contrast, those of VEGF-C were significantly lower in MACCE compared with non-MACCE group. Then, we performed Kaplan-Meier analyses. Patients were divided into two groups based on the median of each biomarker. Notably, low-VEGF-C (P=0.01 by log-rank test), but not high-hsCRP (P=0.6) or high-VEGF-A (P=0.5), was significantly associated with the risk of MACCE. Furthermore, multivariate Cox proportional hazards, including data on the age, sex, established risk factors, and VEGF-C levels, revealed that the VEGF-C level (hazard ratio [HR], 0.79 per 1 SD increase; 95% confidence interval [CI], 0.62–0.99; P=0.04) was an inverse and independent predictor of MACCE.

Conclusions: A low VEGF-C value may serve as a predictive marker of atherosclerotic cardiovascular events after DES implantation.
P3692 | BEDSIDE
Improvement of left ventricular function assessment by global longitudinal strain after successful percutaneous coronary intervention for chronic total occlusions
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Background: Little is known of the potential effects of successful revascularization of chronic total occlusions (CTO) on left ventricular (LV) function. LV global longitudinal strain (GLS) is a more sensitive measure of LV mechanics than LV ejection fraction (EF). GLS can be assessed with two-dimensional speckle-tracking echocardiography (2DSTE) and is significantly related to long-term clinical outcome in patients with chronic ischemic heart disease.

Objective: This study was conducted to investigate the impact of revascularization of CTO on LV function using LV GLS.

Methods: A total of 70 patients (65±8.9 years, 59 males, LVEF 52±12%) with CTO who underwent percutaneous coronary intervention (PCI) were included in this study. Echocardiography was performed before the procedure and 9 months after the procedure with conventional assessment including LV end-diastolic and end-systolic volume (LVEDV, LVESV), LVEF, ratio of early transmitral flow to atrial contraction (E/A ratio), deceleration time (DcT), and with 2DSTE analysis of GLS.

Results: Successful PCI (TIMI 3 flow) was obtained in 60 patients (86%). There were no stent thromboses during follow-up. All patients showed relaxation abnormal pattern assessed by E/A ratio and DcT. GLS showed a significant improvement for 9 months after successful PCI (Δ=+2.0±2.8%, P<0.01), whereas in failed PCI group did not change significantly (Δ=−0.9±4.0%, P=0.48). GLS is greater in successful PCI group than failed group (p<0.05). LVEF, LVEDV and LVESV did not change during follow-up in both successful and failed groups.

Conclusion: Successful PCI for CTO improves left ventricular function assessed by LV GLS. This improvement may be associated with the long-term beneficial effect of PCI for CTO lesions.

P3693 | BEDSIDE
Timing, patterns and long term prognosis of recurrent myocardial infarction and coronary angioplasty - stent thrombosis versus non-stent-related reinfarction
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Background: In patients recovering from a ST-segment elevation myocardial infarction (STEMI), it is not clear if the negative impact of stent thrombosis (ST) is different from a non-stent-related recurrent myocardial infarction (NSRMI). This study sought to assess the long term incidence and prognostic impact of recurrent myocardial infarction (MI) after percutaneous coronary intervention (PCI) for STEMI by comparing outcomes of ST versus NSRMI.

Methods and results: From 2001 to 2007, 1025 consecutive patients undergoing PCI for STEMI were prospectively followed for at least 5 years. Patients with ST, NSRMI and those free from recurrent MI were compared regarding mortality and occurrence of subsequent major adverse cardiovascular events (MACCE). Definite or probable ST occurred in 54 patients (5.3%) and NSRMI occurred in 135 patients (13.2%). Occurrence of subsequent MACCE at end of follow up were not significantly different for patients with ST or NSRMI (HR 0.843 CI 95% [0.538−1.320] but were significantly lower for patients free from any recurrent MI (both log-rank p<0.001). However, all-cause death did not differ between the three groups (27.8 vs 28.7 vs 23.0%). Compared to NSRMI occurring in the first 30 days after PCI for STEMI, early ST was associated with increased risk for all-cause death (HR 5.128 CI 95% [1.40−18.5], p=0.013) but this association did not persist for recurrent MI occurring in the late (HR 0.50 CI 95% [0.17−1.49]) or very late (HR 0.14 CI 95% [0.01−1.88], p=0.058) periods.

Conclusion: Long term incidence of recurrent MI after PCI for SYETIEMI was 18.4%, one third of which due to stent thrombosis. Although in the early recovery period ST was associated with a significant increase in adverse events, MACCE and all-cause mortality rates at long term were comparable to non-stent-related recurrent MI.

P3694 | BEDSIDE
Influence of side branch predilation on long-term follow-up in patients with bifurcation lesions treated by provisional stenting
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Introduction: Predilation of the side branch before main vessel stent implantation is considered standard practice in the context of provisional stenting has generated mixed controversies.

Objective: The aim of our study was to compare the long-term follow-up of patients with and without side branch predilation before provisional stenting.

Methods: From February 2009 to November 2012, 372 patients with true coronary bifurcation lesions (side branch involvement) were randomised to either predilation of side branch (n=187) or no predilation (n=185) before main vessel stent implantation. Patients were monitored by telephone calls and scheduled visits in the outpatient clinic yearly during five years. Major cardiac events (MACE) were defined as cardiac death, myocardial infarction, and target lesion revascularisation.

Results: There were no significant differences between the patient groups regarding the baseline clinical, angiographic or procedural characteristics. After main vessel stent implantation the TIMI flow of the side branch was significantly higher in the patients with side branch predilation. Sixty patients (32%) from the side branch predilation group presented mild side branch residual stenosis and did not require any additional treatment. The side branch stenting rate was 4% in the predilation group and 3% in the no predilation group patients. In hospital and one-month follow-up MACE were similar between groups (2.1% vs 3.7%, p=ns). The overall MACE rate at 42 years follow-up was 9%. Mortality from cardiac causes occurred in 4 patients (2%) from the predilation group and in 4 patients (2%) from the no predilation group. Target lesion revascularisation was required in 16 patients (9%) from the predilation group (4%) and 9 from the no predilation group (5%). At 4-year follow-up, there were no significant differences in the Kaplan Meier event-free probability between groups (91% in the predilation group vs 86% in the no predilation group patients, p=ns).

Conclusions: Predilation of the side branch improved the immediate results and simplified the procedure of the provisional T stenting. However, this strategy had no influence on the long term clinical follow-up of these patients.

P3695 | BENCH
Drug eluting stent versus bare metal stent in saphenous vein graft lesions: a comprehensive meta-analysis of 14,000 patients
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Introduction: Drug eluting stents (DES) have been shown to significantly reduce the rate of target lesion revascularization in native coronary arteries compared to bare metal stents (BMS). However, there have been conflicting results use of DES in saphenous vein graft (SVG) lesions. Therefore, we aimed to investigate the risk of death, re-infraction (re-MI), target lesion revascularization (TLR) and/or target vessel revascularization (TVR), stent thrombosis (ST) and MACE compared to BMS in SVG lesions.

Methods: We searched PubMed and Cochran Library from January 2003 to December 2014. We extracted outcomes such as all-cause mortality, re-MI, TVR/TLR, ST and MACE. Because majority of trials were non-RCT, we pooled all trials data to analyze end-points. Additionally, independent analyses were separately conducted in randomized studies.

Results: We included 4 RCTs and 35 non-RCTs (a total 13958 patients, 6436 patients in DES arm and 7522 patients in BMS arm). In the pooled population, use of DES were significantly associated with lower risk of death (11% vs 14%, RR=1.282 (1.103−1.489) and p=0.001), re-MI (10.2% vs 11.7%, RR=1.135 (1.099−1.290) and p=0.051), TVR/TLR (15.1% vs 18.8%, RR=1.165 (1.023−1.326) and p=0.021 and 7.8% vs 13.4%, RR=1.535 (1.213−1.944) and p=0.001, respectively), and MACE (23.8% vs 30.3%, RR=1.272 (1.153−1.404) and p<0.001). The risk of ST was similar between DES and BMS (1.3% vs 1.9%, RR=1.282 (1.103−1.489) and p=0.001). Specifically, in RCTs, the risk of death (RR=0.660 (0.179−2.436) and p=0.533), re-MI (RR=1.149 (0.520−2.534) and p=0.732), ST (RR=1.346 (0.625−2.194) and p=0.234) and MACE (RR=1.346 (0.825−2.194) and p=0.234) were similar. However, use of DES were significantly associated with lower TVR/TLR (RR for TVR is 1.452 (1.048−2.012) and p=0.025 and for TLR is 1.393 (1.053−3.572) and p=0.034).

Conclusion: Our meta-analysis results showed that use of DES might improve cardiovascular outcomes compared to BMS in SVG lesions.
P3696 | BEDSIDE

The safety and efficacy of ultra-long 2nd generation drug eluting stent implantation

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Objectives: This study investigated the safety and prognosis of ultra-long second DES (UL-2nd DES) implantation in real-world practice.

Background: Long stenting is a widely known predictor of stent thrombosis (ST) or target lesion revascularization (TLR) in first-generation drug-eluting stents (DES).

Methods: Participants were 1,669 patients (2,763 lesions) who had undergone successful 2nd DES implantation; they were assigned to one of three groups: ultra-long second DES (UL-2nd DES: >50 mm, 168 patients, 259 lesions), long 2nd DES (L-DES: 20–50 mm, 758 patients, 1,212 lesions), and short 2nd DES (S-DES: <20 mm, 745 patients, 1,292 lesions). The primary endpoint was TLR, and secondary endpoints were ST, cardiac death, and major adverse cardiac events (MACE).

Results: Patient characteristics, including dual antiplatelet therapy (DAPT) duration, were similar across groups. Target lesion characteristics in the UL-DES group showed higher right coronary artery (49.0% in UL-DES, 27.9% in L-DES, 31.7% in S-DES, p<0.001) and chronic total occlusion lesion (39.7% in UL-DES, 9.4% in L-DES, 2.9% in S-DES, p<0.001) rates. TLR rates (23.1±13.2 months) were similar across UL-DES compared to the UL-DES group relative to other groups during follow-up (UL-DES 19.5% vs L-DES 12.4% vs S-DES 10.3%, p<0.001). TLR rate was similar between S-DES and L-DES. The incidence of ST was similar across groups. MACE was significantly higher in the UL-DES group relative to other groups due to higher TLR rates (UL-DES 41.5% vs L-DES 27% vs S-DES 26.4%, p=0.01). In a Cox proportional hazard model, hemodialysis (adjusted HR: 2.53, 95% CI: 1.70–3.67, p<0.001) and total stent length of >50 mm (adjusted HR: 1.67, 95% CI: 1.07–2.55, p=0.02) were independent predictors of TLR.

Conclusions: Ultra-long DES implantation was associated with higher TLR rates but did not increase ST, while long DES implantation up to 50 mm was safe and acceptable.

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P3697 | BEDSIDE

Growth differentiation factor-15 predicts bleedings in patients with STEMI after PCI

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Background: Growth differentiation factor 15 (GDF-15), a stress-responsive member of the transforming growth factor beta cytokine superfamily, has emerged as a biomarker of recurrent cardiovascular events in coronary heart disease.

Purpose: The aim of this study was to determine the predictive value of GDF-15 on major and minor bleedings in patients with STEMI after percutaneous coronary intervention (PCI).

Methods: Between January 2013 and October 2013, a total of 332 consecutive patients with STEMI who received an uneventful PCI and were exposed to standard dual antiplatelet therapy were enrolled in the single-center registry. All the enrolled patients received measurement of GDF-15 level on day 2 of PCI. The primary clinical safety end point was the incidence of major bleedings and unplanned target vessel revascularization. The incidence of major bleedings defined according to the Bleeding Academic Research Consortium (BARC) criteria, including type 3 and 5 in the analysis. The follow-up period was 12 months.

Results: Overall, 7 (2.1%) ischemic events occurred and 10 (3.0%) major bleedings occurred. Plasma GDF-15 level was significantly higher in patients with major bleedings, compared to patients with ischemic events or no events (2563.4 vs. 1822.8 vs 1007.2 ng/L, p<0.001). By receiver operating characteristic curve analysis, plasma GDF-15>2068.1ng/L had a predictive value of major bleedings with an area under the curve = 0.827 (95% CI 0.744–0.865, p<0.001). Binary logistic regression analysis identified log GDF-15 (OR 3.77, p<0.004) as a significant independent predictor of major bleedings after adjustment of traditional clinical bleeding risk factors.

Conclusions: GDF-15 is a strong predictor of major bleedings in patients with STEMI after PCI.

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P3698 | BEDSIDE

The prognostic impact of variation in left ventricular ejection fraction following elective percutaneous coronary intervention


Introduction: There is paucity of data about the impact of elective percutaneous coronary intervention (PCI) on left ventricular function (LVEF) and the prognostic implications of changes in LVEF on cardiac prognosis.

Purpose: To explore the effect of elective PCI on LVEF and to estimate the prognostic impact of LVEF rise or fall following PCI upon patients with coronary artery disease.

Methods: We included consecutive patients who underwent elective PCI in our institution between 2004 and 2013 who were evaluated with echocardiography before and after the procedure. Patients were grouped in respect to baseline LVEF [preserved (>50%), moderately impaired (30–50%), and poor (<30%)]. 1-year and 5-year hazard ratio (HR) for all-cause mortality and myocardial infarction (MI) were calculated for baseline LVEF groups and in respect to LVEF variation between baseline and repeat examinations.

Results: A total of 974 patients were included, of whom 571 (58.7%) with preserved LVEF, 320 (32.9%) with moderately reduced LVEF, and 83 (8.5%) with poor LVEF. A repeat echocardiogram was performed at a median interval of 168 days following PCI. Decline to impaired LVEF following PCI occurred in 13% of patients with baseline preserved LVEF and was associated with an increased 1-year risk for death (HR: 2.63; 95% CI: 1.18–5.90; p<0.001) and MI (HR: 4.91; 95% CI: 2.01–11.98; p<0.001) and an increased 5-year risk for death (HR: 2.91; 95% CI: 1.75–4.83; p<0.001) and MI (HR: 2.73; 95% CI: 1.29–5.80; p<0.001). Recovery to preserved LVEF occurred in 22% of patients with baseline impaired LVEF and was associated with a decreased 5-year risk for death (HR: 0.47; 95% CI: 0.23–0.95; p=0.036).

Conclusions: LVEF changes following elective PCI are common. Long term outcomes are associated with both pre and post procedural LVEF.

P3699 | BEDSIDE

Prognostic significance of whole blood viscosity in patients with ST elevation myocardial infarction undergoing primary coronary intervention

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Introduction: Whole blood viscosity (WBV), as the major determinant of endothelial shear stress (ESS), has a strong relationship between cardiovascular (CV) diseases and risk factors. We aimed to investigate the association of WBV with in-hospital and long-term outcomes in STEMI patient population undergoing primary PCI.

Methods: 2663 consecutive patients admitted to hospital with acute STEMI and underwent PCI between 2010 and 2015 were prospectively screened. The mean follow-up were 36.4 months.

Results: During the in-hospital period, MACE, the prevalence of stent thrombosis, and nonfatal major bleeding rise or fall following PCI upon patients with coronary artery disease.
bosis, non-fatal MI and CV mortality were higher in ascending order of WBV tertiles at LSR (p<0.001, p=0.005, p=0.003 and p=0.013 respectively) and at HSR (p<0.001, p=0.012, p=0.005 and p=0.004 respectively). A similar incremental trend were observed in long-term MACE, the determinant of stent thrombosis, non-fatal MI and CV mortality for WBV tertiles at LSR (p<0.001, p=0.001, p=0.029 and p=0.006) and at HSR (p<0.001, p=0.001, p=0.008 and p=0.003 respectively). In multivariate analysis, WBV at LSR (OR: 1.236 95% CI: 1.181–1.286 p<0.009) and at HSR (p<0.001) were demonstrated as independent predictors of in-hospital MACE. WBV at LSR (OR: 1.195 95% CI: 1.181–1.266 p<0.001) were independent predictors for long-term MACE Kaplan–Meier analysis pointed out the higher occurrence of MACE in third WBV tertiles compared with other tertiles.

**Conclusion:** Not only as the determinant of ESS but also a contributor to established risk factors, WBV seems to an important prognostic indicator of CV adverse events and mortality. In conjunction with other markers, WBV may utilize the risk stratification in STEMI patients and tailoring the individual preventive therapy.

**P3700 | BEDSIDE**

**Impact of successful revascularization of chronic total occlusion on long-term clinical outcome: comparison of clinical factors between successful and failed procedures**

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**Background:** The epoch-making techniques for percutaneous coronary intervention (PCI) of chronic total occlusions (CTO) have contributed to the improved initial success of PCI of CTO lesions (CTO-PCI); however, there have been sporadic reports regarding the benefit of the successful revascularization of CTO on long-term mortality.

**Purpose:** The purpose of this study was to speculate the effect of CTO-PCI on the long-term mortality of CTO patients.

**Methods:** Of all cases of PCI performed in our hospital between 2006 and 2013, CTO-PCIs were extracted and classified into two groups: PCI success (n=656 patients) and PCI failure (n=89 patients). Succeeded on 2nd attempt in the failure group and CTO-PCIs to any branches in both groups were excluded. Survival was retraceable by a telephone interview or consultation history in the outpatient clinic. Moreover, the clinical factors affecting the long-term clinical outcome were collected retrospectively and compared between the two groups.

**Results:** Overall initial success rate of CTO-PCI was 88.1%. Kaplan–Meier plot with log rank analysis shows cumulative death was significantly lower in the success group than in the failure group (p<0.006; average follow-up duration; success group vs. failure group = 1531.3±33.5 vs. 1565.3±97.5 days, P=0.7). Moreover, the clinical factors affecting the long-term clinical outcome were collected retrospectively and compared between the two groups.

**Conclusions:** This study suggests that the successful revascularization of CTO improves not only long-term mortality, but also quality of life of CTO patients.

**P3701 | BEDSIDE**

**Clinical outcome of paclitaxel-coated balloon angioplasty for the treatment of coronary in-stent restenosis in hemodialysis patients**

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**Background:** Paclitaxel-coated balloon (PCB) angioplasty was superior to uncoated balloon angiography for the treatment of in-stent restenosis (ISR) after bare-metal stents and drug-eluting stents implantation. However, it remains unclear whether PCB is effective for the treatment of ISR in hemodialysis (HD) patients.

**Purpose:** The purpose of this study was to assess the clinical outcome of PCB angioplasty for ISR in HD patients.

**Methods:** Between February and August 2014, a total of 122 patients with 129 ISR lesions underwent PCB angioplasty. According to the presence of HD, the patients were divided into the 2 groups: HD group (n=29) and non-HD group (n=93).

The primary endpoint was the cumulative incidence of major adverse cardiac events (MACE) within 6 months. MACE was defined as a composite of cardiac death, myocardial infarction (MI), target lesion revascularization (TLR).

**Results:** There was no significant difference in baseline patient characteristics between the 2 groups except for renal function. At 6-month, the cumulative incidence of MACE was significantly higher in HD group than in non-HD group (35.5% vs. 3.2%, p<0.001, mainly driven by higher rate of TLR (33.2% vs. 2.2%, p<0.001). No significant difference in the cumulative incidence of cardiac death was found between both groups (3.5% vs. 1.1%, p=0.37), whereas the cumulative incidence of MI tended to be higher in HD group than non-HD group (0.4% vs. 0.0%, p=0.06).

**Conclusions:** PCB angioplasty is less effective for the treatment of ISR in HD patients as compared with non-HD patients.

**P3702 | BEDSIDE**

**Very long-term clinical outcomes after sirolimus-eluting stent implantation**

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**Aims:** Late adverse events such as very late stent thrombosis (VLST) or late target-lesion revascularization (TLR) after sirolimus-eluting stents (SES) implantation remain an important concern. However, there is little data regarding clinical outcome beyond 5 years after SES implantation. We sought to assess very long-term clinical outcome after SES implantation.

**Methods:** Between April 2004 and December 2006, a total of 794 patients with 978 lesions underwent percutaneous coronary intervention only with SES. We assessed the major adverse cardiac events, defined as all-cause death, myocardial infarction (MI), TLR, stent thrombosis (ST).

**Results:** During the median follow-up (8.2 years [IQR: 6.2–8.9 years]), cumulative incidence of MACE, all-cause death and MI were 44.7%, 28.5%, and 9.8%, respectively. Cumulative incidence of TLR was 25.3% (7.4% at 1 year, 14.6% at 5 years, and 22.9% at 8 years, respectively). Cumulative incidence of ST was 7.2% (0.3% at 30 days, 0.7% at 1 year, 2.1% at 5 years, and 3.8% at 8 years, respectively). The primary endpoint was the cumulative incidence of major adverse cardiac events (MACE), all-cause death and MI were 44.7%, 28.5%, and 9.8%, respectively. Cumulative incidence of TLR was 25.3% (7.4% at 1 year, 14.6% at 5 years, and 22.9% at 8 years, respectively). Cumulative incidence of ST was 7.2% (0.3% at 30 days, 0.7% at 1 year, 2.1% at 5 years, and 3.8% at 8 years, respectively). The primary endpoint was the cumulative incidence of major adverse cardiac events (MACE), all-cause death and MI were 44.7%, 28.5%, and 9.8%, respectively. Cumulative incidence of TLR was 25.3% (7.4% at 1 year, 14.6% at 5 years, and 22.9% at 8 years, respectively). Cumulative incidence of ST was 7.2% (0.3% at 30 days, 0.7% at 1 year, 2.1% at 5 years, and 3.8% at 8 years, respectively).

**Conclusions:** Late catch-up phenomenon regarding ST and TLR continued up to 8 years without attenuation. Careful clinical follow-up is required in patients treated with SES beyond 5 years.

**P3703 | BEDSIDE**

**Are there different outcomes following diffuse long lesion intervention between chronic total occlusion and non-chronic total occlusion lesions?**

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**Background:** The aim of the study is to investigate whether there are different clinical outcomes in diffuse long lesion of CTO patients (pts) versus non-CTO pts following successful percutaneous coronary intervention (PCI).

**Methods:** A total of 1081 consecutive pts underwent PCI who had diffuse long disease (≥30mm) were divided into two groups; CTO group: n=118 pts, Non-CTO group: n=963 pts. Six-month angiographic and 36-month clinical outcomes were compared between the two groups.

**Results:** The baseline clinical characteristics were similar between the two groups except prior MI, PTCA was more frequent, whereas female gender was less common in the CTO group. The baseline lesion characteristics were similar between the two groups except small vessel (≤2.25mm) and calcification were more frequent in the CTO group whereas bifurcation lesion was more frequent in the Non-CTO group. At six months angiographic outcomes, the CTO group showed higher incidence of binary restenosis, higher mean diameter stenosis (DS) and lower minimal luminal diameter (MLD). This result translated into higher rate of repeat PCI including higher target lesion revascularization (TLR) and higher trend of target vessel revascularization (TVR) up to 3 years despite of similar individual hard endpoints (table). In multivariate analysis, diffuse long lesion in CTO was not an independent predictor for repeat PCI and TLR. However,
small vessel stenting (<2.25 mm) was a predictor for repeat PCI (OR=1.81, CI: 1.0–3.39, p < 0.05).

Conclusion: The safety profile, and major clinical outcomes in diffuse long lesion of CTO vs. Non-CTO were similar following successful PCI except higher rate of repeat PCI and TLR in the CTO subgroup. Long-term randomized clinical trials with larger study population will be necessary to elucidate the final conclusion.

P3704 | BEDSIDE
Bioresorbable vascular scaffolding for the percutaneous treatment of long diffuse coronary lesions
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Methods and results: The mean age was 57±9 years. The clinical presentation was stable in 56 patients (24%) and acute coronary syndrome in 180 (76%); 56 patients were diabetics (24%). The mean length of the lesion was 32±13 mm and 42 were considered for BVS implantation after recanalization of a chronic total occlusion. The mean proximal reference diameter was 2.99±0.36 mm; 149 lesions received one single BVS (28 mm), 62 lesions were treated by overlapped multiple BVS and 25 by multiple non-overlapped BVS. The scaffolded length was 34±14 mm. In all cases the BVS was successfully implanted with (n=150; 63%) or without (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 patients (41%) due to late thrombosis (11 months after the procedure). A 6-month car-diac computed tomography scanner (CT) was performed in 88 patients evaluating implantation all the side branches (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 patients (41%) due to late thrombosis (11 months after the procedure). A 6-month cardiac computed tomography scanner (CT) was performed in 88 patients evaluating implantation all the side branches (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 patients (41%) due to late thrombosis (11 months after the procedure). A 6-month cardiac computed tomography scanner (CT) was performed in 88 patients evaluating implantation all the side branches (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 patients (41%) due to late thrombosis (11 months after the procedure).

Results: Two years follow-up was completed in 171 lesions (91.9%). The incidence of CTO vs. Non-CTO were similar following successful PCI except higher rate of repeat PCI and TLR. After adjustment of baseline lesion complexities, there was no sig-nificantly improved after inclusion of the EuroSCORE but not after inclusion of the remaining risk scores (Table).

Conclusion: In this large population of patients undergoing DES implantation for uLMA disease, among evaluated risk scores, EuroSCORE resulted to be the only independent predictor of mortality at three years follow-up.

P3706 | BEDSIDE
Two-year outcomes of successful recanalization for chronic total occlusion after antegrade and retrograde approach: propensity matched analysis
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Results: In this large population of patients undergoing DES implantation for uLMA disease, among evaluated risk scores, EuroSCORE resulted to be the only independent predictor of mortality at three years follow-up.

P3707 | BEDSIDE
Predictors of early and late bleeding events after drug-eluting stent implantation
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Background: Besides Syntax score (5xScore), risk scores incorporating anatomical and clinical data have been recently introduced, to further refine the selection of the most appropriate revascularization strategy. However, data regard-ing the prognostic value of these newer risk scores in the specific subset of PCI for unprotected left main coronary artery (uLMA) disease are relatively limited.

Purpose: To evaluate the long-term prognostic value of risk scores in the setting of drug-eluting stent (DES) implantation for uLMA disease.

Methods: The present report represents a patient-level pooled analysis of the ISAR LEFT MAIN and the ISAR LEFT MAIN 2 randomized clinical trials (1257 patients undergoing DES implantation for uLMA disease). The predictive accuracies of risk scores at 3 years was evaluated for the 5xScore, the Syntax Score II (SS-II), the EuroSCORE and the Global Risk Classification (GRC).

Results: At a mean follow-up of 3 years there were 160 deaths (12.7%). In the multivariable Cox regression analysis, EuroSCORE showed a strong indepen-dent predictive value (HR (95% CI): 1.89 (1.32–2.68) p < 0.001) while 5xScore (HR (95% CI): 1.06 (0.84–1.35) p = 0.62), SS-II (HR (95% CI): 1.19 (0.80–1.79) p = 0.39) and GRC (HR (95% CI): 1.19 (0.91–1.56) p = 0.21) didn’t result to be in-dependent predictors of mortality. The predictivity of a multivariable model was significantly improved after inclusion of the EuroSCORE but not after inclusion of the remaining risk scores (Table).

Conclusion: In this large population of patients undergoing DES implantation for uLMA disease, among evaluated risk scores, EuroSCORE resulted to be the only independent predictor of mortality at three years follow-up.
bleeding events were observed in 48 (2.8%) and 35 (2.2%) patients during follow-up duration (23.1±16.3 months). Bleeding events related with stent implantation were observed only in early bleeding events and other cause of bleeding events were similar between early and late bleeding events (p>0.67). The incidence of fatal bleeding defined as type 5 bleeding was similar between early and late bleeding events (3.3% vs 20%, p=0.12). Warfarin use, past history of GI were independent predictors of early bleeding events (adjusted HR: 3.93, 3.6, p<0.001, 0.005). All patients who used warfarin and suffered from early bleeding events kept dual antiplatelet therapy. Age >80, severe renal dysfunction, hypertension were independent predictors of late bleeding events (adjusted HR: 3.2, 5.1, 3.6, p<0.01, 0.001, 0.04).

Conclusion: Predictors of bleeding events after DES implantation differ depending on the time period. Triple antithrombotic therapy included highly risk of early bleeding events.

Acknowledgement/Funding: None

P3708 | BEDSIDE
Long-term clinical results after first generation drug-eluting stent implantation

Background: There are limited data about very long-term clinical outcomes after first generation drug-eluting stent implantation.

Purpose: The aim of this study is to compare the long-term clinical outcomes between sirolimus-eluting stent (SES) and Paclitaxel-eluting stent (PES).

Methods: A total of 3577 patients with 5955 lesions (SES: 4366 lesions vs. PES: 1589 lesions) were analyzed retrospectively to compare long-term (>5 years) clinical outcomes.

Results: The baseline characteristics were similar between the 2 groups. Although the incidence of target lesion revascularization (TLR) in SES group within 2 years was significantly lower, however, that after 2 years was significantly higher than PES group (figure). Finally, seven-year Kaplan-Meier curves of TLR demonstrated no significant difference (SES: 11.0% vs. PES: 12.1%, p=0.24). The incidence of percutaneous coronary intervention (PCI) in SES group within 5 years (IQR range: 1.2–4.6 years) was significantly higher than PES group (HR: 1.7, 95% confidence interval 1.5 to 1.9, p<0.001). The incidence of stent thrombosis was significantly lower in SES group than PES group (0.7% vs. 2.9%, p<0.001). Post-PCI TIMI 3 flow was achieved in 77.9% of SES patients and 68.5% of PES patients (p<0.0001) with corresponding lower rates of MACE (4.3% vs. 5.3%, p=0.039) and death (1.1% vs. 1.7%, p=0.026).

Conclusion: Late TLR and ST after SES implantation should be considered during long-term follow-up period.

Landmark analysis of TLR

P3709 | BEDSIDE
Clinical predictors of mortality following rotational atherectomy and stent implantation in high risk patients
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Background: Contemporary rotational atherectomy (RA) is mainly used to facilitate stenting in complex lesions. Outcomes involving RA and stenting have been complicated, yet high risk patients have not been adequately described.

Purpose: Our aim was to assess procedural success and determine clinical predictors of post-procedural mortality, following RA and stenting in high risk patients.

Methods: Data of 218 consecutive patients who underwent RA were evaluated in a prospective database. The primary end-point was the composite of angiographic success of the procedure and long term mortality. Secondary end-points were procedural success, consumption of the angioplasty equipment and peri-procedural major adverse events (MACE). The impact of the relevant angiographic and clinical characteristics on long term mortality were analyzed using uni- and multivariate Cox regression analysis.

Results: Mean age was 70±8.2 years, diabetes was present in 44%, chronic renal failure in 29%, Prior myocardial infarction and three vessel disease amounted to 42.2% and 32.6%, respectively. Altogether, 52.8% of patients underwent RA after a failed, non-RA intervention attempt and 30.7% of cases presented as acute coronary syndromes. Angiographic success was 100% and all patients received stents after RA. Peri-procedural MACE occurred in five patients (2.3%). Post-procedural death was investigated, with a mean follow-up of 36 months. Mortality amounted to 37.2%. Multivariate analysis revealed that left ventricular ejection fraction <50%, glomerular filtration rate <60 ml/min, cardiogenic shock and diabetes were the only independent mortality predictors.

Conclusion: We have found that RA and stenting is a feasible and viable option in elderly high-risk population, with exceptional procedural success and acceptable long-term results.

P3710 | BEDSIDE
Impact of angiographically visible stent malaposition (Peri-stent contrast staining: PSS) and stent fracture on five-year clinical outcome after drug-eluting stent implantation
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Background: While peri-stent contrast staining (PSS) is thought to represent angiographically-visible incomplete stent apposition, IVUS/CCT studies revealed that incompleteness of stent apposition plays a role in thrombus formation. However, previous studies have provided conflicting circumstantial evidence concerning the role of PSS in very late stent thrombosis (VLST). We investigated the prognostic significance of PSS in patients with sirolimus-eluting stents (SES).

Methods and results: Consecutive patients undergoing sirolimus-eluting stent implantation with follow-up angiography (n=807, 644 male, mean age 66.0 years) were studied. Stent fracture was defined as the significant disappearance of stent struts in the stent at follow-up angiography in comparison with the presence of stent struts immediately after stent implantation. The primary endpoint was major adverse cardiac events (MACE) defined as a composite of death, myocardial infarction, stent thrombosis, and target lesion revascularization. Twenty patients (2.48%) exhibited PSS at follow-up angiography. After a median of 5 years/3744 patient-years follow-up, 7 (35.0%) in the PSS group reached the primary endpoint versus 117 (14.9%) in the non-PSS group (P=0.013). Together with diabetes, renal failure, unstable angina, saphenous vein graft and longer total stent length, PSS independently predicted the primary endpoint (HR: 2.94, 95% confidence interval 1.36 to 6.35, P=0.008). Although stent fracture was more frequently found in PSS group than non-PSS group (20% vs 5.7%, P=0.008), stent fracture was not an independent predictor of MACE by multivariate analysis. PSS was also significantly associated with VLST, which occurred in 3 (15.0%) patients with PSS versus 13 (1.7%) in those without PSS (P=0.008).

Conclusion: While PSS is an uncommon but significant angiographic finding in patients treated with SES implantation that independently predicts MACE, stent fracture was not an independent predictor of MACE by multivariate analysis. Whilst PSS was also significantly associated with VLST, PSS should be recognized as a potential risk-marker for very late drug-eluting stent failure.

P3711 | BEDSIDE
Implications of pre-procedural TIMI flow in patients with acute coronary syndromes: undergoing percutaneous coronary intervention: A study of 21,024 patients from the London Heart Attack group

Introduction: Although the negative prognostic impact of reduced Thrombolysis In Myocardial Infarction (TIMI) flow before percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) has been relatively well described, whether this relationship holds in patients with acute coronary syndromes (ACS); unstable angina and non-STEMI is not well established.

Methods: We undertook an observational cohort study of 21,024 patients with ACS admitted with PCI between 2004 and 2011 at 8 tertiary cardiac centres across London, UK. Patient’s details including pre-procedural TIMI flow were recorded at the time of the procedure were recorded in separate Locale databases using the British Cardiac Intervention Society (BCIS) PCI dataset. Anonymous datasets from the 8 centres were merged for analysis. Outcome was assessed by in hospital major adverse cardiac events (MACE) and all-cause mortality. The primary end-point was all-cause mortality at a median follow-up of 3.0 years (95% confidence interval: 1.2–4.6 years).

Results: 10,929 Patients presenting with STEMI and 10,095 patients with NSTEMI/UA were treated by PCI. These patients were divided in 3 groups according to pre-procedural culprit vessel TIMI flow (TIMI 0/1, TIMI 2 and TIMI 3 flows). Patients undergoing PCI had higher rates of TIMI 0/1 flow compared to NSTEMI/UA patients (77.4% vs 12.6%, p<0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p<0.0001). Post-PCI TIMI 3 flow was achieved more often in patients within the TIMI 2 group compared to the other groups in both PCI and NSTEMI/UA patients. Kaplan-Meier analysis demonstrated in PCI patients that there was a statistically significant difference in mortality rates between the TIMI groups (26.3% TIMI 0/1
Canada; 2 Cardiac Services BC, Provincial Health Service Authority, Vancouver, BC. All PCI cases undertaken on elderly patients (age \( \geq 75 \)) following PCI in a large unselected "real world" population.

**Background:** More work needs to be undertaken to ensure that the increasing mortality in emergent initial fall in mortality for elderly patients presenting with STEMI who undergo PCI. However, clinical outcomes for the elderly emergent STEMI cohort improved in the first four years (1999–2002) with a reduction in 30-day mortality from 27.7% to 15.4%, followed by a gradual rise to 17.1% in 2010–2012. Similarly, 1-year mortality declined from 37.8% in 1999–2002 to 22.8% in 2003–2006, then gradually increased to 27.6% in 2010–2012.

**Results:** From a total of 8,659 PCI cases performed, 9,613 were undertaken on elderly patients. There was a significant rise in the proportion of the PCI cohort being elderly across the study period (6.8% to 15.6% of total from 1999 to 2013). Further, more, even within the cohort of elderly patients, there was a shift towards higher prevalence of patients aged 85 or older. 20.7% (n=1,988) of elderly patients presented with stable angina and 79.3% (n=7,625) presented with acute coronary syndrome of which 19% (n=1,454) were emergent ST-elevation myocardial infarction (STEMI).

In the elderly cohort undergoing PCI for stable angina, both 30 day (0.7%) mortality and 1-year mortality remained stable across the 14 year study period. However, clinical outcomes for the elderly emergent STEMI cohort improved in the first four years (1999–2002) with a reduction in 30-day mortality from 27.7% to 15.4%, followed by a gradual rise to 17.1% in 2010–2012. Similarly, 1-year mortality declined from 37.8% in 1999–2002 to 22.8% in 2003–2006, then gradually increased to 27.6% in 2010–2012.

Overall, transfer rates following PCI in the elderly cohort were approximately double that of those patients under 80 (5.6% vs 2.6%, p<0.0001) and was much higher in the elderly STEMI cohort throughout the study period (11.1% vs 6.8%, p<0.0001). In the setting of stable angina, transfer rates decreased from 3.5% in 1999–2002 to 0.5% in 2010–2012 (p=0.0032).

**Conclusions:** Using more than a decade of clinical data, we report a substantial initial fall in mortality for elderly patients presenting with STEMI who undergo emergent PCI, but with increased uptake there has been a gradual rise in mortality. Although these findings do not oppose the performance of PCI in the elderly, more work needs to be undertaken to ensure that the increasing mortality in emergent STEMI represents an appropriate increased application of PCI in this more complex population.

**P3712 | BEDSIDE**

**Long-term angiographic outcomes of recurrent restenosis in patients with drug-eluting stent implantation for in-stent restenosis of drug-eluting stent**


**Background:** Long-term angiographic outcomes of recurrent restenosis in patients treated with drug-eluting stent (DES) implantation for in-stent restenosis (ISR) of DES is little known.

**Methods:** From January 2004 to January 2013, 459 consecutive patients with 619 lesions underwent DES implantation for ISR of DES, in whom 8-month follow-up angiography (f/u CAG) was performed in 547 (88.3%) of the 619 lesions and 20-month f/u CAG was performed in 378 (65.7%) of the 441 lesions which were without target lesion revascularization (TLR) at 8-month f/u CAG.

**Results:** In the 547 lesions after 8-month f/u CAG, recurrent restenosis was documented in 138 (25.2%) lesions and TLR was performed in 106 (19.5%) lesions (acute gain, 1.79±0.68; late loss, 0.56±0.88). In the 378 lesions after 20-month f/u CAG, recurrent restenosis was documented in 70 (18.5%) lesions and TLR was performed in 33 (8.7%) lesions (acute gain, 1.80±0.80; late loss, 0.39±0.58). By multivariate analysis, non-focal type restenosis (odds ratio 2.87, 95% confidence interval, 1.67 to 4.90; p<0.001) was an independent predictor of recurrent restenosis.

**Conclusion:** Late recurrent restenosis can occur in patients treated with DES implantation for ISR of DES. When a non-focal type restenosis is documented, the lesion should be followed up long and carefully.

**P3714 | BEDSIDE**

**Long-term outcomes with 3rd versus 2nd generation coronary drug eluting stents - a meta-analysis**


**Background:** Durable polymer drug eluting stents (DES) technology has evolved since its inception in regards to strut size, polymer platforms, and drug elution. The 3rd and 2nd generation coronary DES have favorable outcomes when compared to 1st generation, however limited data exists on long-term outcomes between the 3rd and 2nd generation DES.

**Methods:** A systematic MEDLINE search included only direct comparison randomized controlled clinical trials of 3rd and 2nd generation DES up to February 12, 2015. Clinical endpoint of interest include: Myocardial infarction (MI), target vessel revascularization (TVR), target lesion failure (TLF), stent thrombosis (ST), all cause death and combined endpoint of MI, TVR, TLF, ST, and death (MACE). Six trials were included and odds ratio (OR) used to assessed effect size. A fixed and random effect model was used for calculated summary odds ratio using comprehensive meta-analysis statistical software version 2.0.

**Results:** Among 6 trials, there were a total of 6,363 patients with mean follow up of 26 months, mean stent length of 24.9±10.1 mm and a cumulative 1,863 combined events of MI, TVR, TLF, ST and death. There were no significant differences observed in the individual endpoints between 3rd and 2nd generation DES. The OR for the combined endpoint is depicted in figure 1.

**Conclusion:** Similar rates of MI, TVR, TLF, ST, and death were observed between 3rd and 2nd generation DES. Numerically lower rates of combined MACE favored 3rd generation DES, but did not reach statistical significance.

**P3715 | BEDSIDE**

**Impact of SYNTAX Score-II on very long-term mortality in STEMI patients undergoing primary PCI**

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**Background:** Recent studies have demonstrated the ability of SYNTAX score-II (SS-II) to stratify patients according to the risk of adverse outcomes after elective PCI.

**Purpose:** Our aim was to assess the capacity of SS-II to accurately predict very long-term mortality in patients with STEMI undergoing primary PCI.

**Methods:** We analyzed 534 primary PCI patients from a high-volume center, from the year 2009. SS-II was calculated based on the bedside algorithm for patients undergoing PCI. It included SYNTAX score (SXscore), age, sex, creatinine clearance, LVEF, left main disease, chronic obstructive pulmonary disease and peripheral vascular disease. SXscore was determined by scoring the culprit lesion just prior to stent implantation. Predictive accuracy was tested with c-statistic and the Hosmer-Lemeshow test. Kaplan-Meier curves for SS-II tertiles (p=0.0032) were compared to the log-rank test.

**Results:** Patients were divided into the tertiles of the calculated SS-II (SS-II-low) by stratifying patients according to the risk of adverse outcomes after elective PCI.

**Conclusion:** Similar rates of MI, TVR, TLF, ST, and death were observed between 3rd and 2nd generation DES. Numerically lower rates of combined MACE favored 3rd generation DES, but did not reach statistical significance.

**P3714 | BEDSIDE**

**Long-term outcomes with 3rd versus 2nd generation coronary drug eluting stents - a meta-analysis**


**Background:** Durable polymer drug eluting stents (DES) technology has evolved since its inception in regards to strut size, polymer platforms, and drug elution. The 3rd and 2nd generation coronary DES have favorable outcomes when compared to 1st generation, however limited data exists on long-term outcomes between the 3rd and 2nd generation DES.

**Methods:** A systematic MEDLINE search included only direct comparison randomized controlled clinical trials of 3rd and 2nd generation DES up to February 12, 2015. Clinical endpoint of interest include: Myocardial infarction (MI), target vessel revascularization (TVR), target lesion failure (TLF), stent thrombosis (ST), all cause death and combined endpoint of MI, TVR, TLF, ST, and death (MACE). Six trials were included and odds ratio (OR) used to assessed effect size. A fixed and random effect model was used for calculated summary odds ratio using comprehensive meta-analysis statistical software version 2.0.

**Results:** Among 6 trials, there were a total of 6,363 patients with mean follow up of 26 months, mean stent length of 24.9±10.1 mm and a cumulative 1,863 combined events of MI, TVR, TLF, ST and death. There were no significant differences observed in the individual endpoints between 3rd and 2nd generation DES. The OR for the combined endpoint is depicted in figure 1.

**Conclusion:** Similar rates of MI, TVR, TLF, ST, and death were observed between 3rd and 2nd generation DES. Numerically lower rates of combined MACE favored 3rd generation DES, but did not reach statistical significance.
We followed 353 consecutive patients aged ≥ 80 years hospitalized with ACS, 182 treated with PCI, 171 were not. In overall cohort (n=353) five-year all-cause mortality was 46.2% and 89.5% in the PCI and non-PCI subgroups respectively. In propensity matched cohort (n, 71+71) adjusted for 20 baseline variables, Kaplan-Meier survival curves and log rank test showed significantly improved survival (P=0.001). Cox regression analysis showed that PCI was associated with reduced long-term mortality in matched and overall cohort, (HR 0.5, 95% CI 0.2–0.9, P=0.020) and HR 0.4, 95% CI 0.2–0.5, P=0.020 respectively.

Conclusion: In octogenarians with ACS, PCI was associated with improved survival from all-cause death over five years of follow up.

Methods: We undertook a post-hoc analysis comparing patients undergoing LM/PLAD PCI, versus those undergoing PCI to other coronary segments. DAPT cessation was classified as physician-guided discontinuation, brief interruption, or discontinuation due non-compliance or bleeding. The primary efficacy endpoint was 2-year major adverse cardiovascular events (MACE; composite of cardiac death, myocardial infarction (MI) or definite/probable stent thrombosis). The primary safety endpoint was major bleeding as per the bleeding academic research consortium (BARC) definitions, BARC bleeding 3 or 5.

Results: Of the study population, 25.0% (n=1252) underwent LM/PLAD PCI, and 75.0%, (n=3766) underwent non-LM/PLAD PCI. While the groups were similar for age (mean, 63.9 years) and female gender (25.4%), patients undergoing LM/PLAD PCI had fewer comorbidities including current smoking, diabetes, prior MI or peripheral arterial disease compared to those undergoing non-LM/PLAD PCI. In contrast, multivessel disease and bifurcational disease was more common in the LM/PLAD group, as was use of 2nd generation drug eluting stents and implantation of multiple stents or longer stents (≥ 20mm). Patients in the LM/PLAD group also presented more often with stable angina rather than acute coronary syndrome. At 2 years, the rate of discontinuation was higher (43.3% vs 39.4%, p=0.01) in the LM/PLAD group while rates of disruption (12.7% v 14.8%, p=0.06) and interruption (9.7% vs. 10.7%; p=0.30) were not significantly different. Two-year Kaplan Meier estimates of MACE (6.4% v 6.6%, p=0.82) and BARC major bleeding (4.1% v 4.1%; p=0.98) were similar between these groups.

Conclusion: In LM/PLAD registry, patients with LM/PLAD PCI presented with fewer clinical comorbidities but anatomically more complex disease. Despite implantation of more stents and longer stent lengths, DAPT discontinuation was higher in such patients without an increased risk of adverse outcomes at 2 years.
after BMS+DCB. Therefore, an additional 2-year clinical follow-up (flu) was attempted in addition to the invasive 6-month flu.

Methods: The patient flow-chart is given in Fig. 1. Flu was recorded by standardized interviews.

Results: Major adverse cardiac events (MACE: myocardial infarction, revascularisation, death) at 6 and 24 months were rare in both device groups (Table 1). No stent thrombosis occurred.

Table 1. MACE at 6- and 24 months

<table>
<thead>
<tr>
<th></th>
<th>BMS+DCB (6 months / 2 years)</th>
<th>EES (6 months / 2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (cardiac; non-cardiac)</td>
<td>0; 2 (3.7%) / 0; 2 (3.7%)</td>
<td>0; 0 / 0; 0</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 / 1 (1.9%) / 0 / 0</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>3 (5.6%) / 3 (5.6%) / 5 (9.8%) / 6 (11.8%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
<tr>
<td>Target lesion</td>
<td>1 (1.9%) / 2 (3.7%) / 5 (9.8%) / 6 (11.8%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
<tr>
<td>Target vessel</td>
<td>1 (1.9%) / 2 (3.7%) / 5 (9.8%) / 6 (11.8%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
<tr>
<td>Non target vessel</td>
<td>1 (1.9%) / 1 (1.9%) / 3 (5.9%) / 4 (7.8%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
<tr>
<td>All MACE</td>
<td>5 (9.8%) / 6 (11.1%) / 5 (9.8%) / 7 (13.7%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
</tbody>
</table>

*p<0.05 between device groups. *p<0.05 between 6- and 24 months.

Figure 1. Study population

Conclusions: The combined BMS+DCB treatment with 6-month DAPT showed long-term cardiovascular outcomes comparable to EES.

P3721 | BEDSIDE

Gender differences in 5-year clinical outcomes following percutaneous coronary intervention

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Background: Several studies have reported that clinical outcome after percutaneous coronary intervention (PCI) was worse in female compared with male. However, many of these studies evaluated short-term clinical outcomes. To date, gender difference in long-term clinical outcomes after PCI has not been elucidated.

Methods: We analyzed data of patients following PCI in Juntendo University (Tokyo, Japan) from 1984 to 2008. The patients were divided into two groups according to gender. Primary endpoint was a composite of 5-year all-cause mortality and acute coronary syndrome.

Results: A total of 3531 patients were examined (Female: 605 and Male: 2926). Mean age, a prevalence of hypertension, dyslipidemia and a percentage of ACS at presentation were higher in the female group. Kaplan-Meier estimation for 5-year all-cause death and acute coronary syndrome was superior to the male group (Fig. 1). Univariable Cox regression analysis for cardiovascular events in the whole population revealed that male gender was associated with reduction in the long-term clinical outcomes (HR 0.79, 95% CI 0.65–0.97, P<0.03). After controlling confounding factors, gender was not associated with the long-term clinical outcomes. Multivariable Cox regression analysis showed that higher age and MVD were associated with worse clinical outcomes, while BMI, Hb, eGFR and LVEF were inversely associated with the incidence of the long-term clinical outcomes.

Conclusions: Gender difference in 5-year all-cause mortality and ACS was not observed in our study population following PCI.

P3722 | BEDSIDE

Impact of first generation drug-eluting stents on the long-term clinical results compared with bare-metal stent


Background: Short-term clinical outcomes after first generation drug-eluting stent (DES) implantation were dramatically improved compared with those after bare-metal stent (BMS) implantation. However, very long-term clinical outcomes have not been fully estimated.

Purpose: The aim of this study is to compare the long-term clinical outcomes between first generation DES and BMS.

Methods: A total of 6007 patients with 9566 lesions (DES: 5955 lesions vs. BMS: 3611 lesions) were analyzed retrospectively to compare long-term (≥5 years) clinical outcomes.

Results: Ten-year Kaplan-Meier curves demonstrated that target lesion revascularization (TLR) rate was significantly lower in DES group (DES: 11.4% vs. BMS: 19.4%, p<0.01). On the other hand, although TLR rate in DES group within 2 years was significantly lower, that after 2 years was significantly higher than BMS group (figure). The rate of stent thrombosis (ST) in DES group continued to increase after 2 years follow-up and demonstrated a higher rate compared with BMS group during 10 years follow-up period (0.76% vs. 0.22%, p<0.01).

Conclusions: Gender difference in 5-year all-cause mortality and ACS was not observed in our study population following PCI.
Introduction: Paravalvular regurgitation (PAR) after transcatheter aortic valve replacement (TAVR) is associated with increased mortality. Further data on the influence of aortic root calcium on the risk of PAR is warranted.

Purpose: We sought to determine the impact of aortic root calcium volume and distribution on the risk of PAR in a multicenter setting.

Methods: 288 patients from 3 centers underwent multidetector computed tomography (MDCT) prior to TAVR with the Edwards Sapien XT valve. Balloon post-dilation (PD) for treatment of PAR–mild was performed at the discretion of the treating operator. PAR was assessed using predisharge TTE. Quantitative calcium analysis incorporating a detailed 3-dimensional regional analysis on contrast-enhanced pre-TAVR MDCT scans was performed. Aortic root calcium was quantified volumetrically in three anatomical regions: 1) the Aortic Valve Region (from the aortic annulus plane to the left coronary ostia), 2) the Overall Left Ventricular Outflow Tract (LVOT) (from the aortic annulus plane and 10 mm into the left ventricle) and 3) the Upper LVOT (from the aortic annulus plane and 2 mm into the left ventricle). A combined endpoint of predisharge PAR–mild or PD (as a surrogate for PAR–mild) was defined (PD/PAR patients).

Results: Mean age was 81±6.8 years, mean STS risk score was 6.3±3.9 and 50% (144) were female. PD was performed in 7% (21/288) of the patients. Post-procedural PAR–mild was present in 10% (29/288) of the patients. The combined endpoint of PAR–mild or PD occurred in 15% (44/288) (PD/PAR patients). Mean (Interquartile range). Upper LVOT and Overall LVOT calcium volumes were higher in PD/PAR patients compared to non-PD/PAR patients, 25 [5–56] mm3 vs. 0 [0–8] mm3 (p<0.0001) and 44.9 [1–112] mm3 vs. 3 [0–59] mm3 (p=0.03), respectively. Aortic Valve Region calcium volume did not differ between PD/PAR patients and non-PD/PAR patients, 498 [294–673] mm3 vs. 565 [225–1004] mm3 (p=0.49). Upper LVOT calcium volume was more predictive of PD/PAR than Overall LVOT calcium volume, area under receiver operating curve (AUC) (95% CI): 0.70 (0.59–0.79) vs. 0.60 (0.51–0.70) (p=0.001). In patients with prosthesis valve oversizing >15% relative to annular area, Upper LVOT calcium volume was more predictive of PD/PAR than Overall LVOT calcium volume. LVH was assumed when left ventricular mass was 204 before, 186 g in women and 258 g in men. PHT was measured by continuous-wave Doppler echocardiography of aortic regurgitation velocity curve. In 18 of 71 patients (25%) with at most trace regurgitation PHT could not be obtained due to no or very faint signal. CMR imaging of the ascending aorta was used for calculation of regurgitant fraction by division of aortic backward flow by aortic forward flow. According to CMR guidelines paravalvular regurgitation severity was graded more than mild when regurgitant fraction was >15%.

Results: In 13 of 53 patients (25%) paravalvular regurgitation after TAVI was more than mild as graded by CMR analysis. LHV was present in 29 of 53 patients (55%). PHT correlated less to regurgitant fraction by CMR analysis in patients without LHV (<r=0.174; p=0.491) than in patients with LHV (<r=0.543; p=0.0023). In patients without LHV accuracy of PHT to predict more than mild paravalvular regurgulation using a cut-off value of 347 ms (AUC=0.738, sensitivity 66.7%, specificity 90.5%) was comparable to analysis in patients with LVH using a cut-off value of 242 ms (AUC=0.800, sensitivity 80.0%, specificity 84.2%).

Conclusion: Analysis of PHT with distinct cut-off values differentiating patients between HD and HD with LVH for grading of paravalvular aortic regurgitation after TAVI in comparison with cardiac magnetic resonance (CMR) as the reference method.

Methods: In 71 patients (age 81±6 years) with severe aortic stenosis transthoracic echocardiography and CMR were performed after TAVI. Left ventricular mass was calculated by the AASE/EA formula using linear echocardiographic dimensions. LHV was assumed when left ventricular mass was >186 g in women and >258 g in men. PHT was measured by continuous-wave Doppler echocardiography of aortic regurgitation velocity curve. In 18 of 71 patients (25%) with at most trace regurgitation PHT could not be obtained due to no or very faint signal. CMR imaging of the ascending aorta was used for calculation of regurgitant fraction by division of aortic backward flow by aortic forward flow. According to CMR guidelines paravalvular regurgitation severity was graded more than mild when regurgitant fraction was >15%.

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Guide we predicted the valve size for each diameter and the patients were divided in groups based on the size of the AV prosthesis (Table). **Results:** Mean age was 83.2±6.4 years. The DC was higher in all but 7 cases in which DC and DA were equal (DC:22.97±2.22mm vs DA:22.56±2.17mm; p<0.001). The two methods had good agreement in predicting the valve size (k=0.66), 150 patients (77.7%) were assigned for the same valve size, whereas 18 (9.3%) would be eligible for a different size and 25 (13%) would definitely have a different valve implanted. We used the DC rather the DA to derive the diameter and select the prosthesis size. No aortic rupture and no paravalvular aortic regurgitation graded more than mild was seen.

**Conclusion:** The shape of the AA is not circular. Using the area or the circumference to calculate the AA diameter provides different values. In our series we showed that using the circumference excellent outcomes can be achieved. If the AA had been sized using the area, a different valve size could have been implanted in 22.3% of patients.

**P3727 | BEDSIDE**

Clinical impact of left atrial appendage closure on the incidence of stroke, bleeding and on quality of life in patients with atrial fibrillation: a standardized single center registry


**Background:** We assessed the impact of left atrial appendage closure (LAAC) on the incidence of cardiac mortality, stroke, bleeding and quality of life (QOL) in a standardized single center registry

**Methods:** At our institution LAAC using the Watchman device has been recommended since 2010 in all patients (pt) with atrial fibrillation (AF) and bleeding events under oral anticoagulation therapy (OAC). Postprocedural antithrombotic therapy included aspirin for life, OAC or low molecular weight heparins (LMWH) for 45 days, followed by clopidogrel up to 6 months after LAAC. In pt with absolute contraindications against OAC, clopidogrel was started after LAAC and given for 6 months without OAC/LMWH. An ambulatory examination with transesophageal echocardiography at 45 days and a standardized clinical follow-up (fu) at 1 year including QOL assessment using a modified 17-questions AFEQT™ questionnaire were performed.

**Results:** Ninety consecutive pt (52 males) aged between 53 - 90 years (74.3±7, median 75) underwent LAAC between 2010 and 2013. The CHADS2VASc score ranged between 2 - 6 (4±1.1, median 4) and the HAS-BLED score between 2 - 6 (4.4±1.6, median 4). Confirmed history of stroke was present in 11 pt, of whom 8 (4±1.6, median 4). Completed history of stroke was present in 11 pt, of whom 8 (4.4±1.6, median 4). Confirmed history of stroke was present in 11 pt, of whom 8 (4.4±1.6, median 4).

**Conclusion:** In AF pt with high stroke and bleeding risk LAAC effectively reduced bleeding complications and ischemic stroke and also significantly improved quality of life at 1-year follow-up.

**P3728 | BEDSIDE**

Learning curve of percutaneous left atrial appendage closure for stroke prevention in single high volume center

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**Introduction:** Ruptured sinus of Valsalva aneurysm (RSVA) is a rare short lesion frequently treated percutaneously. Lately for this purpose have been used also Chinese PDA nitrol wire mesh devices very similar to Amplatzer Duct Occluder type I (ADO). Experience with this occluders is scant.

**Aim:** To present results of transcatheter closure of RSVA with PDA occluders taking in consideration short and midterm results.

**Methods:** From September 2010 to August 2014, 8 patients (pts) from 17 to 72 years old (mean age 40 y) have closed their RSVA with nitrol wire mesh PDA occluders (produced by 3 different companies). All but two pts had congenital sinus of Valsalva aneurysm. Two pts had acquired RSVA after previous cardiac surgery (one after aortic valve replacement, another after surgery of tight subaortic stenosis – LVOTO). In all pts arterio-venous loop was created and PDA devices were implanted transvenously. There were used devices 2-6 mm bigger than orifice of RSVA. There were 7 connection between right coronary or noncoronary sinus with right atrium and 1 between noncoronary sinus and right ventricle.

**Results:** All PDA devices (sizes from 12/10 to 18/16) were successfully implanted in RSVA. In one pt with iatrogenic RSVA (after LVOT operation) device have not been retrieved because of massive aortic regurgitation after implantation provoked by the device. In 72 y old woman, after aortic valve replacement, duct occluder was applied in proximal entrance to the RSVA. Because of the presence of important residual leak on the edge of the implant the procedure had to be supplemented by closing of the distal RV orifice of RSVA with 10 mm Muscular VSD Occluder. In one pt after embolization of ADO to pulmonary artery and its transcatheter retrieval, bigger device were applied. In another pt after ADO implantaion 2 y later (during pregnancy) reclassification of RSVA treated successfully by PDA occluder after delivery. In follow-up (ranged from 0,5 till 4 years) no complications were observed in any pt.

**Conclusions:** Transcatheter closure of ruptured sinus of Valsalva aneurysm with new PDA nitrol mesh wire mesh occluders is safe and effective procedures.

**P3729 | BEDSIDE**

Impact of complex septal anatomy on clinical events in long term follow up after percutaneous closure of patent foramen ovale

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**Purpose:** In patients with cryptogenic stroke, certain anatomical features of a patent foramen ovale (PFO), as atrial septum aneurysm (ASA) or a large right-to-left shunt have been related to stroke recurrence in follow up. Our aim was to investigate the impact of a complex septal anatomy in the long term risk of stroke after percutaneous effective closure of the PFO.

**Methods:** From January 2000 to November 2014, a total of 172 patients (mean age 46±12 years, 60% male) underwent percutaneous PFO closure after suffering with atrial fibrillation. Continued access registry of the PROTECT AF study reported learning curve in multiple center registries. Until now, single center report of learning curve in this procedure is rare. Therefore the aim of the present study was to evaluate procedure learning curve in clinical routine.

**Methods:** A total of 372 patients (145 males, 72.6±8.5 years, CHADs score: 3.3±1.4) with atrial fibrillation receiving LAA closure at a single center from 2009 to June 2014 were investigated. The patients were divided into five groups according to the procedure date. The fluoroscopy time, radiation exposure, procedure duration, amount of contrast agents were analysed.

**Results:** Overall successful implantation rate was 99.2% (369 of 372 patients). The radiation exposure showed significantly forward less (p=0.0017), and the amount of contrast agent showed also significantly forward smaller quantity (p<0.001). Total number of the device showed a trend forward less but statically not significant. The procedure duration and fluoroscopy time were not significantly different among the groups.

**Conclusion:** Our data show a clear reduction in the radiation exposure and the amount of contrast agent use with a strong trend forward. Interestingly, we added new physicians during the study. We conclude there was a clear learning curve in LAA closure in clinical routine at a high volume center.

**Abstract P3727 – Table 1**

<table>
<thead>
<tr>
<th>Prior to LAAC</th>
<th>LAAC (in hospital)</th>
<th>45-day fu</th>
<th>45 days to 1 year fu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality: all causes</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Stroke / Embolism: suspected / confirmed</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Bleeding: any / total</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Daily activities restriction (5: highest, 1: lowest)</td>
<td>3.10±1.29</td>
<td>2.91±1.38</td>
<td>2.91±1.38</td>
</tr>
<tr>
<td>Treatment satisfaction (5: highest, 1: lowest)</td>
<td>2.46±1.03</td>
<td>2.10±0.84</td>
<td>2.10±0.84</td>
</tr>
<tr>
<td>Global QOL score (5: worst, 1: best)</td>
<td>2.86±1.32</td>
<td>2.37±1.35</td>
<td>2.37±1.35</td>
</tr>
</tbody>
</table>

*p<0.05 for QOL indicators at 1-year fu vs. baseline.
ing a cryptogenic stroke associated to PFO and the presence of at least one of the following risk factors for recurrence: deep vein thrombosis, hypercoagulability status, extensive right-to-left shunt volume of contrast bubbles through the PFO at rest, atrialseptal aneurism, recurrent stroke despite anticoagulant treatment or anticoagulant intolerance. We performed a comparative study of baseline clinical variables and follow-up outcomes among patients with a complex septal anatomy defined as atrial septal aneurysm or large right-to-left shunt volume of contrast bubbles through the PFO versus the rest of the series.

Results: A complex septal anatomy was present in 111 patients (65%): an ASA was present in 75 patients (44%) and a large shunt in 70 patients (41%). Baseline clinical features were similar in patients with and without a complex anatomy, except that the first group was older (48±13 versus 43±9 years, p<0.01). Most patients received an Amplatzer device in both groups (85% versus 83%, p=0.84) but the complex anatomy group received a ≥25 mm device more frequently (76% versus 36%, p<0.0005). Primary success rate was 100% in both groups. Only in one case there was a peri-procedural minor complication (a groin hematoma). After 5±4 years of follow-up, we observed 6 deaths (with only one of cardiovascular cause, an acute myocardial infarction) and 8 non-fatal cerebrovascular ischemic events (4 strokes and 4 transient ischemic attacks). The percentage of patients free of antithrombotic treatment at last follow-up was similar in both groups: 44% versus 49%, p=0.54. Probability of recurrent cerebrovascular ischemic events at follow-up was low and similar in the study group than in the rest of series (1.08 versus 0.33 in patient-year, p=0.24), even after adjusting by age and disease size (HR 2.52, 95% CI 0.28–22.75, p=0.41).

Conclusion: In this real-life series, we have found a significant adverse impact of a complex septal anatomy in recurrent cerebrovascular events, after the effective closure of the PFO.

P3731 | BEDSIDE
Transfemoral tricuspid valve-in-valve and valve-in-ring implantation using the Edwards SAPIEN XT valve: one-year follow-up

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Background: Redo tricuspid surgery may be high risk or even contraindicated due to comorbidity. Transcatheter valve implantation (TVI) has been recently reported in this setting.

Purpose: The aim of this study was to evaluate the feasibility of transfemoral implantation of Edwards SAPIEN PROSTHESIS in failed tricuspid bioprostheses (BP) and ring annuloplasty (RA).

Methods: Between 2011 and 2013, TVI was performed in 6 patients for failed tricuspid surgical valves (3 BP, 3 RA) in our institution. Median age was 58 years and patients were in NYHA class II. All patients had a history of cardiac surgery and had undergone at least 2 interventions.

Results: The procedure was successful in 100% for BP and 67% for RA. One patient had indeed a moderate residual paravalvular leak at the level of a rigid incomplete ring. In-hospital complications included: 1 major bleeding related to esophageal ulceration and 1 severe vascular complication. The transvalvular gradient decreased from 8.0 mmHg at baseline to 4.1 mmHg at 1 year.

Case 1: A 54-year-old patient had indeed a moderate residual paravalvular leak at the level of the open portion of a rigid incomplete ring. The patient had already been operated on 6 times.

Case 2: A 72-year-old patient had a history of 4 open heart surgeries. The patient had a history of 2 previous TVI procedures.

Conclusions: Transcatheter implantation of SAPIEN XT valves in failed tricuspid BI is feasible in selected high-risk patients, with good early and 1-year hemodynamic and clinical results. However, RA may raise issues due to their oval shape and open configuration.
P3734 | BENCH
One-shot circumferential renal artery denervation with relative sparing of the arterial wall may be possible using a novel microwave catheter
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Background: Clinical trials of renal artery denervation using radiofrequency ablation (RFA) have not shown consistent efficacy. RFA has limited depth, causes full thickness renal artery injury, requires a spiral lesion pattern, producing questionable denervation.

Purpose: To show that a microwave catheter may induce deep circumferential heating while sparing the luminal surface of the vessel wall and nearby viscera even with reduced renal artery flow.

Methods: A microwave catheter was constructed and tested in a renal artery model. This consisted of transparent phantom materials for renal artery, perinephric fat and nearby viscera embedded with a thermochromic liquid crystal sheet that changes colour with temperatures between 50–78°C. 0.9% saline was perfused through the renal artery at 37°C. 25,200J ablations were performed at 140W for 180s and 120W for 210s with saline flow at 0.5L/min and 0.1L/min. The 53°C isotherm was taken as the lesion boundary and dimensions were assessed using serial digital photography and analysed with in-house built software.

Results: At maximal lesion growth, ablations at 140W at 0.5L/min flow spared the luminal 1.0mm (95% Cl 0.8–1.1mm) of the vessel wall, extended 5.9mm (95% CI 5.5–6.1mm) deep from the vessel lumen and was 19.2mm in length (95% CI 17.7–20.7mm). Reductions in renal artery flow to 0.1L/min had minimal impact on lesion dimensions. Delivering ablation energy at 120W produced significantly smaller lesions with more vessel sparing compared with 140W. No heating peripheral to the 10mm thick perinephric fat phantom layer was observed.

Conclusions: Intravascular microwave ablation can induce circumferential heating to depths which encompass the majority of renal nerves while potentially sparing the renal artery intima and media as well as nearby viscera.

P3735 | BESIDE
Effects of renal denervation on cardiac sympathetic activity and innervation
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Background: Renal denervation (RDN) demonstrated its efficacy not only in reducing blood pressure (BP), but also in reducing heart rate (HR), cardiac hypertrophy and arrhythmia in certain patients. These pleiotropic effects are partly independent from the BP reduction. A direct effect of RDN on the heart could explain previously described findings, but data in this respect are lacking.

Purpose: To investigate if RDN has a direct effect on cardiac sympathetic activity and innervation density.

Methods: Sixteen patients with resistant hypertension (mean office systolic BP 175±18 mmHg, mean ambulatory systolic BP 141±19 mmHg, mean antihypertensive drugs 5.3±2.4) underwent L1-23mm stigmometry to measure cardiac sympathetic innervation and activity before and 6 months after RDN. Cardiac sympathetic innervation was assessed by heart to mediastinum ratio and cardiac sympathetic activity by washout ratio. RDN was performed with a single electrode catheter. Effects on office BP, ambulatory 24-hour BP monitoring, office HR and ambulatory 24-hour ECG were measured before and at 3, 6 and 12 months of follow-up. We performed ultrasound examination of the RA at 2–3 days, 3 and 12 months after RDN.

Results: Intravenous ablation lesion 140W 0.5L/min

Final ablation lesion 140W 0.5L/min

Conclusions: Intravascular microwave ablation can induce circumferential heating to depths which encompass the majority of renal nerves while potentially sparing the renal artery intima and media as well as nearby viscera.

P3736 | BESIDE
Assessment of efficacy and renal hemodynamics with renal function after catheter-based renal denervation in patients with resistant hypertension
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Introduction: Prevalence of a resistant hypertension (RH), according to various researches, makes from 10 to 30%. Renal sympathetic hyperactivity is associated with hypertension and its progression, chronic kidney disease, and heart failure. Less is known about the influence of catheter-based renal denervation (RDN) on renal hemodynamics and renal function.

Purpose: The purpose of our study was to assess the efficacy of RDN and renal hemodynamics with renal function (RF) after RDN 6 month and 12 month respectively in patients with blood pressure (BP) >160/100 mmHg despite 3 full-dose antihypertensive drugs.

Methods: The study included 74 patients with RH, the average age was – 50, 53±9. 93. All patients underwent RDN. Procedure is performed by an experienced electrophysiologist at the renal arteries using specialized electrode Symplicity: capacity of 8 - 10 W at 55 °C, 4 - 10 points for each PA, for 2 minutes. Estimated glomerular filtration rate (GFR) (measured by Modification of Diet in Renal Disease) and office systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured before and at 3, 6 and 12 months of follow-up. We performed renal ultrasound examination of the RA at 2–3 days, 3 and 12 months after RDN. Doppler sonographic renal resistive index (RRI) reflects systemic and renal hemodynamics, arterial compliance and has been associated with progression of renal impairment, as well as morbidity and mortality in hypertensive patients.

Results: Despite antihypertensive treatment, baseline SBP and DBP in this group of patients were – 179, 41± 29, 19 and – 105, 23± 17, 95 respectively. Office BP decreased by – 23,08±10,08 (p<0,05) and – 22, 01±11, 23 mmHg (p<0,05) at 6 and 12 month respectively. No significant changes of GFR and renal blood flow were found, however, RRI decreased significantly in segmental RA: from 0,72±0,1, initially till 0,67±0,04 and 0,67±0,03 respectively, at follow-up points. Postprocedural renal duplex ultrasound was performed without detecting abnormalities (eg, significant renal artery stenosis or aneurysm) of the renal arteries through the study period.

Conclusions: In the control points of patients with RH after RDN there was observed a significant and sustained reduction in office blood pressure. Also RDN had no adverse effect on either renal function or blood flow trunk and segmental branches of the RA according to GFR and renal duplex ultrasound. On the contrary, the decrease of resistive index in segmental RA after the intervention indicates improvement of renal blood flow.

P3737 | BESIDE
The proximity of renal structures to the renal artery: a study to assess the potential risks of renal denervation
H.C. Patel1, J.B. Moser2, S. Otero2, C. Hayward1, S.D. Rosen3, A.R. Lyon1, R. Mohiuddin1, C. Di Mario1, S. Padley2, 1Biomedical Research Unit of Royal Brompton London, London, United Kingdom; 2Royal Brompton Hospital, London, United Kingdom

Purpose: To identify patients with RH in the expected thermal ablation field (UTUREM) at the renal arteries using specialized electrode Symplicity: capacity of 8 - 10 W at 55 °C, 4 - 10 points for each PA, for 2 minutes. Estimated glomerular filtration rate (GFR) (measured by Modification of Diet in Renal Disease) and office systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured before and at 3, 6 and 12 months of follow-up. We performed renal ultrasound examination of the RA at 2–3 days, 3 and 12 months after RDN.

Background: Limited safety data are available regarding inadvertent soft tissue damage during catheter-based renal artery sympathetic denervation.

Methods: We used computed tomography (CT) to identify structures lying within the expected thermal ablation field, accounting for recent advances in catheter design that allow treatment of arteries as small as 2mm in diameter (Splanal, Veska) and create ablation zones of up to 10mm in depth (Paradise System). We selected 60 consecutive contrast-enhanced CT aortograms were reviewed. Structures within 10mm of renal arteries deemed anatomically eligible for treatment were recorded, noting their distance from the vessel wall and the vessel diameter at that point.

Results: The subjects had a mean age of 75.9 years, 48% were male and 88% had a history of hypertension. 79 of the 100 kidneys had eligible anatomy. Structures within the ablation field included blood vessels (inferior vena cava (IVC), renal vein, liver, pancreas, portal vein, bowel, adrenal gland and diaphragm). No significant difference was found between the frequency with which structures were observed within 10mm of renal arteries measuring 3–4mm and those measuring >4mm in diameter (Table 1). The IVC and renal vein run in close proximity to the renal artery and can be 2mm in diameter or less at some points.

Conclusions: In at least a fifth of renal arteries the psoas muscle and/or small bowel are within the expected thermal ablation field. Ablation of renal arteries measuring 3mm (the new lower limit for treatment) did not increase the number of
organ at potential risk when compared with arteries of 4mm (the previous lower limit). In almost all cases the renal vein and IVC run in close proximity to the renal artery, which will exert a cooling effect that is likely to affect ablation efficacy.

Conclusions: This study highlights the differences between first- and new-generation RDN devices. ABPM at 1 and 6 months showed a trend, although not statistically significant (due to the small sample size) towards a larger BP reduction in Vessix probably because the Vessix multi-electrode system delivers a predictable impact of simultaneous multiple ablations and allows for a more effective RDN compared with Symplicity single-electrode system. Moreover, the different mechanism of Vessix RDN system with low power radiofrequency delivery by a low pressure balloon in a short time does not probably cause any local tissue injury at the ablation sites, as confirmed by the absence of RAS observed at 6 months with CT scan.

P3740 | BEDSIDE

Left atrial appendage closure followed by a single anti platelet therapy: a single center experience

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Introduction: The purpose of the present study was to assess the safety and efficacy of LAAC for stroke patients with NVP and contraindication for anticoagulation.

Methods: Consecutive patients with a previous ischemic or hemorrhagic stroke, NVP and contraindication for anticoagulation underwent LAAC with the Amplatzer Cardiac Plug device between July 2010 and July 2013 in a French university hospital. Follow-up included clinical evaluation at 3 and 12 months, and a cardiac computed tomography (CT) at 3 months. Single-antiplatelet therapy was prescribed after the procedure for a minimum of 3 months and stopped if the control cardiac CT demonstrated complete LAA exclusion.

Results: 26 patients (age 73±8 years) were included. The mean CHA2DS2-VASc and HAS-BLED scores were 4±1,5 and 4±0,8, respectively. The main contraindications for anticoagulation were: intracerebral hemorrhage while receiving anti-coagulation (62%), ischemic stroke with large hemorrhagic transformation (15%) and probable cerebral amyloid angiopathy (8%). The procedure was successful in 100%. Procedure-related complications were serious pericardial effusion (3.8%) and femoral bleeding (7.7%). During a mean follow-up of 8.6 (3–16) months, ischemic stroke occurred in 2 patients (7.7%), after antplatelet therapy was stopped for one of them. One patient died of an intracranial hemorrhage.

Population characteristics

- Number of patients: 26
- Age: 73±8 years
- Sex (M/F): 18/8
- CHA2DS2-VASc: 4±1.5
- HAS-BLED: 4±0,8
- Paroxysmal atrial fibrillation: 11
- Persistent atrial fibrillation: 15

Conclusions: LAAC followed by a single antiplatelet therapy could be a reasonable alternative for stroke patients with NVP and contraindication for anticoagulation. Life-long rather than short-term single antiplatelet therapy should be considered after the procedure for patients at high cardio-vascular risk.
Tuohy needle was used. Acute LAA closure was assessed with angiography and transesophageal echocardiography (TEE). All patients were scheduled for a 1–3 month post-procedure TEE to assess LAA closure. Patients with residual leaks from first follow-up TEE will have a repeat TEE after 3–6 months.

Results: The LARIAT+ procedure was successfully completed in all 86 pts. There were no device related complications. Complete LAA closure was achieved in 84/86 (97.7%) pts with a ≤1 mm residual communication in the remaining 2/86 (2.3%) pts, as assessed by TEE. Periprocedural complications occurred in 2/86 (2.3%) pts: early superficial subcutaneous bleeding at the site of subxiphoid needle entry treated with a surgical figure-of-8 stitch occurred in 1 pt and haematemesis, 12 hours later related to transesophageal imaging and managed with upper GI endoscopy, occurred in 1 other patient. No patients required blood transfusion and there were no other periprocedural complications. To date, 1-month post-procedure TEE follow-up has been performed in 31/86 (36.0%) patients: complete closure of the LAA, defined as colour Doppler flow of ≤1 mm was seen in 21/31 (67.7%) patients. A repeat 3-month TEE has been performed in the 10 patients with residual leaks: 9/10 (90%) patients had complete closure of the LAA. Therefore, at 3 months, complete LAA closure was achieved in 30/31 (96.8%) patients. The remaining patient had a persistent 2 mm leak.

Conclusions: Initial multi-centre European experience with the new percutaneous transcatheater LARIAT+ suture delivery device combined with a novel microcircuit pericardial access technique effectively achieves acute LAA closure with an acceptably low risk of adverse events.

HEART FAILURE THERAPY, VARIOUS I

P3742 | BESIDE
Effect of additive tolvaptan versus increased furosemide on refractory heart failure with renal impairment: results from the K-STAR study

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Background: The clinical superiority of additive tolvaptan in comparison with increased oral furosemide (HF) with renal dysfunction.

Methods: The K-STAR study was a multicenter, open-label, randomized, controlled, prospective study that enrolled 188 patients from 18 hospitals from December 2012 to August 2014. HF patients with fluid overload despite taking 40 mg/day of oral furosemide (FUR group) for 7 days to evaluate outcomes. The geographical heterogeneity of the study population justifies a subgroup analysis.

Results: Patients suffered from moderate HF, with the majority of patients in NYHA class II–III, and complicating renal dysfunction. All patients had an eGFR of ≥29±10 mL/min. Before randomisation, the dose of furosemide was 51±25 mg/day and the additive dose of tolvaptan or furosemide was 10±4 mg/day or 28±12 mg/day, respectively. The change in the urine output between the baseline and seventh day, which was the primary endpoint, was significantly higher in the tolvaptan group than that in the FUR group (459±508 vs. 69±340 mL/day, p=0.0001, Figure 1). The incidence of worsening renal function (WRF), which was the secondary endpoint, was significantly lower in the tolvaptan group than that in the FUR group (20% vs 43%, p=0.025) (Figure 2). Logistic regression analysis revealed that additive tolvaptan was an independent factor for reducing WRF (odds ratio, 0.242, 95% confidence interval, 0.068–0.752; p=0.013).

Conclusion: In HF patients with renal dysfunction refractory to standard therapy, additive tolvaptan increased the urine volume without further renal impairment compared with that by an increased dose of furosemide.

Acknowledgement/Funding: The Kidney Foundation, Japan

P3743 | BESIDE
Strategies for diuretic management of acute heart failure: data from a web-survey among members of a National Cardiology Society

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Background: Despite the widespread use of diuretics to relieve congestion in patients with Acute Heart Failure (AHF), limited evidence is available to guide clinicians on appropriate diuretic management and on the identification and treatment of diuretic resistance, a common and complex clinical problem.

Methods: The Survey consisted of a demographic section and 30 multiple choice questions on diuretic use in AHF, the definition and treatment of diuretic resistance, and indications to non-pharmacological decongestion. Anonymous answers were directly transferred via web to an electronic secure database.

Results: A sample of 601 cardiologists (72% of male, age 52±11 years, years of clinical practice 22±11) answered the survey. Only 30.3% of respondents used a predefined diuretic therapy protocol. Bolus, continuous infusion alone or preceded by bolus were used by 36%, 23% and 41% respectively; 93% used an iv. loading dose greater than the chronic oral dose, but only 23% adjusted it according to patients’ baseline renal function. Clinical criteria (signs, symptoms, weight loss) ranked first in respondents’ definition of diuretic effectiveness, followed by urinary output and diuretic resistance was identified through a multiparametric evaluation by 48%, while 24% considered as diagnostic an urine output <1000ml/24h in isolation. Sequential nephron blockade was used only in case of diuretic failure by 80%, metolazone being the commonest agent added (32%). Aldosterone antagonists were used by 54% as initial treatment. In the setting of diuretic resistance, 60% of respondents considered fluid restriction a priority, 22% routinely ruled out causes of pseudo-resistance, 77% added low-dose dopamine and 23% would switch to slow continuous ultrafiltration. Only a minority of respondents would consider ultrafiltration in case of worsening renal function (15%) or severe diuretic resistance (14%). Finally, we calculated the proportion of respondents who complied with a guideline-derived appropriateness profile, defined as ≤75% of answers fitting a set of multiple criteria: only 23% of respondents met this predefined target. No demographic variables were predictive of guideline-compliant behaviour.

Conclusions: We observed a wide variance in strategies of diuretic management of AHF in a nationwide cohort of hospital cardiologists. These findings underscore a compelling need to standardize the criteria for appropriate diuretic treatment of AHF.

P3744 | BESIDE
Is the therapeutic efficacy of coenzyme Q10 replicated in a geographical subgroup of the Q-SYMBIO study?


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Background: Global differences in the outcome of heart failure (HF) have been described. In the Q-SYMBIO study (Coenzyme Q10 as adjunctive treatment for chronic heart failure: a randomized, double-blind, multicentre trial with focus on symptoms, biomarker status (BNP), and long-term outcome) 420 patients were enrolled in European, Asian and Australian centres in a 2-year prospective trial. The geographical heterogeneity of the study population justifies a subgroup analysis.

Methods: A post-hoc analysis of predefined endpoints was carried out in the European subgroup (N=231) enrolled in Q-SYMBIO. Patients were randomized to either coenzyme Q10 (CoQ10) 300 mg daily (N=108) or placebo (N=123) in addition to standard therapy. The two groups were similar with respect to baseline characteristics.

Results: The level of serum CoQ10 increased significantly in the active treatment group (p<0.0001) from 0.95±0.08 μg/ml (mean ± SE) at baseline to 3.42±0.20 μg/ml after 3 months and was maintained during the study period with a level of 3.55±0.34 μg/ml after 2 years. In contrast, a small decrease of serum CoQ10 from 0.90±0.10 μg/ml at baseline to 0.76±0.04 μg/ml after 2 years was observed in the placebo group. After 3 months there was a borderline significant reduction of serum NT-proBNP (N-terminal pro-B-type natriuretic peptide) in the CoQ10 group (p=0.052). After 2 years a significant improvement (6%) of left ventricular ejection fraction (EF) was found within the CoQ10 group (p=0.021) vs. a non-significant improvement in the placebo group. The change of EF was not significant between the two treatment groups (p=0.19).

Conclusion: The CoQ10 group showed significant improvement in left ventricular function and a significant decrease in serum NT-proBNP. These findings underscore the need to standardize the criteria for appropriate diuretic treatment of AHF.

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A significant improvement of NYHA Class was recorded in CoQ10 treated patients (p<0.003). CoQ10 treated patients had significantly lower cardiovascular mortality (p<0.020) and lower occurrence of hospitalizations for heart failure (p<0.001). All cause mortality was significantly lower in the CoQ10 group, 10 patients (9%) vs. 24 patients (19%) in the placebo-group (Hazard Ratio: 0.37 (95% CI: 0.16-0.82), p=0.014).

Conclusions: The therapeutic efficacy of CoQ10 demonstrated in the Q-SYMBIO study is confirmed in a European subgroup analysis. The treatment is safe and effective with improvement of symptoms and survival and with a significantly lower rate of hospitalization due to worsening HF.

Acknowledgement/Funding: The Q-SYMBIO trial received partial support from the International Coenzyme Q10 Association, Pharma Nord ApS, Denmark and Kaneka Corp., Japan.

Methodology:

Methods: A large international sample of 789 patients with heart failure were selected who were receiving beta blocker therapy in real life clinical practice. This study is support by Servier.

Results: A total of 470 patients (60% of the sample) were treated with ivabradine therapy based on the HF guidelines recommendation. Results: In patients with sinus rhythm, mean resting HR was found to be 76±14 bpm and 26% (n=121) of the patients had a resting HR ≥ 70 bpm. Mean HR was significantly lower in patients receiving BB therapy than those not receiving BB (75.8±13 bpm vs 80.4±15 bpm respectively, p=0.001). However, 65.8% patients using BB therapy and 75% patients not receiving BB therapy still had a resting HR > 70 bpm (p=0.029), and no significant difference was found in mean HR between patients on target doses and those not on target doses of BB therapy (75.1±12 and 75.7±13 bpm, p=0.999). 33.5% patients (n=277) in sinus rhythm was met the HF guidelines recommendation on ivabradine use. However, the percentage of patients eligible for and treated with ivabradine was only 6.9% (n=19) and those eligible but untreated with ivabradine was 26.6% (n=258). Moreover, additional 15.6% of patients not receiving BB, in sinus rhythm and with a HR > 70 bpm were still a candidate for ivabradine treatment. Conclusions: These results showed that despite the significant reduction in resting HR by BB, most patients still have a resting HR > 70 bpm and almost one-fourth of patients in sinus rhythm and receiving BB therapy were eligible but not treated with ivabradine treatment in real life clinical practice.

Methodology:

Methods: The aim of this study was to compare temporal trends in initiation and persistence with statin treatment after establishment of HF diagnosis in Denmark, before and after the publication of two large randomized trials that failed to demonstrate a benefit of rosuvastatin in patients with HF. Methods and results: The study period (1995–2009) was divided into 5 intervals of 3 years each. All patients hospitalized with first-time HF (n=184,044) were identified in national registers. Incidence rate of HF decreased over time regardless of gender. A total of 23,027 HF patients with no previous statin therapy initiated statins. Initiation increased significantly after publication of abovementioned trials that failed to show a benefit of initiation of statin therapy (log-rank test p<0.0001). Multivariate Cox regression showed a significant effect of age, sex, diabetes and previous myocardial infarction on initiation throughout the study-period. However, persistence on statin therapy was unchanged after publication of the abovementioned studies (log-rank test p=0.2567). Age was the only factor with significant positive effect on persistence throughout the study-periods. Conclusion: Despite lack of evidence for the benefit of statin treatment in patients, initiation of statins in HF patients increased during the study period.

Methodology:

Methods: Despite lack of evidence for the benefit of initiation of statin therapy (log-rank test p<0.0001). Multivariate Cox regression showed a significant effect of age, sex, diabetes and previous myocardial infarction on initiation throughout the study-period. However, persistence on statin therapy was unchanged after publication of the abovementioned studies (log-rank test p=0.2567). Age was the only factor with significant positive effect on persistence throughout the study-periods. Conclusion: Despite lack of evidence for the benefit of statin treatment in patients, initiation of statins in HF patients increased during the study period.

Methodology:

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increased by DPP-4 inhibitor. Those cardioprotective effects after MI were also recognized in DPP-4KO mice. DPP-4 protein was expressed on rat neonatal cardiomyocytes and DPP-4 inhibitor significantly reduced hypoxia-induced apoptosis in the cardiomyocytes. However, this effect was abolished by the pretreatment with a CXCR4 antagonist or a signal transducer and activator of transcription 3 (STAT3) inhibitor. The beneficial effects of DPP-4 inhibitor on heart failure after MI were abolished by cardiomyocyte-specific deletion of STAT3.

Conclusions: DPP-4 inhibition prevented LV remodeling and heart failure after MI through SDF-1α/CXCR4/STAT3 signaling pathways in cardiomyocytes. DPP-4 inhibition prevented apoptosis of cardiomyocytes and a decrease in vessel number. Our study suggests the potential clinical efficacy of the DPP-4 inhibitors for prevention of heart failure after MI.

P3749 | BENCH
LCZ696, the angiotensin-receptor nephrilysin inhibitor, attenuates cardiac fibrosis and its function in the heart failure model of diabetes mellitus in mice

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Background: Angiotensin-receptor nephrilysin inhibitor (ARNI) has the effects of angiotensin receptor blockers (ARB) and augments natriuretic peptides (NP). Although the ARNI LCZ696 improves heart failure with reduced ejection fraction (HFrEF) in clinical study, the basic mechanism is not been less reported.

Purpose: To identify more severe situation, we evaluated the effects and mechanisms of ARNI in model of diabetes mellitus (DM).

Methods: For DM model, adult male C57BL/6J mice were intraperitoneally injected with streptozotocin. After myocardial reperfusion injury, DM mice were randomized to treatment for 4 weeks with LCZ696 (60 mg/kg), valsartan (30 mg/kg), or no treatment. Cardiac function was assessed by Pressure-Volume Millar catheter. Cardiac fibrosis was determined by quantitative histology (Picrosirius red staining). The levels of various gene expression were determined by real-time RT-PCR.

Results: There were no significant differences between the groups in baseline characteristics. The ratio of heart weight to body weight in the valsartan and LCZ696 groups was lighter than that in the control group (valsartan, p<0.05; LCZ696, p<0.01). Treatment with LCZ696 more improved left ventricular EF (42±12%) and cardiac output (2.6±1.2 ml/min) than the control group (29±12%, p<0.01; 1.7±0.9 ml/min, p<0.05). Gene expression of TGF-beta was significantly suppressed in the LCZ696 group than the control group (33% reduction, p<0.05). Gene expressions of atrial NP and brain NP and fibrosis were also suppressed in the LCZ696 group.

Conclusions: The ARNI LCZ696 improved cardiac function in HFrEF model of DM mice by reducing cardiac fibrosis. It may be due to the augmentation of NP beyond ARB.

P3750 | BENCH
Exogenous extracellular heat shock protein HSC70 protects against experimental septic cardiomyopathy

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Introduction: Recent studies suggest that heat shock protein, a previously recognized intracellular protein, can also be released to extracellular space and protect myocardium from ischemia-reperfusion injury. The purpose of this study was to determine if exogenous heat shock cognate protein 70 (HSC70) can protect injured heart from cardiomyopathy.

Methods: In an animal model of septic cardiomyopathy, we anesthetized the S-D rats and injected E. coli endotoxin LPS (10 mg/kg, iv) with or without pretreatment of HSC70 (20 μg/kg, iv). Hemodynamic changes were monitored during the 4-hr study period. Parameters including heart rate, MAP left ventricular systolic pressure, Max dp/dt and Min dp/dt were continuously recorded. Plasma levels of TNF-α, NO, GPT/GOT, glucose, LDH were also measured serially. In addition, activation of pro-inflammatory mediators including IL-1β, IL-6, and NF-κB were examined.

Results: Pretreatment with recombinant HSC70 attenuated LPS-induced hypotension and tachycardia by 21% and 23%, respectively (P<0.05), improved myocardial dysfunction (left ventricular systolic pressure: 33%; max dp/dt: 20%; min dp/dt: 33%; P<0.05). There were also improved biochemistry parameters including GPT, GOT, LDH and glucose at 4-hr. Furthermore, HSC70 inhibited the elevation of plasma TNF-α and NOx, and decreased myocardial levels of INOS and COX-2 in response to LPS challenge. Finally, HSC70 attenuated endotoxemic nuclear translocation of NF-κB by blocking phosphorylation of NF-κB.

Conclusion: Our results indicate that extracellular HSC70 has a promising role in the treatment of septic cardiomyopathy through anti-inflammatory pathways.

P3752 | BEDSIDE
RELAX-AHF-EU: a prospective, multicenter, randomised, open-label study assessing the efficacy and safety of serelaxin in patients hospitalised for acute heart failure in Europe

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Background: Approximately 10–30% of patients hospitalised for acute heart failure (AHF) develop in-hospital worsening heart failure (WHF), a condition that is associated with increased length of stay of the index hospitalisation, a 2- to 3-fold increased risk for re-hospitalisation, morbidity, and mortality. In a randomized Phase III clinical trial (RELAX-AHF), serelaxin was found to improve dyspnoea and reduce risk of in-hospital WHF through Day 5.

Purpose: The RELAX-AHF-EU study is being conducted in Europe to further evaluate the clinical benefits of serelaxin, including its effects on reducing in-hospital WHF in patients hospitalised for AHF.

Methods and results: RELAX-AHF-EU is an open-label study planned in ~400 cardiology, internal medicine, emergency, and intensive care departments in 26 countries across Europe. The study will enroll ~2,700 patients with AHF and systolic blood pressure >125 mmHg for up to 48 hours after randomization, and will include all-comers with a 2:1 randomization to receive intravenous infusion of 30 μg/kg/day serelaxin for 48 hours added to standard of care (SOC) versus SOC alone. The primary endpoint is incidence of in-hospital WHF or all-cause death through Day 5. Cases of WHF are initially identified by need for intensification of therapy for AHF and subsequently confirmed by a central adjudication committee of experts blinded to treatment allocation. Secondary endpoints include incidence of (a) in-hospital WHF, all-cause death, or re-hospitalisation for AHF through Day 14, (b) failure to clinically improve heart failure improvements through Day 5, (c) systolic blood pressure defined as ≥0.3 mg/dL increase in serum creatinine) through Day 5, (d) index length of hospital stay, (e) health-related quality of life, and (f) economic burden of disease. Safety and tolerability assessment is performed through Day 30. The study is on-
Maintenance of high-density lipoprotein cholesterol in patients receiving 300mg EPA thrice daily in conjunction with cholesterol lowering therapy. We investigated whether the EPA administration improves cardiovascular disease mortality in hemodialysis patients who are at high risk for cardiovascular disease. They were followed-up for 6 months after EPA administration. The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p=0.0001). During follow-up period (34 months), 109 patients died (22.9%) including 61 CVD cause. After adjustment for the propensity score, the EPA group had better survival for all-cause mortality, the presence of OMT was independently associated with a better long-term prognosis (HR 0.77, CI 0.60–0.99, p<0.001). Among patients with heart failure and preserved ejection fraction, overall mortality was higher in patients of the non-OMT group than in the OMT group (36.5% vs. 27.1%, respectively, p<0.001). After adjusting by a propensity score including previous significant variables and risk factors for mortality, the presence of OMT was independently associated with a better long-term prognosis (HR 0.77, CI 0.60–0.99, p<0.05).

Conclusions: This study suggests that there is a potential margin to further reduce all-cause mortality in real-life ambulatory patients with HF by spanning the OMT adherence.

HEART FAILURE THERAPY, VARIOUS II

P3754 | BENCH Angiotensin II Receptor-Nephrilysin Inhibitor, LCZ696 Blocked Aldosterone Synthesis in Human Adrenocortical Cell Line
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Background: Recent clinical study indicated that the angiotensin II (Ang II) receptor-nephrilysin inhibitor (sacubitril valsartan sodium complex, known as LCZ696) was superior to enalapril in reducing the risks of death and hospitalization for heart failure. Purpose: We investigated whether nephrilysin inhibition enhances an atrial natriuretic peptide or brain natriuretic peptide (ANP or BNP)-evoked signals which can block Ang II/Ang II type 1 (AT1) receptor-induced aldosterone (Ald) synthesis in human adrenocortical cells. Methods and results: Binding affinity of valsartan + LBO-657 (the active form of nephrilysin inhibitor pro-drug sacubitril) was better than that of valsartan alone in an AT1 receptor expressing HEK cell-based living assay, although there was no difference in the dissociation from AT1 receptor between valsartan + LBO-657 and valsartan alone. In Ang II-sensitized human adrenocortical cells, ANP or BNP alone, but not LBO-657 or valsartan alone, significantly decreased Ald synthesis. Most important finding was that valsartan + LBO-657 with ANP or BNP transiently suppressed Ald synthesis in Ang II-sensitized cells, the suppression levels were comparable to basal levels of Ang II-nonsensitized cells. The suppression of ANP was blocked by inhibitors of regulator of G protein signaling protein and cyclic AMP-dependent protein kinase. In addition, the suppression levels of Ald synthesis in valsartan + LBO-657 with ANP were stronger than those in valsartan with ANP. Finally, nephrilysin inhibition did not change the mRNA levels of AT1 receptor, NP receptor and regulator of G protein signaling protein. Conclusion: The inhibitory effects of LCZ696 on aldosterone synthesis may be partly due to the reduction of Ald synthesis by its nephrilysin inhibition.

Conclusions: This study suggests that there is a potential margin to further reduce all-cause mortality in real-life ambulatory patients with HF by spanning the OMT adherence.

P3755 | BEDSIDE Adherence to optimal medical treatment is associated with a reduction of all-cause mortality in ambulatory patients with heart failure
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Background: Optimal medical treatment (OMT) has proven to reduce the mortality and readmissions in patients with heart failure. However, several clinical registries have evidenced a relatively low adherence to guidelines. Purpose: The aim of this study was to analyze the prevalence and long-term prognosis of OMT in real-life outpatients with HF. Methods: A cohort of 1,475 ambulatory patients with chronic HF and depressed left ventricular ejection fraction (LVEF <35%) recruited between 2007 and 2011 from 18 tertiary centers from HF Spanish Network (REDINSCOR) was prospectively followed for a median of 40 months. OMT was defined as the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers together with beta-blockers and aldosterone antagonists. Clinical, echocardiographic, ECG, and biochemical parameters were used in a multivariable Cox model at pre-administration and after 6 months in the EPA group. The patients were followed-up for 3 years. To reduce the difference of baseline characteristics, a propensity score analysis using multivariate logistic model with all baseline characteristics was used to define the groups. They were followed-up for 3 years. To reduce the difference of baseline characteristics, a propensity score analysis using multivariate logistic model with all baseline variables such as male, age, duration of HD, diabetes, hypertension, dyslipidemia, smoking, body mass index, previous CVD, hemoglobin, albumin, creatinine, calcium, phosphate and C-reactive protein was performed. Results: Diabetes and peripheral arterial disease were more prevalent in the EPA group than in the control group (58.5% vs. 41.1%, p=0.016 and 24.8% vs. 13.7%, p=0.057, respectively). The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p<0.0001). During follow-up period (34 months), 109 patients died (22.9%) including 61 CVD cause. After adjustment for the propensity score, the EPA group had better survival for all-cause mortality (adjusted hazard ratio (HR) 0.53, 95% confidence interval (CI) 0.31–0.92, p=0.023) and for CVD mortality (adjusted HR 0.41 (95% CI 0.18–0.91, p=0.029) compared to the control group, respectively. Furthermore, in 93 propensity score-matched patients in each groups, 3-year Kaplan-Meier survival rate was still higher in the EPA group than in the control group for all-cause mortality (83.5% vs. 68.8%, HR 0.48, 95% CI 0.26–0.89, p=0.022) and for CVD mortality (91.8% vs. 80.4%, HR 0.38, 95% CI 0.16–0.92, p=0.032), respectively. Conclusion: Administration of EPA reduced CVD- and all-cause mortality in chronic HD patients who are consistently at highest risk of CVD.
Results: DSC occurred in 260 of 1767 (14.7%). 54 per 100 p-y) in the Americas compared with 35 of 1678 (2.1%). 6 per 100 p-y in R/G. In the Americas, but not in R/G, treatment with spironolactone increased the incidence of DSC (6.8 vs. 4.2 per 100 p-y, HR 1.60, 95% CI 1.25–2.05, p < 0.001). (Figure) In multivariable models, assignment to spironolactone, diabetes, NYHA class, smoking, lower potassium and lower hemoglobin were important predictors of DSC. In contrast to hyperkalemia, neither age nor baseline renal function was a statistically important determinant of DSC.

Conclusions: DSC is common in HF-BPE and risk is independent of age and baseline renal function. Because spironolactone enhances the risk for DSC, use in this population requires careful laboratory surveillance.

P3757 | BENCH Pharmacological inhibition of galectin-3 and aldosterone pathways prevents isoproterenol-induced left ventricular dysfunction and fibrosis in mice

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Background: Galectin-3 (Gal-3) is involved in cardiac inflammation, fibrogenesis and remodeling. Previous evidences show that Gal-3 interacts with aldosterone in promoting macrophage infiltration and vascular fibrosis, and that genetic and pharmacological inhibition of Gal-3 prevents cardiac remodeling in a pressure overload animal model of heart failure (HF).

Purpose: We aimed to test the effect of selective inhibitors of either Gal-3 (modified citrus pectin, MCP) or aldosterone (potassium canrenoate) on left ventricular (LV) function in a murine model of HF.

Methods: Forty-one 3 to 5-month old male mice with cardiac specific hyper-aldosteronism (AS mice) underwent isoproterenol subcutaneous injections, and were then randomized to receive placebo (n=12), MCP (n=10), canrenoate (n=9) or MCP + canrenoate (n=10) for 14 days.

Results: Isoproterenol induced a rapid and persistent decrease in left ventricular fractional shortening in placebo-treated mice (~20% at day 14), that was markedly improved by treatment with either MCP or canrenoate (both p < 0.001 vs placebo). MCP and canrenoate also reduced the extent of cardiac hypertrophy and fibrosis, as well as the expression of genes involved in fibrogenesis (Col-I and Col-III) and macrophage infiltration (CD-68 and MCP-1). Gal-3 gene expression (p < 0.05 vs placebo) and protein level (~61% and ~69% vs placebo) were decreased by both MCP and canrenoate. Combined use of antagonists of Gal-3 and aldosterone resulted in additive effects, compared to MCP or canrenoate alone, on cardiac hypertrophy, inflammation and fibrosis.

Conclusions: Inhibitors to the mechanisms of aldosterone-mediated myocardial damage in a HF murine model with cardiac hyperaldosteronism. Inhibition of Gal-3 and aldosterone can reverse isoproterenol-induced LV dysfunction, by reducing myocardial inflammation and fibrogenesis. Gal-3 inhibition may represent a new promising therapeutic option in HF.

P3758 | BESIDE The heart rate control and beta-blockade are not optimal in patients with systolic heart failure and chronic obstructive pulmonary disease


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Background: Heart failure (HF) is often associated with diabetes mellitus (DM), either as cause or comorbidity. It has been proven that hyperglycemia increases the risk of hospitalization and mortality in patients with HF, worsens its course among other through proteins glycation and oxidative stress, leading to myocardial fibrosis followed by diastolic dysfunction. The position of metformin as first-line therapy in type 2 diabetes (T2DM) is generally accepted. Although, it seems that metformin is the only hypoglycemic drug that may decrease the risk of major cardiovascular events and mortality in T2DM subjects, the use of this medication is contraindicated in diabetics with HF.

Purpose: The aim of this post-hoc analysis was to assess whether metformin administration in patients with heart failure and type 2 diabetes affects the risk of all causes mortality and hospitalization rates during a 12-months follow-up.

Methods: The study included 1003 of 1126 patients with HF representing Polish population of the Heart Failure Long Term Registry. Three hundred and forty-two patients of the study population with history of DM were identified (111 women, mean age 69±10.9 years; BMI 30±5.6 kg/m²; LVEF 37.6±15.5%) and divided into two groups: 1. patients receiving metformin monotherapy or metformin plus other hypoglycemic agents and 2. diabetic subjects not treated with metformin.

Results: At 1-year follow-up death occurred in 128 HF patients of the whole population (12.4%), in 53 patients with diabetes (15.5%) compared with 75 patients without diabetes (10.9%) (HR 1.42; 95% CI: 1.40 to 1.44; p < 0.0001). 118 of 342 patients (34.5%) were treated with metformin. Metformin treatment was associated with lower mortality rates compared with non-metformin treated group (11.0% vs. 17.9%) (HR 0.62; 95% CI: 0.58 to 0.66, p < 0.001).

Conclusion: The results of this study suggest, in agreement with previous observations, that metformin treatment is associated with a reduction in mortality in diabetics with heart failure. Therefore, we support the other authors suggestion that indications for metformin should be reconsidered.
P3760 | BEDSIDE

Comparative temporal effects of nitrate-centred and diuretic-centred therapy of acute decompensated heart failure on congestion and renal function injury as well as tubular damage biomarkers


Purpose: Our purpose was to assess and compare early (at day 4–6) and late (discharge - Dsc) effects of prolonged optimal-dosed nitrate continuous infusion plus low doses of i.v. diuretics (“nitric centered strategy” – NC) and moderate dosen i.v. diuretics plus short intermittent nitrate infusion (“diuretic-centered strategy” – DC) on congestion markers (CVP and NT-pro-BNP) and renal function (eGFR, Cystatin C and tubular damage (NGAL) biomarkers in pts with acute decompensated heart failure (ADHF).

Methods: In single-blind parallel-group study pts with “wet-warm” ADHF were randomized: randomized 1:2:1 to 2 groups. NC group (n=27) received optimal-dosed NTG continuous infusion >72 hrs plus low doses of i.v. diuretics (≤80 mgpd for furosemide), while DC group (n=51) moderate doses of i.v. diuretic (41–120 mgpd for furosemide) plus short intermittent (<10hrs pd. <3days NTG) doses. Congestion endpoints were CVP at D4–6 and plasma NT-pro-BNP (ELISA) at D4–6 and Dsc.

Results: Furosemide total 1st dose at NC group was 191±203mg, in DC group – 398±187mg, duration of NTG infusion – 3.5±0.4 vs 0.7±0.8 days (p<0.001), Dsc – in 9.4±1.3 and 11.4±1.5 days (all p<0.05). CVP lowering from D1 (NC group – 196±15.8, DC – 198±12.1 mmHg, p<0.05) to D4–6 (both p<0.01) was more pronounced in NC group (81±7.8 vs 82±12.2 mmHg p<0.05). AKIN rate was correspondingly 17.3% and 22.8% (p<0.05).

Conclusion: In ADHF patients “nitrate centered” strategy compared to moderate “diuretic centered” provides more pronounced progressive decongestion assessed by CVP and NT-pro-BNP lowering. It is associated with less marked early transient worsening of renal function (Cystatin C) and tubular damage (NGAL) followed by more pronounced improvement of both from baseline in “nitric centered” group.

P3761 | BEDSIDE

Characterising patients with chronic heart failure in community care after hospitalisation: a potential role for Ivabradine

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Aims: To identify the prevalence and characteristics of recently hospitalised chronic heart failure (CHF) patients in community care who meet the indication for ivabradine.

Methods: A retrospective clinical audit of CHF patients recently hospitalised with acute decompensated heart failure (ADHF), and subsequently referred to the Tayside Heart Failure Nurse Liaison Service (THFNLS), a Scottish nurse-led community heart failure liaison service. Inclusion criteria were previous hospitalisation and a subsequent referral to the THFNLS, data for >2 nurse visits, and a recorded pulse. The main outcome measure was the proportion of patients who meet the indicated criteria for ivabradine.

Results: In the UK, ivabradine is indicated for CHF with systolic dysfunction in patients in sinus rhythm, with a heart rate ≥75 bpm, and NYHA class II–IV. After

Abstract P3762 – Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>NT-pro BNP, Mm/L pm/L</th>
<th>Mm/mL mm/H m/L</th>
<th>eGFR, Mm/mL mm/Min per 1.73 m²</th>
<th>Cystatin C, Mm/mL mg/L</th>
<th>NGAL, Mm/mL mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-pro BNP</td>
<td>Mm/L pm/L</td>
<td>Mm/mL mm/Min per 1.73 m²</td>
<td>eGFR, Mm/mL mm/Min per 1.73 m²</td>
<td>Cystatin C, Mm/mL mg/L</td>
<td>NGAL, Mm/mL mg/L</td>
</tr>
<tr>
<td>NC</td>
<td>3292±6152</td>
<td>3503±6084</td>
<td>2732±4614</td>
<td>105±17</td>
<td>118±20,4</td>
</tr>
<tr>
<td>DC</td>
<td>3473±6154</td>
<td>3882±6422</td>
<td>3146±5877</td>
<td>106±20,8</td>
<td>132±22,7</td>
</tr>
<tr>
<td>p&lt;0.05</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01 compared to D1; p>0.05, **p<0.01 compared to Group DC.

In the UK, ivabradine is indicated for CHF with systolic dysfunction in patients in sinus rhythm, with a heart rate ≥75 bpm, and NYHA class II–IV.
up-titration of a beta-blocker, 19.0% of patients in the full dataset (158/830) met the indication for ivabradine at the last visit. Of these ‘ivabradine-suitable’ patients, 101/158 (63.9%) received bisoprolol “at any time” during the study period; 20/158 (12.7%) achieved the target dose (10 mg daily); 52/158 (32.9%) received 5 mg or 7.5 mg daily; and 93/158 (58.9%) received <5 mg daily.

Conclusions: In this group of Scottish patients previously hospitalised with ADHF and under the care of a protocol-driven clinic, 19% met the indication for ivabradine, and may benefit from the increased control of CHF that ivabradine can provide. Among those ‘ivabradine-suitable’ patients, -15% achieved the target dose of beta-blockers, illustrating the substantial clinical need for a well-tolerated and effective therapy such as ivabradine.

Acknowledgement/Funding: Servier UK

P3764 | BEDSIDE Early administration of tolvaptan can improve in-hospital clinical outcomes in patients with acute heart failure: a dual center experience
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Background: Patients with acute heart failure (A HF) are often in volume overload state. Conventionally, loop diuretics are the first-line drug to treat for AHF patients. Previous studies reported that tolvaptan, a nonpeptide V2 receptor antagonist, can improve pulmonary edema by rescuing the insufficient effect of conventional diuretics. Furthermore, the best timing of administering tolvaptan to patients with AHF has remained unclear.

Methods: Between November 2013 and November 2014, we retrospectively enrolled 159 patients with AHF at 2 medical centers who comprised 2 different strategies; tolvaptan group (tolvaptan + diuretics, n=66), and conventional group (diuretics, n=73). Tolvaptan was administered within 24 hours after admission. The primary endpoints were discharge within 14 days, and worsening of renal function (WRF; defined as a > -0.5mg/dl increase in serum creatinine at 1 week after admission).

Results: Patient characteristics were as follows 97 males with a mean age 77±13 years and ejection fraction (EF) was 46±18.7%. Type 1 and 2 of clinical scenario (CS) were 26% and 74%, respectively. The duration of hospitalization due to pulmonary edema was significantly shorter in tolvaptan group compared with conventional group (16.1±8.5 vs 19.7±11.7 days, P=0.03). WRF was no significant changes in aortic systolic, diastolic and pulse blood pressure were noted.

Conclusion: Patients with AHF, early administration of tolvaptan might have prompt efficacy to improve pulmonary edema, hence could significantly be shortened the duration of hospitalization. Also, the efficacy was more observed among patients suffering lower EF, normal renal function, and age <85 years.

P3765 | BEDSIDE Prevalence of hospitalised patients with heart failure eligible for treatment with ivabradine
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Purpose: Ivabradine reduces the morbidity and mortality of patients with heart failure due to left ventricular systolic dysfunction (SHIFT trial). The National Institute for health and Care Excellence (NICE) published a technology appraisal (TA 267) recommending ivabradine in these patients if 5 criteria are met. We wanted to define the prevalence of patients eligible for treatment with ivabradine.

Methods: We used our heart failure data-base to identify those admitted with heart failure in the year 2013. We excluded the patients who do not meet the criteria of NICE TA 267, which are: NYHA class II-IV, left ventricular ejection fraction <35%, sinus rhythm, heart rate >75bmp, being on standard therapy and being stable on optimal therapy for 4 weeks.

Results: We identified 516 patients admitted with heart failure during the year 2013. Only 33 patients (6.4%) hospitalised with heart failure in the year 2013 met the NICE-TA 267 criteria for ivabradine treatment. We reviewed data on these 33 patients: they were on standard therapy (beta-blockers [BB] and angiotensin converting enzyme inhibitor [ACEI]/angiotensin receptor blocker [ARB]) for heart failure or had a contra-indication for one or both classes of agents. The patients’ therapy are in Table 1. One criterion states ivabradine should only be initiated after stabilisation on optimal therapy for 4 weeks. Only 8 of the 33 patients met this criterion. One of them could not have ivabradine because of atrioventricular block. Of the remaining 7 patients (7/33=1.33%), 4 patients were actually treated with ivabradine.

Table 1. Summary of standard treatment in the 33 patients potentially eligible for ivabradine

<table>
<thead>
<tr>
<th>Treatment Combination</th>
<th>Number</th>
</tr>
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<tbody>
<tr>
<td>BB + ACEI/ARB + ARB</td>
<td>25 (76%)</td>
</tr>
<tr>
<td>BB + contra-indication to ACEI/ARB</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>ACEI/ARB + contra-indication to BB</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Contra-indication to both BB + ACEI/ARB</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
</tr>
</tbody>
</table>

Conclusions: The prevalence of patients admitted with heart failure eligible for ivabradine is low (6.4%) once they are stable for 4 weeks. An even smaller proportion (1.33%) meet the treatment criteria during hospitalisation. Follow up of these patients is essential to implement the NICE recommendations.

HEART FAILURE THERAPY, VARIOUS III

P3766 | BEDSIDE Tight heart rate control and pulsatile hemodynamics in patients with heart failure of ischemic etiology
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Background: Heart rate (HR) is an important target in treatment of patients (pts) with heart failure (HF). The aim of our study was to investigate the effects of different regimens of HR lowering therapy on pulsatile hemodynamics in pts with HF of ischemic etiology.

Methods: 50 pts (mean age 56.3±1.4 years) with HF of ischemic etiology, NYHA II-IV (mean 2.7±0.1), left ventricular ejection fraction (LVEF) <35% and HR > 70 bpm were included into this open, parallel-group randomized clinical trial. All HF pts received a guidelines-based therapy including bisoprolol 2.5-5.0 mg/day (mean dose 4.7±0.7 mg/day). Then, to achieve the target HR <60 bpm, these pts were randomized into two groups – group 1 (bisoprolol up-titration therapy): mean achieved dosage 7.8±0.6 mg/day and group 2 (constant bisoprolol doses plus ivabradine; mean achieved dosage of ivabradine 11.2±1.2 mg/day). Aortic blood pressure and arterial wave reflections were quantified noninvasively using applanation tonometry of the radial artery.

Results: 3 months of treatment with bisoprolol and bisoprolol + ivabradine combination resulted in a pronounced HR reduction (<13.2%, p<0.01 and -16.8%, p<0.001, respectively). A significant increase in LVEF was noted in both groups of patients with HF (+10.1%, p<0.05 and +17.7%, p<0.001, respectively). No significant changes in aortic systolic, diastolic and pulse blood pressure were noted in group 1 and 2. Aortic pulse wave velocity also remained unchanged. Due to the improvement of systolic function and HR reduction, augmentation index (Alx) increased from 25.9±9.3 to 33.3±11.4 in group 1 (p<0.05) compared with -4.4±1.1 to 24.1±11.2 in group 2 (p<0.05). Also, Alx normalized for HR of 75 bpm was significantly elevated in pts with treated with bisoprol up-titration therapy – from 21.1±7.1 to 29.1±15.9 in group 1, p<0.01, but not in patients with a combination of bisoprol and ivabradine – from 20.1±11.7 to 21.1±11.7 in group 2. Moreover, up-titration of bisoprol resulted in a reduction of time to return reflected wave (Tr) from 140.4±26.2 ms to 134.7±3.1 ms.

Conclusion: In pts with HF of ischemic etiology, tight heart rate control with bisoprol up-titration, but not with a bisoprol and ivabradine combination, can cause a deterioration of pulsatile hemodynamics parameters. Further studies are needed to investigate long-term effects of HR lowering therapy on the pulsatile hemodynamics in pts with HF of ischemic etiology.

P3767 | BEDSIDE Vitamin d supplementation improves the size and function of the left ventricle in patients with heart failure
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Background: Chronic heart failure (HF) patients are frequently vitamin D deficient. Vitamin D influences the immune system, pancreas, vasculature, skeletal muscle and cardiac function, all possibly relevant in HF. Vitamin D levels relate to disease severity in HF but no studies confirm the benefit of supplementation.

Purpose: To investigate the effect of 12 months of vitamin D supplementation on left ventricular function in HF patients.

Methods: This abstract reports the echocardiographic results from a 12 month double-blind, placebo-controlled randomised study in vitamin D-deficient HF patients, allocated to 100 μg vitamin D3 or placebo per day. Echocardiograms
recorded at baseline and after 12 months were analysed by a physiologist blinded to allocation and date. Changes in echocardiographic variables between the groups were compared using unpaired t-tests.

**Results:** 54 patients (44 men), mean age 72, SE (1.3) years were recruited; due to death (3) and withdrawal (3), 48 completed the study (25 in intervention group and 23 in placebo group). Baseline clinical variables were comparable between the groups. After 12 months, vitamin D levels in the intervention group increased significantly compared to the placebo group (96.19 ng/mL versus 1.01 ng/mL; p = <0.001), with no adverse effect on any biochemical marker including calcium. At 12 months there were statistically significant differences in change in systolic and diastolic LV volumes (mean reductions of 11.25 mls and 6.08 mls respectively (p=0.007 and p=0.015) (figure 1)), in LV end systolic diameter (−4.46 mm; p=0.047) between groups and a trend towards increased LVEF in the vitamin D group.

**Conclusion:** Twelve months of vitamin D supplementation improved LV systolic and diastolic volumes in patients with HF and vitamin D deficiency.

**P3769 | BENCH**

Treatment with ranolazine attenuates cardiac hypertrophy and contractile dysfunction in a murine model of heart failure induced by chronic beta-1-adrenergic stimulation

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**Background:** Chronic stimulation of the β1-adrenergic pathway, as in mice over-expressing the beta-cardiac adrenergic receptor (β1-OE), leads to cardiac hypertrophy and heart failure. Changes in Ca2+ handling at an early stage play a pivotal role. Relaxation of cardiomyocytes is impaired due to slower Ca2+ removal via the Na+/Ca2+ exchanger (NCX) related to higher cytosolic Na+ levels. Therefore we investigated the influence of Na+ via the late component of the Na+ current (Iray) in an early stage of the disease and evaluated the effect of a chronic therapy with ranolazine, a selective blocker of the Iray current on cardiac hypertrophy and dysfunction.

**Methods:** Single left ventricular (LV) myocytes were isolated from young (8–12 weeks) male β1-OE mice (N=4) and wild-type controls (WT, N=6). The late component of the Na+ current (Iray) was measured as end of pulse current sensitive to 30 μM tetrodotoxin, normalised to cell capacitance. Moreover 6 weeks old male β1-OE mice were treated with 30mg/kg body weight (BW)/day per os ranolazine (10 mg/kg/day, CTRL, N=18) or vehicle (CTRL, N=20) from 2 weeks and were also compared to WT CTRL (N=15). Pressure volume measurements and echocardiography were performed at the end of the chronic treatment period. After sacrifice, organ morhophy, LV hypertrophy, and LV cardiomyocyte function were determined.

**Results:** In young β1-OE mice, Iray was significantly increased (−0.063±0.018 pA/pF in WT, n=9 vs. −0.149±0.034 pA/pF in β1-OE, N=10; p<0.05) as well as the integrated current (85±17 pC/pF in WT, n=9 vs 138±17 pC/pF in β1-OE, n=10; p<0.05). In 6 month old mice, weight/BW (HW/BW), LV mass and lung volume/LW/BW (BW) were significantly increased in β1-OE compared to WT. LV end-systolic pressure (ESP), dp/dtmax and dp/dtmin were decreased whereas LV end-diastolic pressure (EDP) and LV isovolumetric relaxation constant tau (IvRC) were increased. Chronic ranolazine treatment significantly attenuated HW/BW, LV mass as well as LW/BW in β1-OE, significantly decreased LVEDP. IvRC, Tau and improved dp/dtmax and dp/dtmin. Cardiomyocytes from 6 months old β1-OE mice showed significantly elevated Ca2+ transient amplitudes (CaT) at 1 Hz and 0.5 Hz stimulation with a prolongation of the CaT decay (0.5 Hz compared to controls). Ranolazine did not influence the amplitude of the CaT but normalized the prolonged CaT decay in β1-OE cardiomyocytes.

**Conclusion:** Early elevated cytosolic Ca2+ was related to increased Na+ influx via Iray. Chronic treatment with ranolazine improves cardiomyocyte Ca2+ transients, adverse remodeling and cardiac function in this heart failure model.

**P3770 | BENCH**

Efficacy of long-term ivabradine therapy on prognosis, left and right heart functional parameters in patients with chronic heart failure and preserved left ventricular systolic function

K.G. Adamyan, L.R. Tumasyan, A.L. Chillingaryan, L.G. Tunyan, Institute of Cardiology, Yerevan, Armenia

The aim of study was to assess the efficacy of long-term ivabradine (i, 15 mg) therapy on prognosis, left (LV) and right ventricular (RV), left (LA) and right (RA) atrial parameters, NT-pro-BNP and hsCRP levels in pts with III NYHA FC CHF and preserved LV ejection fraction (PVE).

**Methods:** 104 pts (age 63.2) with CHF and PEF were randomly assigned to groups A (n=53, non receiving I) and B (n=51, receiving I) in addition to ACE inhibitors, beta-blockers and diuretics. Deceleration time of transmitial (DTm) and transtricuspidal (DTt) E waves, E/A ratio of transmitial flow (E/A), RV fractional area change (FAC), tricuspid annulus plane systolic excursion (TAPSE), pulmonary artery (PA) ejection (ET) time, RA and LA fractional contribution (FC), functional Q index (FI), relation of pulmonary vein (PV) systolic and diastolic fractions (S/D), systolic contribution (SC), difference between duration of reaerial flow arterial (Ar) and late (A) transmitial filling, NT-pro-BNP and CRP levels were assessed at baseline, 12, 24 and 36 months.

**Results:** 1, 2- and 3-year mortality were 34%, 43.1% and 50.9% and 25.5%, 33.3% and 37.2% in groups A and B, respectively. Event-free analysis showed lower probability (RR reduction) of 1-, 2- and 3- year mortality at 25.1%, 22.7% and 26.7%, respectively, in group B compared to A (p<0.05). 1-year I treatment increased RV FAC at 28.5%, TAPSE at 42.1%, DTt at 32.1%, PA ET at 17.9%, RA and LA at 48.8% and 46.7%, FC at 28.2% and 29.3%, PV SD at 35.2%, SC at 39.9%, E/A at 51.1%, decreased Ar-A at 82.7% and 80% were associated with significant improvement of prognosis compared to decrease of NT-pro-BNP >30%, CRP >20% and HR >15% (RR 0.33, 0.33 and 0.32, p<0.01, respectively). Similarly, changes of RA and LA FI, PV SC ≥50%, RA and LA FC, RV FAC, DTt, PAET ≥25% and Ar-A and Dm >80% were associated with significant improvement of prognosis.
compared to changes of RA and LA FL, PV SC−30%, RA and LA FC, RV FAC, DT, PAET −15% and ArA and DTm −60% (RR 0.37, 0.36, 0.35, 0.34, 0.36, 0.37, 0.35, 0.34, 0.35 and 0.33, p < 0.01), respectively.

Conclusions: 1) Decrease of NT-pro-BNP: >50%, ArA >80%, CRP >40%, HR >25% and increase of DTm >80%, RA and LA FC, PV SC >50%, RA and LA FC, RV FAC, DT and PAET at 25% identified pts with cardiac risk reduction. 2) Use associated with lower mortality and morbidity due to significant improvement of LV, RV, LA and RA functional parameters, neurohormonal and inflammation status and HR reduction.

Results: Across studies, 337 pts received ZS-9 tid in the acute phase: 50% had mild, 37% moderate, and 13% severe HK. In pts with severe HK, significant K+ reduction occurred immediately (1 hr) after initial ZS-9 dose (Figure). After 48h of ZS-9 treatment, K+ reduction was greater in pts with severe HK (1.5 mmol/L; 23.2%) compared to mild (0.78 mmol/L; 14.7%) and moderate (1.2 mmol/L; 20.5%); P < 0.0001, all comparisons).

Conclusions: ZS-9 rapidly reduced serum K+ in pts with severe HK, who had significantly greater K+ decline than pts with milder HK, suggesting ZS-9 may reduce K+ to a greater amount in highest risk pts. Pending further studies in the emergency setting, these findings suggest ZS-9 may be an attractive therapeutic option in management of severe HK.

Acknowledgement/Funding: Supported by ZS Pharma, Inc., Coppel TX, USA.

P3773 | BENCH

Does higher stimulation dosage in cardiac contractility modulation increase patient outcome? Data from the FIX HF 13 Trial

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Aims: Cardiac contractility modulation (CCM) signals are non-excitatory electrical signals delivered during the absolute refractory period intended to improve contraction and cardiac function. Clinical trials have shown that CCM treatment significantly improves exercise tolerance and quality of life in symptomatic heart failure patients.

Studies with CCM therapy typically include CCM delivery for 3, 5 or 7 hours per day, although other configurations are also commonly used. Each has been associated with improved outcomes in heart failure, but it is not clear whether different application durations are associated with different degrees of benefit. The purpose of the current study was to evaluate quality of life, exercise tolerance, and cardiac function, over a 6 month period when CCM was delivered for 5 hours/day vs. 12 hours/day.

Methods: This single center study involved 19 medically refractory symptomatic patients with heart failure and reduced LV function who underwent implantation of an Optimizer™ system. Patients were randomized into one of two treatment groups: 5 hours/day CCM treatment or 12 hours/day CCM treatment. Subjects and evaluating physicians were blinded to study group. Subjects returned to the hospital after 12 and 24 weeks for evaluations. Efficacy was measured in terms of changes in MWHFQ, Peak VO2, NYHA, 6 min W, and EF.

Results: At the end of 24 weeks, clinical improvement was observed in the entire cohort in all efficacy measures (mean change from baseline of −17.1 in ML-WHFQ, −0.86 in NYHA, and improvement trend of 1.48 ml O2/kg/min in Peak VO2; 31.25 in 6 min W, and 2.25% in EF). There were no significant differences, either clinically or statistically, between the groups receiving CCM for 5 vs. 12 hours/day.

Conclusions: Together with previously reported experience with CCM, delivery of CCM therapy is safe and effective over the range of shorter (5 hours) to longer (12 hours) daily periods of application.

P3774 | BEDSIDE

Safety and efficacy of G-CSF and autologous bone marrow-derived cells in ischaemic cardiomyopathy: Results of the REGENERATE-IHD Phase II trial


Aims: The effect of combined cytokine and cell therapy in ischaemic cardiomyopathy is unknown. Meta-analyses suggest improved cardiac function with cell therapy. The optimal cell delivery route remains unclear. We investigated whether granulocyte-colony stimulating factor (G-CSF) alone or in combination with intramyocardial (IC) or intramyocardial (IM) injection of autologous bone marrow-derived cells (BMC) improves cardiac function.

Methods and results: 90 patients with symptomatic ischaemic cardiomyopa- thy and no further treatment options were enrolled in the randomised, placebo-
controlled, single-centre study. Randomisation was to 1 of 3 arms: peripheral, IC or IM. In each arm, patients were randomised to active treatment or placebo. All patients, except 5 patients in the peripheral placebo group (saline only) received G-CSF for 5 days. The IC and IM arms received either BMC or serum (placebo). The primary endpoint was change in intramyocardial cell infiltration (IC) and intramyocardial cell infiltration (IM) arms. Only the IM BMC group showed a significant improvement in LVEF: 4.99% (95% CI 0.33–9.6%; p=0.038) at 1 year. This group also showed a reduction in NYHA class at 1 year and a fall in NT pro-BNP at 6 months. None of the other groups showed a significant change in LVEF.

Conclusion: We have shown that G-CSF combined has no effect in patients with ischemic cardiomyopathy. However, G-CSF combined with autologous BMC, when delivered intramyocardially, had a beneficial effect on cardiac function and symptoms. Given the lack of treatment options for this patient group, a clinically driven outcome study is warranted.

P3775 | BEDSIDE
Chronic vagus nerve stimulation reduces cardiac electrical instability assessed by quantitative T-wave alternans analysis and suppresses ventricular tachycardia in heart failure patients
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Introduction: Autonomic regulation therapy (ART) by way of chronic vagus nerve stimulation (VNS) improves ventricular function in heart failure (HF) patients, but its effects on cardiac electrical instability remain unknown.

Purpose: Effects of ART on T-wave alternans (TWA), a marker of cardiac electrical instability and risk for life-threatening arrhythmias, were studied in patients with chronic, symptomatic HF and reduced ejection fraction enrolled in the ANTHEM-HF study (NCT01823887).

Methods: TWA quantified using modified Moving Average method and ventricular tachycardia (VT) incidence were assessed in 24-hour ambulatory ECG recordings. Measurements were made prior to ART system (Cyberonics, Inc., TX) implantation involving the left or right vagus nerve, and after 6 months of therapy (10 Hz, 250 μs pulse width, 18% duty cycle, maximum tolerable current amplitude after 10 weeks of titration). Effects of low (<2 mA, n=9) vs high-intensity (≥2 mA, n=11) stimulation levels were investigated.

Results: TWA levels were 68±5 μV at baseline (abnormal: >47 μV). After 6 months, TWA amplitude increased with low-intensity VNS and decreased with high-intensity VNS, and the change was significantly different between the two groups (29±17 vs. 14±5 μV, p=0.026). Figure shows typical QRS-aligned TWA template response to VNS. The occurrence of VT was also lower in the high-intensity group (2 patients vs. 4, p=0.039).

Conclusion: High-intensity chronic VNS in patients with symptomatic HF can decrease cardiac electrical instability, as reflected in reduced TWA levels and suppression of VT. These findings underscore the importance of appropriate VNS parameter selection to optimize the potential benefits of ART.

Acknowledgement/Funding: Cyberonics Inc., Houston USA

P3777 | BEDSIDE
Tolvaptan in patients with acute decompensated heart failure, could reduce renal worsening from randomized controlled trial two
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Background: Prevention of worsening renal function (WRF) is very important in the treatment of acute decompensated heart failure (ADHF). Tolvaptan is known to induce free water diuresis without impairing renal function. However, its clinical efficacy for patients with ADHF remains controversial. We evaluated the effects of tolvaptan on the renal function in ADHF patients with volume overload.

Methods: We enrolled 105 patients with ADHF. They were divided to three groups (A group: Conventional therapy only (including lupus, thiazide and carper- tile), B group: Conventional therapy with 7 days of administration of tolvaptan 7.5mg/day, C group: Conventional therapy with 7 days of administration of tolvaptan 15mg/day.) We evaluated the rate of changes of serum creatinine, eGFR, WRF, body weight, daily urine volume, serum sodium, serum potassium. We defined WRF as the serum creatinine increase ≥0.3 mg/dL between admission and 15th hospital day.

Results: Urine output in 48 hours after admission was significantly higher in the both tolvaptan groups than the conventional groups. Serum creatinine elevation was 0.17. 0.10. 0.03 in the group A, B, C respectively. Incidence of WRF was significantly lower in the tolvaptan groups (B: 8%, B plus C: 12%) than in the conventional therapy group A; 33% (P=0.02) in the group B (P<0.03) by Paired T test).

Conclusion: Additional treatment with tolvaptan could prevent WRF in patients with ADHF.
Effects on beta-blockers on heart failure with preserved ejection fraction; from the Korean Acute Heart Failure (KoA HF) registry

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Background: Beta-blockers are indicated in patients with heart failure with reduced ejection fraction. However, the efficacy of these drugs in patients with heart failure with preserved ejection fraction (HFpEF) is uncertain.

Purpose: To investigate the hypothesis that beta-blockers are associated with reduced adverse events in patients with HFpEF.

Methods: The KoA HF is a prospective observational multicentre cohort study. Patients hospitalized for acute heart failure syndrome in 10 tertiary university hospitals across the country have been consecutively enrolled 5,660 patients between March, 2011 and February, 2014. Of these patients, 2,152 patients with HFpEF (ejection fraction ≥ 40%) were investigated. We compared adverse outcomes (all-cause death, rehospitalization, a composite of all-cause death and rehospitalization) with the use of propensity-score matching and the inverse probability of treatment weighting (IPTW).

Results: Median follow-up in HFpEF was 139 days. In the overall HFpEF cohort, beta-blockers were not associated with all-cause death (hazard ratio [HR], 0.86; 95% confidence interval [CI], 0.51–1.40) but significantly associated with reduced rehospitalization (HR, 0.75; 95% CI, 0.59–0.94). In the propensity-score matching cohort, beta-blockers were not associated with all-cause death (HR, 0.76; 95% CI, 0.57–1.30) but significantly associated with reduced rehospitalization (HR, 0.75; 95% CI, 0.59–0.94) and a composite outcome (HR, 0.74; 95% CI, 0.60–0.94).

Conclusions: In Korean patients with HFpEF, use of beta-blockers was not associated with lower all-cause death but with lower rehospitalization.

Acknowledgement/Funding: The Korea National Institute of Health
Purpose: We tested the hypothesis that DPP-4 inhibitor reduces adverse cardiac remodeling and left-ventricular (LV) dysfunction in obese-IR rats with MI.

Methods: Rats were fed either normal-diet (ND) or high-fat diet for 12 weeks to induce obese-IR, followed by left anterior coronary artery ligation to induce MI. Then, rats in each dietary group were divided into 5 subgroups to receive vehicle, enalapril (E; 10 mg/kg/day), metformin (M; 30 mg/kg/day), DPP-4 inhibitor vildagliptin (V; 3 mg/kg/day), or combined metformin and vildagliptin (V+M) for 8 weeks. Heart rate variability (HRV), LV function, pathological and biochemical studies for LV remodeling, and myocytes apoptosis were determined.

Results: Obese-IR rats had severe insulin resistance, LV dysfunction, and had a higher mortality rate than the ND group. Although all drugs improved insulin sensitivity, HRV, LV ejection fraction as well as reduced cardiac hypertrophy and fibrosis, vildagliptin effectively reduced myocyte cross-sectional areas more than enalapril (Figs. 4B and 5B) related to markedly decreased p-ERK1/2. In ND rats with MI, metformin neither improved LVEF nor reduced cardiac fibrosis. The infarct size and TGF-β expression were not different among groups.

Conclusion: In obese-IR rats with chronic MI, DPP-4 inhibitor vildagliptin and metformin ameliorated diabetes cardiomyopathy by decreasing LV dysfunction and restoring autophagy via FoxO activation.

P3785 | BEDSIDE

Introduction: Vasoressin promotes the renal and cardiovascular responses to hypotension. Aims: To determine the mechanism of VAS in the setting of severe hypotension with refractory shock.

Methods: An ex vivo model of human microvascular tissue was used. The arterial pressure was decreased in a stepwise manner until a defined level of hypotension was reached. The dose response of vasopressin to hypotension was determined.

Results: Vasoressin was able to increase the arterial pressure in a dose-dependent manner. The maximal response was observed at a concentration of 10^{-6} M. The response was reversed by the specific V1 receptor antagonist, D-tubocurarine.

Conclusions: Vasoressin is a potent vasoconstrictor in the setting of severe hypotension. The mechanism of action involves activation of the V1 receptor.

P3786 | BENCH

Methods: The effects of Bendavia on mitochondrial function were assessed using a mitochondrial function assay kit. The isolated mitochondria were incubated with different concentrations of Bendavia for 30 minutes. The changes in mitochondrial membrane potential and complex I activity were measured.

Results: Bendavia treatment resulted in a dose-dependent increase in mitochondrial membrane potential and complex I activity. The maximum effect was observed at a concentration of 10^{-5} M.

Conclusions: Bendavia improves mitochondrial function, which may contribute to its therapeutic effects in HF.

P3787 | BENCH

Conclusion: Bendavia reduces cross-sectional area in rat heart failure.

P3788 | BEDSIDE

Methods: The study included 50 patients with acute heart failure syndrome (AHFS) who were randomly assigned to either the vasodilator group or the control group. The primary endpoint was the change in 6-minute walk distance (6MWD) from baseline to 24 hours after hospital discharge.

Results: The 6MWD improved significantly more in the vasodilator group compared to the control group (30±5 m vs. 10±3 m, p<0.05).

Conclusions: Vasodilators improve functional capacity in patients with AHFS.

P3789 | BEDSIDE

Introduction: Fractional sodium excretion (FENa) is a strong predictor of response to diuretics in patients with heart failure. Aims: To determine the relationship between FENa and diuretic response in patients with heart failure.

Methods: A total of 100 patients with heart failure were included in the study. FENa was measured before and after diuretic treatment. The relationship between FENa and diuretic response was assessed using linear regression analysis.

Results: The FENa before diuretic treatment was 0.8±0.2%, and the FENa after diuretic treatment was 0.6±0.2%. The diuretic response was significantly higher in patients with lower FENa (r=0.6, p<0.01).

Conclusions: Low FENa is associated with a better diuretic response in patients with heart failure.
fur 125 mg (14 pts.), fur 250 mg (13 pts.) and fur 500 mg (9 pts.). Fur diluted in 150 ml of normal saline (initial) and hypertonic saline (after 24 hrs) was infused over 20 minutes. Diuresis, natriuresis, urinary osmolarity and fur urine delivery in all patients and at all detected times. No significant changes in serum sodium,BUN, serum creatinine and creatinine clearance estimated by MDRD formula were observed while body weight decreased significantly (p<0.0001). Furosemide concentration increases over time and was observed to rise into urine at all different doses when dilute in HSS. In 31 pts (86%), curves fit with sigmoid function (ALLFIT) confirming that HSS addition to fur. have positive effects on diuresis and natriuresis.

**Furosemide Dose response curves**

**Conclusion:** This study demonstrates that addition of HSS to high dose fur. improves fur dose response curves, total diuresis, and natriuresis in acute HF. These results serve as pathophysiological basis of an innovative approach to manage acute HF.

**References:**

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- **Mahidol University, Thalassemia Research Center, Institute of Molecular Biosciences, Nakhon Pathom, Thailand**

**Background:** Iron overload cardiomyopathy is an important complication and responsible for high mortality rate in β-thalassemia major and hereditary hemochromatosis patients. Currently, 3 available iron chelators for clinical use including parenteral iron chelator deferoxamine (DFO), and 2 oral iron chelators including deferoxamine (DFP), and deferasirox (DFX) are used to prevent iron-overloaded complications. Since their effective chelating effects, there are no reports on head-to-head comparison regarding the efficacy of these 3 iron chelators on cardiac function in iron-overloaded rats.

**Purpose:** To compare the therapeutic effects of DFO, DFP, and DFX on the iron accumulation and cardiac function in iron-overloaded rats.

**Methods:** Iron overload condition was induced in male Wistar rats by high iron (HFe) diet consumption for 4 months. At 2 months, iron-overloaded rats were divided into 4 groups (n=6/group) to receive treatment with DFO, DFP, DFX, or control (HFe) diet consumption for 2 months. Cardiac structure, left ventricular (LV) function, heart rate variability (HRV), and cardiac iron concentration were determined.

**Results:** Iron-overloaded rats had increased cardiac iron deposit and decreased %LV fractional shortening (%LVFS) compared with the normal diet control group. All 3 iron chelators exerted similar efficacy in reducing cardiac iron deposit (Fig A) and improving HRV and LV function in iron-overloaded rats (Fig B).

**Conclusion:** DFO, DFP and DFX treatments were effective in reducing cardiac iron deposit, and improving cardiac autonomic balance as well as LV function in iron overload cardiomyopathy.

**Acknowledgement/Funding:** A NSIDC Research Chair Grant (NC), the Thailand Research Fund RTA5580006 (NC), BRG5780016 (SC), Chiang Mai University Center of Excellence Award (NC)

**HEART FAILURE THERAPY, VARIOUS V**

**P3787 | BEDSIDE**

**Different impacts of statin therapy on clinical outcomes in acute decompensated heart failure patients with or without ischemic cardiomyopathy**

J.Y. Cho1, K.H. Kim1, Y. Ahn1, E.S. Jeon1, J.J. Kim1, S.C. Chae4, S.H. Baek1, S.M. Kang1, D.C. Cho1, B.H. Oh1 on behalf of KorAHF investigators.

**Background:** It remains unclear whether statin treatment benefits the patients with heart failure (HF) in terms of clinical outcomes. The aim of this study was to evaluate the effectiveness of statin treatment on HF in patients with various comorbid conditions including ischemic cardiomyopathy and acute coronary syndrome.

**Methods:** A total of 4,183 patients (68.7±14.5 years, 2,252 males) from 10 regionally-representative tertiary university hospitals with acute heart failure (AHF) were consecutively enrolled in Korean AHF registry (KorAHF) between March 2011 and July 2013. They were divided into two groups according to use of statin, statin group (n=1,695, 70.4±12.4 years, 939 males) vs. non-statin group (n=2,488, 67.5±15.6 years, 1,313 males). Adverse clinical events including all cause death, and rehospitalization at short-term follow-up were compared between the groups.

**Results:** Adverse clinical events were developed in 1045 patients (25.0%); 186 deaths (4.4%), 955 rehospitalizations (22.8%). The development of short-term adverse events were not different between the groups (28.1% vs. 29.1%, p=ns). In subgroup analysis between AHF patients with and without ischemic etiology, however, the use of statin reduced composite adverse events only in ischemic etiology (27.4% vs. 34.1%, p=0.033 by log-rank test), but did not in non-ischemic one (Fig 1).

**Conclusion:** Overall, the use of statin failed to show favorable effect on short-term clinical outcomes in Korean patients with AHF. However, the use of statin showed favorable effect in AHF patients with ischemic etiology. These results suggested that statin therapy may be useful in treatment of this category of patients.

**Acknowledgement/Funding:** This work was supported by a grant from Korea Centers for Disease Control and Prevention.

**Figure 1. Event-free survival between groups**

**P3788 | BENCH**

**GH differentially modulates skeletal muscle proteins in rats with aortic stenosis-induced heart failure**


Although chronic heart failure is usually associated with skeletal muscle atrophy, the physiopathological mechanisms involved in muscle mass loss are not completely established. Growth hormone (GH) has anabolic effects. It stimulates IGF-1, which activates the PI3K/Akt pathway to inhibit atrogin-1 and MuRF-1. GH can also modulate myogenic regulatory factors and myostatin and follistatin expression as well as satellite cell activation. However, the effects of GH on skeletal muscle preservation during catabolic diseases are not well understood. In this study we evaluated the effects of GH on trophicity and the intracellular signaling pathways involved in the atrophy process in peripheral skeletal muscles of rats with aortic stenosis (AS)-induced heart failure. After heart failure detection, GH was administered for 14 days (AS-GH group). Results were compared...
with those from Sham and non-treated AS groups. Transthoracic echocardiogram was performed before and after treatment. Tropilicin was analyzed in solesus and white part of gastrocnemius muscles. Protein expression was evaluated by Western blot and satellite cell activation by immunofluorescence. Statistical analyses: ANOVA and Tukey or Kruskal-Wallis and Student-Newman-Keuls. Before treatment, AS, Sham, and HFS groups presented similar echocardiographic parameters. GSH attenuated systolic dysfunction. Gastrocnemius fiber cross-section areas did not differ between groups; soleus fiber cross-section areas were lower in both AS groups than Sham. In gastrocnemius, MRF-4 and atrogin-1 were higher in AS and AS-GH groups. GH attenuated MRF-4 increase. Immunofluorescence showed that staining with anti-neural cell adhesion molecule (NCAM) and anti-neoantial myosin heavy chain isoform was statistically more intense in AS-GH than AS and Sham. In soleus, GH activated IGF-1 and PI3K proteins; NCAM immunofluorescence was increased in both AS groups. In conclusion, GH treatment attenuates left ventricular systolic dysfunction in rats with aortic stenosis-induced heart failure. GH administration for 14 days does not change skeletal muscle tropilicin. However, GH differentially modulates expression of proteins involved in satellite cells activation and muscle atrophy. In preferably glycolytic muscles (gastrocnemius), GH activates satellite cells and attenuates MyOd expression increase. In predominantly oxidative muscles (soleus), GH activates IGF-1 and PI3K protein expression.

P3789 | BEDSIDE Clinical, biochemical and echocardiographic phenotyping of patients with cardiac dysfunction stratified according to prescription of loop diuretics
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Background: Congestion due to cardiac dysfunction is an important cause of symptoms and signs of heart failure. Diuretics are the mainstay of treatment for congestion. Patients treated with loop diuretics have a worse prognosis but whether this is because of their association with congestion or because they cause adverse neuroendocrine activation is uncertain.

Aim: To explore whether the relationship between loop diuretic use and outcome is explained by underlying evidence of congestion amongst patients referred for diagnosis and management to a heart failure clinic.

Results: Of 1190 patients enrolled, 979 (82%) had cardiac dysfunction (either a reduced left ventricular ejection fraction (LVEF < 50%) or raised plasma NT-proBNP > 1000 ng/l; 350 (18%) did not). Of those with or without cardiac dysfunction, 71% and 37% respectively were prescribed loop diuretics.

Patients with cardiac dysfunction taking diuretics were older, had more evidence of congestion [more severe symptoms and signs, higher NT-proBNP (320 ml/40 mg furosemide). Patients with low 24hDR and more signs of congestion, lower systolic blood pressure (SBP) and more comorbidities, namely renal dysfunction, at admission. Although patients with low 24hDR were treated with significantly higher doses of furosemide and more frequently inotropes, they had higher levels of NT-proBNP at discharge (3139 ng/ml vs 2018 ng/ml, p<0.001). In a linear regression model the predictors of the 24hDR were SBP, renal function, and signs of congestion at admission. Low 24hDR was associated with higher in-hospital mortality and worsening renal function. The incidence of the primary endpoint was significantly higher in the low 24hDR group (p<0.001, Figure 1).

In a multivariable model, 24hDR was an independent predictor of long-term events [HR 0.60 (0.37–0.96), p=0.032] and resulted superior to 5DDR.

Conclusions: DR at 24 hours is a predictor of long-term events in patients with AHF. Further studies are needed to investigate the possible role of this parameter to optimize diuretic strategy.

P3791 | BEDSIDE Impact of loop diuretic infusion modalities on congestion signs and outcomes in patients with acute heart failure
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Background: Intravenous loop diuretics are the cornerstone of therapy in acute heart failure (AHF). However there are poor data regarding the relation between diuretic modality administration and the effects on decongestion as well the acute clinical impact.

Purpose: We sought to determine if there are any differences in decongestion signs and clinical outcomes between intravenous intermittent (IV) and continuous infusion (Civ) of loop diuretics. Therefore we aim to evaluate the effects of two modalities administration on worsening renal function (WRF) and B-type Natriuretic Peptide (BNP) reduction.

Methods: Subjects with AHF within 12 hours of hospital admission were randomly assigned to continuous infusion or twice daily bolus therapy with furosemide. There were 2 co-primary endpoints: persistence of 2 or more congestion signs at the end of hospitalization treatment, and clinical outcome during six months follow-up post discharge period.

Results: 51 patients received Civ and 46 received IV. At discharge, the persistence of congestion signs in the Civ was higher than Civ (38% versus 14%; p=0.009). After treatment, the mean change in weight loss (∼3.6±2.9 kg vs 2.7±2.5 kg vs 0.01) and the mean urine output (251±730 ml vs 225.4±551 ml vs 0.04) were higher in the Civ group than IV. There was no significant difference in the reduction in BNP over the hospital course. Finally, the rate of WRF was higher in the Civ group compared to IV (39% vs 15% p=0.01). 6 months follow up analysis demonstrated an higher rate of re-admission or death in the Civ (54% versus 28%, p=0.011). Univariate and multivariate analysis are showed in table 1.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rehospitalization or death</th>
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<tbody>
<tr>
<td></td>
<td>Univariate</td>
</tr>
<tr>
<td>BNP <strong>A</strong></td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>Creatinine <strong>A</strong></td>
<td>3.17 (1.98–5.08)</td>
</tr>
<tr>
<td>Persistence of congestion</td>
<td>2.19 (1.09–4.38)</td>
</tr>
<tr>
<td>Continuous vs bolus</td>
<td>3.43 (1.64–7.15)</td>
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Conclusions: In ADHF, Civ of loop diuretics resulted in greater reductions of congestion signs despite an increased rate of WRF. In hospital WRF and continuous infusion appeared both associated with poor outcome.

P3792 | BEDSIDE Efficacy of addition of ivabradine to bisoprolol in patients with essential hypertension, coronary artery disease and reduced left ventricular systolic function
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Objective: Essential hypertension (EH) and coronary artery disease (CAD) contribute synergistically to high cardiovascular risk. The aim of this study was to...
compare the efficacy of treatment with combined beta-blocker Bisoprolol (B) and If inhibitor Ivabradine (I) or beta-blocker B monotherapy in patients with EH, CAD and left ventricular (LV) systolic dysfunction.

Methods: Fifty two patients with mild EH, documented CAD and LV systolic dysfunction (ejection fraction-EF=35% or lower), who were in sinus rhythm and with a resting heart rate >70 beats/min., were treated with B at a constant dose (5 mg once a day) for 30 days or longer. 26 patients, aged 51–62 years (group A), were randomly assigned to receive 5 mg of I twice daily; 26 patients, aged 49–61 years (group B), were treated only with B until the end of the study. Echocardiography was performed at baseline and after 6 months of therapy. Parameters of LV systolic function [EF, endocardial and midwall fractional shortening (end FS and mid FS)] were calculated. Differences in the efficacy parameters were analysed using 2-tailed Student’s t test for quantitative parameters.

Results: At the end of the study blood pressure was lowered in both groups to less than 140/90 mm Hg. Mean number of anginal attacks per week decreased by 38.6% in group A (p < 0.001) and by 23.1% in group B (p < 0.01). EF increased in group A (p < 0.001) from 34.1±1.1% to 37.4±1.2%, in group B (p < 0.01). End FS and mid FS also increased at the end of the study in both groups (p < 0.001). 35.3±1.2 vs 24.8±1.3% and 20.4±0.6 vs 16.3±0.5% in group B, respectively. The combined therapy with B and I showed greater effects on clinical symptoms of CAD and LV function compared to monotherapy with B in patients with EH and CAD. Treatment with I is associated with significant improvement in all parameters of LV systolic function.

P3793 | BEDSIDE

Sodium zirconium cyclosilicate (ZS-9) for hyperkalaemia treatment: efficacy and tolerability in heart failure patients on renin-angiotensin-aldosterone system inhibitors (RAASI) in a phase 3 study

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Background: Renin-angiotensin-aldosterone system inhibitors (RAASI) increase the risk of hyperkalaemia (HK; serum K+ >5.3 mmol/L) in the general population. In patients with heart failure (HF), HK may be transient and does not appear to impact survival. In patients failing to wean following cardiothoracic surgery treated with iNO, the presence of PH may be transient and does not appear to impact survival.

Methods: From a single-institution database of 177 patients receiving iNO for failure to wean after CTS, 121 had echos performed after surgery and prior to initiation of iNO. PH was defined by estimated right ventricular systolic pressure (RVSP) ≥ 35 mmHg. In-hospital mortality was compared based upon the presence of PH.

Results: PH was present in 51% of the cohort. PH patients were similar to non-PH patients with respect to age, demographic features, cardiovascular morbidities and operative interventions. RVSP was expectedly higher in the PH cohort (69±16 vs 35±8 mmHg, p < 0.001). Patients received iNO for an average of 82±62 hours, with no difference based upon the presence of PH. Among patients with echo during iNO administration, drop in RVSP was similar in both groups. Survival among patients based on the presence of PH was also remarkably similar (Graph). Pre-discharge echos were available in 98 patients and demonstrated greater median RVSP decrease in the PH population (24 vs. 3 mmHg, p < 0.001), suggesting that PH was transient and reversible in most of these patients.
BLOOD PRESSURE, MONITORING VARIABILITY AND ARTERIAL STIFFNESS

P3796 | BEDSIDE
Classification of blood pressure by office and ambulatory readings in hypertensive type 2 diabetic patients—results of the German T2Target registry in primary care
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Objective: The target blood pressure for hypertensive patients with type 2 diabetes (age 64±12.3 years) with treated hypertension was obtained using validated monitors. Corresponding values of office and day-time-ABPM values were calculated by the percentile method. ABPM recordings were analysed by a central, independent and blinded reference centre according to recent ESH guidelines.
Results: Mean office blood pressure was 151.7±19.6/87.5±11.5 mmHg. ABPM daytime values were 141.3±15.2/81.8±10.2 mmHg, night-time values were 131.1±18.3/72.6±11.1. During night-time 285 patients showed non-dipping and 138 patients showed normal nocturnal hypertension. Masked white-coat hypertension was more common (14%) than white-coat hypertension (8%). As assessed by office blood pressure isolated systolic hypertension (ISH) was more common than combined systolic/diastolic hypertension. However, with ABPM combined systolic/diastolic hypertension was the predominant form of hypertension. Corresponding ABPM values for stage 1 hypertension (day-time: 134/86 mmHg) and stage 2 hypertension (day-time: 151/96 mmHg) were in excellent agreement with previously published NICE guidelines. In our study an office target blood pressure for stage 1 hypertension (day-time: 134/86 mmHg) was the predominant form of hypertension.
Conclusions: The non-dipping pattern is less common with ABPM than with office blood pressure measurement.
Acknowledgement/Funding: Servier

P3797 | BEDSIDE
Greater night-time blood pressure variability in acute coronary syndrome patients with more impaired reactive hyperemia index
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Background: Although night-time blood pressure (BP) variability is associated with cardiovascular events, the mechanism is poorly understood. There is little information about the relationship between night-time BP variability and endothelial dysfunction or lipid content of coronary plaque that are important factors of atherosclerosis.
Purpose: The aim of this study was to examine the relationship between night-time BP variability and reactive hyperemia index (RHI) or lipid content of coronary plaque assessed by integrated backscatter intracoronary ultrasound (IB-IVUS).
Methods: We prospectively screened 157 patients with acute coronary syndrome who underwent primary percutaneous coronary intervention. Patients with any unanswerable plaque for IVUS examination were not included. Finally 47 patients underwent ambulatory BP monitoring to evaluate BP variability and measurement of RHI to assess endothelial function. The standard deviation (SD) of systolic BP was used as BP variability. Plaque components of non-culprit coronary plaque in the culprit vessel were determined as lipid, fibrosis, dense fibrosis, and calcification (IB-IVUS).
Results: The mean night-time systolic BP SD and RHI were 11.1 mm Hg and 1.92, respectively. The night-time systolic BP SD showed a trend negatively correlated with RHI (r=−0.30, p=0.06). Additionally, Patients with abnormal RHI (-1.67) had significantly higher night-time systolic BP compared to those with the normal RHI (≥1.67) (13.4±4.9 vs. 10.6±3.8 mm Hg, p=0.05). On the other hand, there was no significant correlation between the night-time systolic BP SD and percentage of lipid plaque volume (r=0.04, p=0.78).
Conclusions: This study indicates that night-time BP variability was associated with endothelial function, which may partly explain a higher incidence of cardiovascular event in patients with greater night-time BP variability.

P3798 | BEDSIDE
Ambulatory blood pressure monitoring in adolescent girls, reproductive-age women and postmenopausal women with obesity
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Excess adiposity is the strongest known risk factor for hypertension (HT). The aim of this study was to compare the characteristics of ambulatory BP (ABPM) among women with obesity and normal body weight of different age groups.
Methods: 382 pts without known history of HT, DM or CVD were included: 111 adolescent girls (54 obese, 15–20 y), 127 reproductive-age (65 obese, 20–40 y), 144 postmenopausal women (77 obese, 40–65 y). Levels of lipids, blood pressure, ESH criteria of left ventricular hypertrophy (LVH), carotid-femoral pulse wave velocity (PWV), LV mass index (LVM), glomerular filtration rate (GFR, EPI) were measured, 24-hour ABPM was performed.
Results: In all groups obese pts had higher rates of HT (39 vs 4; 48 vs 8; 70 vs 32%, p<0.01), higher night SBP than age-matched non-obese pts (p<0.01). In 1st group obese pts had higher day, night pulse pressure (PP), SBP variability and rates of high night SBP (28 vs 0% ,p<0.01). In 2nd group obese pts had higher night DBP, SBP variability, rates of high day DBP, lower night-day BP ratio (p<0.01). In 3rd group obese pts had higher day SBP, day, night DBP and PP, rates of elevated day and night SBP (p<0.01). Obese girls with HT (n=21) had higher levels of HbA1C, dyslipidemia (DLT) than obese girls without HT (p<0.01). In 2nd group obese pts with HT (n=31) had higher rates of abdominal obesity, DLT (p<0.01). In 3rd group obese pts with HT (n=54) had higher PWV (10±3 vs 7±2 m/s, p<0.01, 0.001), LVM, DLP low apoA1 (p<0.01, 0.001). On univariate analysis, in 1st group there was a correlation between day and night SBP and CCA-IMT (ρ=0.40, p<0.001), LVM (ρ=−0.33, p=0.42), day and night DBP and PWV (ρ=0.31, day, and night SBP variability and CCA-IMT (ρ=−0.56, p=0.25), LVM (ρ=−0.47, night systolic variability and PWV (ρ=−0.42, night SBP and eGFR (ρ=−0.31), in 2nd between day and night SBP and PWV (ρ=0.26, p=0.31), LVM (ρ=−0.34, p=0.31); in 3rd between night SBP and LVM (ρ=0.25), night SBP variability and PWV (ρ=0.24), eGFR and day SBP and DBP (ρ=−0.82, p=0.77), night DBP (ρ=−0.77, day SBP variability (ρ=−0.71), p=0.05).
Conclusion: Female pts with obesity have higher rates of undiagnosed HT. High levels of night SBP seem to be a distinguishing feature of obesity. ABPM allow to find out elevated night-time BP and BP variability, which are associated with asymptomatic organ damage (heart, blood vessels, kidney). ABPM is an important adjunct to conventional office BP measurement and should be used for screening and diagnosis of HT in all age groups of female patients with obesity. Adolescent girls with obesity represents an important group for screening of nocturnal HT.

P3799 | BEDSIDE
Multiple office blood pressure measurement is not inferior to home blood pressure monitoring compared with 24-hour ambulatory blood pressure monitoring: a prospective multicenter study
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Background: It is not well known the difference of office machine blood pressure measurement (AOBP), home blood pressure monitoring (HBPM), or doctor’s manual BP measurement (DBPM), compared with 24-hour ambulatory blood pressure monitoring (ABPM) as a standard reference for the diagnosis of hypertension.
Purpose: The authors prospectively compared DBPM, AOBP and HBPM with ABPM at Ambulatory blood pressure monitoring under controlled circumstances by a well-trained nurse. HBPM (WatchBP Home, Microlife, Switzerland) was measured for 7 days. The 24-hour ABPM (Mobil-O-Graph, IEM GmbH, Germany) was measured on the 7th day after HBPM.
Results: Compared with ABPM, mean systolic BP was higher in DBPM (152.6±14.3 mmHg vs. 132.7±12.5 mmHg, p<0.001), AOBP (141.6±12.4 mmHg vs. 132.5 mmHg, p<0.001) and HBPM (137.8±12.5 mmHg, p<0.002) in order. However, correlation coefficients (r) of systolic BP, DBPM, AOBP and HBPM with ABPM were 0.25 (p<0.001, 95% confidence interval (CI): 0.13 - 0.36), 0.73 (p<0.001, 95% CI: 0.66–0.78), and 0.55 (p<0.001, 95% CI: 0.46–0.63), respectively, suggesting the best correlation between AOBP and ABPM. Bland-Altman analyses showed mean bias of −13.9% with 95% limits of agreement extending from −35.0 to 7.3% in DBPM, mean bias were −6.6% and −1.7%, 95% limits of agreement were −19.8 to 6.6% and −17.4 to 13.9%, in AOBP and HBPM, respectively (Figure 1).
Conclusion: Multiple measurement of AOBP under controlled circumstances by a well-trained healthcare personnel is easy and comparable to HBPM compared with ABPM.
Blood pressure, monitoring variability and arterial stiffness 675

Methods: Our study included 100 subjects: 34 normotensive (19 male, mean age 53.4±6.9 years), 33 dipper (18 male, mean age 54.4±11.7 years) and 33 non-dipper (12 male, mean age 56.7±9.7 years) newly diagnosed HT patients. Vitamin D and PTH levels of hypertensive dipper and non-dipper patients and normotensives were compared, factors affecting non-dipper BP were analyzed.

Results: Mean log (vitamin D) level was significantly lower in non-dipper patients than that of dipper and control groups (0.8±0.3 ng/ml, 1.0±0.3 ng/ml and 1.0±0.4 ng/ml respectively, p<0.001). Mean log (PTH) level was significantly high in non-dippers than that of dipper and control groups (1.9±0.3 pg/dl, 1.7±0.2 pg/ml, 1.7±0.2 pg/dl respectively, p<0.001). Vitamin D levels were negatively correlated with 24-hr systolic and diastolic BP [(r=−0.366, p=0.003), (r=−0.295, p=0.018)], and likewise with all mean arterial pressures (MAP). PTH was positively correlated with systolic and diastolic BP and MAP levels. We found that vitamin D and PTH levels and 24-hr MAP were independent predictors of non-dipper HT.

Table 1. Levels of vitamin D and PTH

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Control (n=34)</th>
<th>Non-dipper (n=33)</th>
<th>Diper (n=33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male [%]</td>
<td>45 [45.0]</td>
<td>15 [44.1]</td>
<td>12 [36.4]</td>
<td>0.335</td>
</tr>
<tr>
<td>Female [%]</td>
<td>55 [55.0]</td>
<td>19 [54.9]</td>
<td>21 [63.6]</td>
<td></td>
</tr>
<tr>
<td>log(VitD) (ng/ml)</td>
<td>1.0±0.4</td>
<td>1.1±0.2</td>
<td>0.8±0.3</td>
<td></td>
</tr>
<tr>
<td>log(PTH) (pg/ml)</td>
<td>1.2±0.1</td>
<td>1.7±0.2</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
</tbody>
</table>

P3801 | BEDSIDE
Ambulatory monitoring derived blood pressure variability is associated with cerebral white matter lesions in elderly hypertensive patients

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Introduction: Cerebral white matter hyperintensities (WMH) are highly prevalent in the elderly population and increase the risk of dementia and stroke. Hypertension is one of the most important factors for WMH progression. According to recent studies, blood pressure (BP) variability is recognized as a cardiovascular risk factor; however, little is known about the association between BP variability and WMH.

Purpose: The purpose of this study is to evaluate the relationship between ambulatory monitoring derived BP variability and WMH volumes among elderly hypertensive patients with controlled office BP.

Methods: This cross-sectional study comprised 81 hypertensive patients aged between 65 and 75 years without symptomatic heart failure, ischemic heart disease, atrial fibrillation, stroke, or cognitive dysfunction. We obtained brain magnetic resonance imaging to quantify the volume of WMH. BP profile was assessed using 24-h ambulatory blood pressure monitoring (ABPM). BP variability was calculated using a standard deviation (SD) of systolic BP.

Results: Linear regression analysis revealed that office BP, Hba1c, LDL, HDL and TG were not associated with WMH volume increases. Raised nighttime systolic BP (p=0.035) was associated with greater WMH volumes as reported previously. Furthermore, higher SD of daytime systolic BP was positively related with WMH volume (p=0.013), but not SD of 24-h and nighttime BP. To clarify the association of blood pressure variability with WMH volume, we classified patients into two SD groups of daytime systolic BP as follows: <17 (n=40) and >17 (n=41). Baseline characteristics were similar in both groups. However, WMH volume was greater in the group with higher SD group (7.86±7.58 ml vs 4.38±4.77 ml, p=0.021).

Conclusion: Ambulatory monitoring derived BP variability was observed to contribute greater WMH volumes in elderly hypertensive patients. Further investigation is required to elucidate whether blood pressure variability can be a potential target for preventing WMH progression.

P3803 | BEDSIDE
How do vitamin D and PTH affect diurnal blood pressure rhythm in newly diagnosed hypertensive patients and normotensives

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Background: Non-dipper hypertension (HT) is a strong predictor of cardiovascular complications. Vitamin D deficiency has been reported to be associated with HT, coronary artery disease and heart failure. Also parathyroid hormone (PTH) excess has been shown to be a predictor of cardiovascular mortality.

Purpose: We aimed to investigate the effects of vitamin D and PTH on diurnal blood pressure variations in newly diagnosed HT and normotensive patients.

P3802 | BEDSIDE
Role of ambulatory blood pressure monitoring in long-term follow-up of gestational hypertension

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Background and aim: Many studies have shown that women with pregnancy complicated by gestational hypertension and preeclampsia have a higher risk of developing hypertension later in life than women with normotensive pregnancy. However, in these studies, the diagnosis of hypertension was made only on the basis of clinical measurements. The purpose of the study was to assess the incidence of hypertension after a long-term follow-up (mean: 8.5 years) in women with previous gestational hypertension, preeclampsia and previous normotensive pregnancy using ambulatory blood pressure monitoring (ABPM).

Patients and methods: We enrolled 150 women who delivered at the Department of Obstetrics of our city hospital between 2002 and 2005: 50 with gestational hypertension, 50 with preeclampsia and 50 with normotensive pregnancy. The inclusion criteria were: pre-existing hypertension, history of diabetes mellitus and cardiovascular events. The groups were matched for age and body mass index. Office blood pressure (OBP) and ABPM were measured in every woman. We collected lipid profile, glucose and creatinine at baseline and follow-up. We collected history of gestational hypertension and preeclampsia developed hypertension more often than women with previous normotensive pregnancies (respectively 56% and 38% vs 20%, p=0.001), confirmed by the Kaplan-Meier analysis (log rank p 0.001). New diagnoses of hypertension made by ABPM were more than those made by OBP (28% vs 12% in gestational hypertension, 26% vs 12% in pre-eclampsia and 20% vs 12% in the control group, p=0.05). It has been found a higher rate of masked hypertension in women with previous gestational hypertension and preeclampsia than in the control group (26% and 24% vs 12%, p=0.07). There were no differences between the groups regarding glucose and lipid profile and renal function neither at baseline nor at follow-up.

Conclusions: ABPM appears a more reliable method than OBP when assessing the presence of hypertension in women with a history of hypertension in pregnancy, given the high incidence of masked hypertension in this setting.
Methods: The study included 503 untreated normotensive and hypertensive subjects who underwent 24-hour ambulatory blood pressure monitoring (ABPM). In all participants, left ventricular mass index (LVMi), mitral pulse-wave Doppler E/A ratio, left atrial (LA) volume and LV end-diastolic diameter (LVEDD) were assessed by echocardiography. Creatinine clearance was estimated by the Cockcroft-Gault formula, while serum cystatin-C and brain natriuretic peptide (BNP) levels were measured by ELISA. INH was defined as nighttime systolic BP > 120/70 mm Hg and systolic BP < 135/85 mm Hg.

Results: Based on ABPM, 15.9% of participants had INH. Notably, INH group compared to normotensive controls exhibited higher values of LVMi (84.5±2.2 vs 74.2±1.1 g/m², p<0.001), while they did not differ regarding LA volume (41.1±1.0 vs 40.5±0.6 ml, p=0.629) and LVEDD (4.6±0.5 vs 4.6±0.3 cm, p=0.742). Also, INH group had decreased E/A ratio compared to controls (1.0±0.4 vs 1.1±0.3, p=0.042). However, serum cystatin-C levels were higher in INH subjects compared to normotensive controls (825±34.7 vs 737±13.5 ng/ml, p=0.004) but the two groups did not differ with respect to BNP levels (22.6±3.8 vs 23.4±2.2 pg/ml, p=0.218). Notably, using linear regression analysis, we found a positive correlation between cystatin-C levels and LVMi (r=0.21, p=0.005) in the group of INH.

Conclusion: According to this study, the presence of INH is accompanied by structural and functional abnormalities of the left ventricle. Cystatin-C, as an early marker of kidney function and a potential contributor to cardiac remodeling, is correlated with LVMi in this under diagnosed high risk population.

P3804 | BEDSIDE
Effect of liver transplant in circadian variation of blood pressure in patients with familial amyloid polyneuropathy
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Patients (pts) with Transthyretin familial amyloid polyneuropathy (TTR-FAP) are at risk of developing progressive heart failure. We sought to investigate the impact of liver transplantation (LT) on the circadian variation of blood pressure (BP)

Methods: 135 liver transplant recipients (M:F=63:72, age 57±12 years) who underwent ABPM for 24 hours before and 1 month after LT.

Results: Before LT, INH was present in 70 pts (52%). After LT, INH was abolished in 52 of these pts, and developed in 3 pts. Abolition of INH after LT was associated with significant reductions in LVMi (84.5±2.3 vs 76.4±2.2 g/m², p=0.01), left atrial volume (40.1±1.1 vs 34.6±0.9 ml, p=0.01), LVEDD (4.6±0.3 vs 4.4±0.2 cm, p=0.04), and systolic BP (135±8/87±6 vs 118±7/74±5 mm Hg, p=0.001).

Conclusion: Liver transplantation can significantly reduce INH and improve left ventricular function in familial amyloid polyneuropathy.

P3806 | BEDSIDE
Reversing the clock of vascular aging: the effect of antihypertensive treatment
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Purpose: Vascular aging, as assessed by structural and functional properties of the arteries, is an independent indicator of cardiovascular risk. Antihypertensive treatment has shown beneficial effects on prognosis. We sought to investigate the effect of different classes of antihypertensive drugs on the progression of vascular aging.

Methods: One hundred and forty-two subjects (mean age 51.9±10.8 years, 94 men, 61 hypertensives) with no established cardiovascular disease were investigated. Two examinations over a 2-year period (mean follow-up visit 1.8 years).

All hypertensives were under treatment for at least 1 year and had well-controlled blood pressure. Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (PWV).

Results: Treatment with angiotensin receptor blockers was associated with slower progression of arterial stiffening after adjustment for relevant confounders [0.033/m/year (95% CI: 0.020 to 0.046), p=0.04] or thiazide diuretics [0.031/m/year (95% CI: 0.018 to 0.044), p=0.002] compared to control.

Conclusion: Angiotensin receptor blockers seem to slow down progression of vascular aging, compared to other classes of antihypertensive drugs. These results warrant further investigation in larger outcome studies.

P3807 | BENCH
The influence of antihypertensive treatment on arterial stiffness, shear stress and activity of chosen matrix metalloproteinases
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Objective: Comparison of therapeutic effects of chosen antihypertensive drugs on arterial stiffness, shear stress in carotid arteries and metalloproteinases activity, moreover analysis of relationship of these variables in the course of treatment.

Design/methods: 71 hypertensive patients found no correlation of DBP and PWV. The patients were randomized to 6 months therapy with: quinapril, amlopidine, hydrochlorothiazide, losartan or bisoprolol. All therapeutic group consisted of 19 patients (N=19). Before and then after 1, 3 and 6 months of treatment carotid-
pulse wave velocity (PWV) by using a Compilor device, ultrasound of carotid arteries were performed. Blood samples for the measurement of whole blood viscosity were taken during each visit. Shear stress (SS) was calculated on the basis of the formula. Serum concentration of metalloproteinase 3 (MMP-3) and plasma concentration of tissue inhibitor of metalloproteinase 1 (TIMP-1) were measured at the initial visit and after 6 months of treatment.

Results: ANOVA for repeated measurements revealed for all groups significant decrease of PWV and MMP-3 concentration and increase of shear stress in carotid artery and TIMP-1 concentration (p < 0.05). No between groups differences appeared in above effects (p > 0.05).

Conclusion: Irrespective of chosen drug we observed similar effect for PWV drop. Reduction of arterial stiffness as a result of antihypertensive therapy is strongly connected with shear stress increase that is secondary to blood flow velocity growth and changes in connective tissue metabolism.

INFLAMMATION AND IMMUNITY

3942 | BENCH
Increased risk of abdominal aortic aneurysm in patients with psoriasis: A nationwide study

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Purpose: Abdominal aortic aneurysm (AAA) is a complex multifactorial disease associated with a high morbidity and mortality. Increased inflammation including cytokines, chemokines, and socioeconomic status was identified by individual-level linkage of administrative registers. Incidence rates for AAA were calculated and incidence rate ratios (IRRs) adjusted for age, gender, comorbidity, medications, and socioeconomic status were estimated in time-dependent Poisson regression models.

Results: A total of 5,108,593 subjects were eligible for analysis. During the study period we identified 60,477 patients with mild psoriasis and 12,285 patients with severe psoriasis. The overall incidence rates of AAA were 3.80, 8.17, and 10.70 per 10,000 person-years for the reference population (25,409 cases), mild psoriasis (272 cases), and severe psoriasis (55 cases), respectively. The corresponding adjusted IRRs for AAA were markedly increased in patients with psoriasis with IRR 1.35 (95% confidence interval [CI] 1.19–1.52) and IRR 1.89 (CI 1.45–2.47) for subjects with mild and severe disease, respectively.

Conclusion: In a nationwide cohort, psoriasis was associated with a disease severity-dependent increased risk of incident AAA. The mechanisms underlying this novel finding require further study.

3943 | BENCH
Oxidized LDL induce tissue factor expression in CD3+ T-lymphocytes: a possible link between immunity, inflammation and thrombosis

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Background: Recent data suggest that inflammation contributes not only to the genesis of the atherosclerotic plaque, but also to its complication, the key event in the pathophysiology of acute coronary syndromes (ACS). Plaque rupture involves exposure of Tissue Factor (TF) within the plaque, which culminates in the formation of an intravascular thrombus. It has been shown that oxidized low-density lipoprotein (oxLDL) induce TF expression in endothelial cells, macrophages, smooth muscle cells. At present, however, is not yet known whether oxLDL may directly induce TF expression in T lymphocytes.

Methods: CD3-positive cells were isolated from buffy coat of healthy volunteers and stimulated with LDL or OxLDL (25, 50 and 100mg/mL). Expression of TF was assessed at 24, 48 hours at gene level and at 72 hours for protein expression after stimulation.

Results: OxLDL induced TF gene expression in T-lymphocytes in a dose dependent manner up to 40 times the baseline value; this resulted in a significant expression of TF protein at 72 hours. LDL had no effect on TF expression in T-lymphocytes. Interestingly, in human carotid plaques obtained at surgery, TF expression co-localized with CD3+, suggesting that T-lymphocytes express TF in vivo.

Conclusions: Our data indicate that oxLDL induce TF expression in T-lymphocytes, suggesting a role for these cells also in the thrombotic process, thus adding a new piece to the complex puzzle of ACS pathophysiology.

3944 | BENCH
Indoleamine 2,3-dioxygenase (IDO) enzyme: linking innate immunity and altered T-cell differentiation in acute coronary syndromes

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Background: Atherosclerosis is a chronic inflammatory disease characterized by complex interplay of innate and adaptive immune responses. Dendritic cells (DC) play a key role in the activation and regulation of T-lymphocyte by presenting antigens to naïve T-cells, which in turn differentiate in effector T-cells, such T helper 1 (Th1), induced regulatory T-cells (iTreg), T helper 17 (Th17) and T helper 2 (Th2). DCs can promote a tolerogenic environment through the production of IL-10 and TGFβ or the expression of the immunosuppressive enzyme indoleamine 2,3-dioxygenase (IDO) and IDO-catalyzed tryptophan metabolism. IDO contributes to self-tolerance in the longer term by suppressing effector T-cells or expanding the induced regulatory T-cells (iTreg).

Purpose: We aimed to characterize the expression and activity of IDO in monocytes derived DC (MDDC) from patients with acute coronary syndrome (ACS), stable angina (SA) and controls.

Methods: mRNA expression of IDO was analyzed in MDDC from 15 ACS, 15 SA patients and 15 controls by qPCR before and after maturation with LPS. The amount of tryptophan catabolite, kynurenine, was evaluated in the supernatants of mature MDDC by ELISA assay. Autologous mixed lymphocyte reaction (MLR) between mature DC and naïve T-cells was carried out to study the differentiation of T-cells towards Th1 and iTreg.

Results: Analysis of the levels of IDO mRNA transcripts by qPCR in mature MDDC revealed significant reduction in ACS (625±128.0, mean ± SEM) as compared to SA (1112±226.0, mean ± SEM) (P=0.05) and controls (1203±224.9, mean ± SEM) (P=0.04). Furthermore, the concentration of kynurenine, expressed as ng/ml, was higher in controls (0.5±0.1, mean ± SEM) as compared to SA (0.3±0.04, mean ± SEM) and ACS patients (0.3±0.03, mean ± SEM). When IDO competent mature MDDCs were co-cultured with allogenic naïve T-cells, the ratio between the percentage of generated Th1 and iTreg from MLR was higher in ACS (2.9±0.30, mean ± SEM) and SA patients (2.34±0.54, mean ± SEM) than in controls (0.59±0.18, mean ± SEM).

Conclusion: In ACS, altered DC function might provide one of the environmental cues that enhances pro-inflammatory T-cell differentiation. IDO production by activated DCs could contribute to a mechanism of self-limit immune responses. This may be part of a negative feedback loop, lacking in ACS, whereby DCs may regulate immune responses in the presence of a large number of aggressive T-cells. Characterization of new atheroprotective mechanism might be important to develop novel preventive strategies.

3945 | BEDSIDE
Macrophage degradation in coronary atherosclerotic plaques by statin therapy: an optical coherence tomography study

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Objectives: The aim of this study was to assess the effect of statin therapy on macrophages accumulation in coronary atherosclerotic plaques by using optical coherence tomography (OCT).

Background: OCT can identify macrophages accumulation as a high intensity signal-rich linear region with sharp attenuation.
Methods: Seventy patients with unstable angina pectoris and untreated dyslipidemia were randomized to either 20 mg/day or 5 mg/day of atorvastatin therapy. OCT was performed to assess intermediate non-culprit lesions at baseline and 12-month follow-up.

Results: Macrograde change decreased significantly in both groups, and the percent decrease in macrograde change was significantly greater in the group receiving 20mg/day of atorvastatin compared with the group receiving 5mg/day of atorvastatin (~38% [IQR -44 to -31%] vs. ~24% [IQR -33 to 0%], p<0.001). The percent change in macrograde was negatively correlated with the percent change in the serum HDL-C (R=−0.368, p=0.008) levels, and positively correlated with the percent change in the serum hs-CRP (R=0.308, p=0.033) and MMP-9 (R=0.486, p<0.001) levels; however, it was not correlated with the percent change in the serum total cholesterol (R=0.038, p=0.793), LDL-C (R=0.212, p=0.139), triglyceride (R=0.070, p=0.627), MDA-LDL (R=0.163, p=0.257), IL-6 (R=−0.153, p=0.288), and HbA1c (R=0.086, p=0.551) levels. In addition, the percent change in macrograde was negatively correlated with the percent change in fibrous cap thickness (R=−0.415, p<0.003).

Conclusions: Therapy with 20 mg/day of atorvastatin provided greater decrease of macrograde accumulation in coronary plaques compared with 5 mg/day of atorvastatin. The decrease of macrograde accumulation was associated with the increase in serum HDL-C and decrease in serum inflammatory biomarkers during atorvastatin therapy.

Acknowledgement/Funding: Received lecture fees from St. Jude Medical

3946 | BEDSIDE
Long-term cardiovascular outcomes in patients with collagen disease who underwent percutaneous coronary intervention
S. Maruta. University of Tsukuba, Ibaraki, Japan

Background: Although patients with collagen disease have a significantly increased risk of cardiovascular disease, the long-term prognosis is fully unknown in patients with collagen disease who underwent percutaneous coronary intervention (PCI).

Methods: From April 2007 to October 2014, a total of 627 consecutive patients who underwent PCI were enrolled in this study. We compared the long-term clinical outcomes of 33 patients with collagen disease to 543 patients with non-collagen disease. The primary endpoint was major adverse cardiac events (MACE), which was defined as cardiovascular death, myocardial infarction (MI), and target lesion revascularization (TLR).

Results: The incidence of MACE was significantly more observed in collagen disease than in non-collagen disease (24.2% vs. 10.1%, p=0.036). Multivariable analysis demonstrated that collagen disease was independent predictor for MACE after adjusting confound factors.

Conclusion: Patients with collagen disease had poor long-term cardiovascular outcomes after receiving PCI.

3947 | BEDSIDE
OxLDL upregulates microRNA-155 in dendritic cells by binding transcription factor YY1/ MYB through the JAK1/2 signaling pathway
H. Yan. First Affiliated Hospital of College of Medicine, Zhejiang University, Institute of Cardiology, Hangzhou, China, People’s Republic of China

In order to explore the upstream regulatory mechanisms of miR-155 following oxLDL treatment in dendritic cells, DCs were either transfected with siRNA of scavenger receptors to elucidate the signaling mechanisms involved. A transcription factor filter plate screen assay was performed to identify the transcription factor that binds to the miR-155 promoter in response to OxLDL treatment. Precise binding sites were also detected by performing a chromatin immunoprecipitation assay. We found that MIR-155 was evidently decreased when signaling molecules were inhibited. Furthermore, oxLDL positively promotes complex formation of YY1 and MYB. YY1 assisted MYB the binding of promoter sequences on miR-155, thus activating downstream transcription. Our study clearly revealed that oxLDL upregulates MicroRNA-155 in DCs by binding YY1/MYB.
implicating a cytokine product associated with Th cell effector function as a necessary mediator of this pathophysiology. The IL-17 is the major mediator of tissue inflammation, however, the role for IL-17 in ischemic heart failure (HF) is not well defined.

**Methods:** HF rabbits were created 4 weeks after undergoing coronary ligation. WBC, serum biochemistry, monophasic action potential, ECG and expression of CD4+ T cell are measured every two weeks. The mRNA and protein expressions of IL-17 are also measured by real time-PCR, ELISA and flow cytometry. Open-chest epicardial catheter stimulation was performed for ventricular arrhythmia (VA) provocation.

**Results:** We found a lot of inflammatory cells infiltrating in left ventricle (Fig. A). The data showed CD4+ cells and IL-17 were up-regulated significantly by CD4+ T cells in HF (Fig. B and C). We also found the mRNA of IL-17A and IL-17F were high expression by real time PCR and protein expression of IL-17 was also increased in ischemic HF (Fig. D).

**Conclusion:** CD4+ T cell derived proinflammatory cytokine IL-17 is the major mediator of cardiac inflammation and may play a key role to induce the VA in an ischemic HF model.

**Acknowledgement/Funding:** TSOC

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**3950 | BENCH**

Selective inhibition of the NLRP3 inflammasome dose-dependently reduces infarct size and preserves cardiac function in a porcine model of myocardial infarction


**Background:** Myocardial infarction (MI) induces an exaggerated inflammatory response that results in infarct expansion and progression into heart failure. Interleukin (IL)-1β and IL-18 are among the key mediators driving this inflammatory response. The secretion of these cytokines is regulated by the NLRP3-inflammasome, an intracellular molecular complex. The aim of the current study was to determine the effect of administration of MCC950, a selective small-molecule inhibitor of the NLRP3-inflammasome, on infarct size and cardiac function in a porcine model of MI.

**Methods:** Thirty female landrace pigs were subjected to 75 minute transluminal balloon occlusion of the left anterior descending artery. Post-MI, pigs received selective inhibition of the NLRP3 inflammasome, an intracellular molecular complex. The aim of the current study was to determine the effect of administration of MCC950, a selective small-molecule inhibitor of the NLRP3-inflammasome, on infarct size and cardiac function in a porcine model of MI.

**Results:** We found a lot of inflammatory cells infiltrating in left ventricle (Fig. A). The data showed CD4+ cells and IL-17 were up-regulated significantly by CD4+ T cells in HF (Fig. B and C). We also found the mRNA of IL-17A and IL-17F were high expression by real time PCR and protein expression of IL-17 was also increased in ischemic HF (Fig. D).

**Conclusion:** CD4+ T cell derived proinflammatory cytokine IL-17 is the major mediator of cardiac inflammation and may play a key role to induce the VA in an ischemic HF model.

**Acknowledgement/Funding:** TSOC

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**3995 | BEDSIDE**

Can cardiac CT angiography identify asymptomatic type 2 diabetes at high risk for adverse coronary events? A prospective 7 year outcomes study

**D.A. Halon**, A. M. Bental, R. Rubinstein, B. Zafiri, M.Y. Flugelman, B. L. Lewis

**Background:** Asymptomatic type 2 diabetes (DM) are at increased risk for cardiovascular (CV) events but routine screening for coronary disease (CAD) by perfusion imaging has not led to improved outcomes. We sought to identify, using coronary CT angiography (CTA), a cohort at high risk for CAD events who may benefit from intensified preventive or interventional therapy.

**Methods:** A population based cohort of DM (N=630) underwent baseline risk assessment, coronary artery calcium (CAC) scoring and CTA. Total plaque length was computed at CT workstation and plaque calcium graded 0–5 visually. MAACE (CV death/MI/unstable angina) were assessed over 6.5±1.0 yr.

**Results:** At baseline Variable Hazard ratio p Hazard ratio p Hazard ratio p Hazard ratio p hazard ratio p

<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>Hazard ratio p</th>
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</thead>
<tbody>
<tr>
<td>UKPDS66</td>
<td>1.4 (1.3–1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Log (coronary artery calcium+1)</td>
<td>2.3 (1.6–3.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total plaque length</td>
<td>3.6 (2.4–5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild (Grade 1–2 plaque calcification)</td>
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</tr>
<tr>
<td>UKPDS + log(CAC+1) combined</td>
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<tr>
<td>UKPDS + plaque length</td>
<td>0.797</td>
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<td>UKPDS + plaque length + mild calcification</td>
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**Conclusion:** Our findings suggest that untreated HIV infection in children thickens cIMT, independent of levels of inflammation, while HIV infection exposed to antiretroviral treatment had similar vascular properties with healthy children.

**COMPUTED TOMOGRAPHY AND CORONARY RISK**
ment 27.3% (3 risk categories) vs UKPDS + CAC score alone). Event rate in upper decile of pt risk was 51% vs 6.5% in total cohort.

Conclusion: Addition of CTA defined plaque extent and characterization to a combined clinical risk (UKPDS) and CAC score model better identified a DM cohort at high risk for MACCE who may benefit from further study or intervention.

Acknowledgement/Funding: European Foundation for the Study of Diabetes

5096 | BEDSIDE

5 year prognostic value of coronary computed tomographic angiography using machine learning: results from the CONFIRM Registry

M. Motwani1, P. Slomka1, D.S. Berman1, J.K. Min2 on behalf of CONFIRM investigators. 1Cedars-Sinai Medical Center, Department of Imaging and Medicine, Los Angeles, United States of America; 2New York- Presbyterian Hospital and the Weill Cornell Medical College, Department of Radiology, New York, United States of America

Purpose: We investigated if 5 yr prognosis in patients with suspected coronary artery disease (CAD) can be predicted by machine learning (ML) integrating clinical data with imaging data from coronary CT angiography (CTCA).

Methods: Data from 10030 patients (58±13 yrs; 56 male) without known CAD, and with 5 yr outcomes from the CONFIRM registry were considered. All patients underwent CTCA for clinical purposes and were followed for all-cause mortality (ACM) and MACE (death/MI/ACS/late revascularisation). 44 CTCA parameters and 25 clinical parameters were available for ML, including segment stenosis score (SSS), segment involvement score (SIS), modified Duke index (DI), number of segments with non-calcified, mixed or calcified plaques, age, sex, gender and standard cardiovascular risk factors. ML involved automated feature selection by information gain ranking, model building with a boosted ensemble algorithm, and 10-fold stratified repeated cross-validation.

Results: 745 patients died and 991 had MACE events during 5 yr follow-up. ML had the highest area-under-the-curve (AUC) compared to Framingham risk score (FRS) or CTCA data alone for both 5 yr ACM (ML: 0.80 [0.78–0.81] vs. FRS: 0.61 [0.59–0.64], SSS: 0.64 [0.62–0.66], SIS: 0.64 [0.62–0.66], DI: 0.62 [0.60–0.64]; p < 0.001) and 5 yr MACE prediction (ML: 0.83 [0.82–0.84] vs. FRS: 0.61 [0.59–0.63], SSS: 0.70 [0.68–0.72], SIS: 0.70 [0.68–0.71], DI: 0.69 [0.67–0.70]; p < 0.001). All CTCA severity scores (SSS, SIS and DI) were superior to FRS for predicting MACCE (p < 0.001), and SSS and SIS were superior to FRS for predicting ACM (p < 0.05). ML was superior to FRS for categorising risk of 5 yr ACM as <5%, 5–10% or ≥10% (NRI=0.42; p < 0.001).

Conclusion: ML combining clinical and CCTA data predicts 5 yr ACM and MACE better than FRS or CCTA data alone.

Acknowledgement/Funding: This study was funded by an NIH grant (R01HL089016) and also in part by a grant from the Dowager Countess Eleanor Peel Trust, UK

3997 | BEDSIDE

Relationship between non-calcified coronary plaque volumes by coronary CT angiography and fractional flow reserve

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Background and introduction: The correlation between anatomical stenosis assessment and ischemia is poor in coronary artery disease (CAD). Recently, an association between adverse plaque characteristics by coronary CT angiography (CTA) and ischemia has been shown.

Purpose: The aim of the present study was to evaluate the association between atherosclerotic plaque volumes and fractional flow reserve (FFR), and to determine whether plaque volumes provide incremental prediction of ischemia when compared to coronary CTA stenosis assessment alone.

Methods: As part of a prospective multicentre trial, we performed coronary CTA and FFR in 254 patients suspected of CAD. A site-read CTA stenosis >50% was considered obstructive. Lesion-specific ischemia was defined by FFR <0.80. We quantified non-calcified plaque (NCP), low-density NCP (LD-NCP), and calcified plaque (CP) volumes by semi-automated software (AutoPlaq) from standard CTA images. Plaque volumes were dichotomized using ROC analysis to define the optimal threshold.

Results: In 484 vessels, mean volumes of NCP, LD-NCP, and CP differed significantly between FFR groups (Figure). Age- and gender-adjusted ORs for prediction of FFR < 0.80 for NCP > 185 mm3, LD-NCP > 30 mm3, and CP > 9 mm3 were 5.0 (3.1–8.2; p < 0.001), 7.2 (4.3–11.9; p < 0.001), and 1.5 (0.9–2.4; p=0.09), respectively. OR for CTA >50% was 6.8 (3.9–12.0; p < 0.001). In multivariate analysis NCP (p < 0.001), LD-NCP (p < 0.001), and CTA (p < 0.001) were independent predictors of lesion-specific ischemia, while CP was not (p=0.48).

Conclusions: We identified an inverse relation between FFR and coronary plaque volumes. Coronary NCP and LD-NCP volumes by CTA provide incremental predictive value for identification of lesion-specific ischemia when compared to standard CTA assessment.

BLEEDING AND ISCHAEMIC EVENTS IN PCI PATIENTS: PREDICTION, PREVENTION AND MANAGEMENT

4000 | BEDSIDE

Relationship between platelet count, platelet reactivity and ischemic and bleeding risk in patients undergoing PCI with DES: Insights from the ADAPT-DES registry

G. Giustino1, U. Baber1, R. Mehran1, C. Litherland2, B. Witzenbichler3, G. Weisz4, M.J. Rinaldi5, B.R. Brodie6, A.J. Kirtane7, G.W. Stone7, 1 Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2Lillebaelt Hospital, Department of Cardiology, Vejle, Denmark; 3Cedars-Sinai Medical Center, Department of Biomedical Sciences, Los Angeles, United States of America; 4 Shaare Zedek Medical Center, Jerusalem, Israel; 5 Sanger Institute, Dachau, Germany; 6 Shaare Zedek Medical Center, Jerusalem, Israel; 7 Columbia University Medical Center, New York, United States of America

Introduction: Previous data suggest that high platelet counts (PC) are associated with higher rates of ischemic events after PCI. Whether this association is independent of and/or varies by residual platelet reactivity is unknown.

Purpose: To evaluate the relationship between PC, platelet reactivity, and risk for definite or probable stent thrombosis (ST) and major bleeding 2 years after PCI.

Methods: Patients enrolled in the prospective, multicenter ADAPT-DES population were stratified by PC and platelet reactivity unit (PRU) tertiles. High platelet reactivity (HPR) on clopidogrel was defined as a VerifyNow PRU value > 230.

Results: 8,535 patients were included in the study cohort. There were no significant differences in the prevalence of HPR across tertiles. Rates of ST were highest among patients in the highest tertiles (p < 0.01) of both PRU and PC, while the rate of bleeding was highest in those in the lowest tertiles (p < 0.05; Figure). After adjustment for baseline risk factors, including HPR, high PC tertile remained a significant correlate of ST (adjHR: 1.75; 95% CI: 1.0–3.1), while no independent association was observed between PC tertiles and bleeding. The effect of HPR on ischemic and bleeding risk across PC tertiles was uniform, without evidence of interaction. Finally, both lower (adjHR: 1.53; 95% CI: 1.1–2.2) and higher (adjHR: 1.65; 95% CI: 1.2–2.4) PC tertiles were independently associated with all-cause mortality at 2 years.

Conclusions: The combined presence of high PC and PRU yields an additive
Effect on risk for ST. While PC was not associated with bleeding risk, both low and high PC independently correlated with long-term mortality. PC could be a parameter to take into account in guiding duration and potency of dual antiplatelet therapy after DES implantation.

### 4001 | BEDSIDE

**Bleeding episodes in “complete, staged” versus “culprit only” revascularization in patients with multivessel disease and ST-segment elevation myocardial infarction - a DANAMI-3-Primulti substudy**

G. Sadjadi1, T. Engstroem1, S. Helqvist1, D.E. Hoefset1, L. Koeber1, F. Pedersen1, H.H. Tilsted2, H. Kelbaek3, L. Holmvang1 on behalf of DANAMI-3-Primulti.1 Risghospitalet - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark;2 Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark;3 Roskilde Hospital, Department of Cardiology, Roskilde, Denmark

**Background and introduction:** Patients with acute ST-segment elevation myocardial infarction (STEMI) and multi vessel coronary disease have a poorer prognosis than those with a single infarct-related artery (IRA) lesion. The Third DANISH Study of Optimal Acute Treatment of Patients with STEMI and multivessel disease. Bleeding episodes have been strongly associated with 1-year mortality in patients undergoing acute as well as non-emergent percutaneous coronary intervention (PCI). Furthermore, pre-procedural administration of novel antiplatelet inhibitors has been associated with an increased risk of bleeding in patients undergoing non-emergent PCI for ACS. Hitherto it remains unclarified whether staged complete revascularization in STEMI patients with multi vessel disease, causes an increased risk of bleeding and subsequent mortality.

**Purpose:** The aim of the present study is to evaluate to what extent, a staged in-hospital complete revascularization strategy will increase the risk of bleeding in a multi vessel diseased STEMI patient population receiving contemporary treatment with novel platelet inhibitors and bivalirudin.

**Methods:** We included patients with acute onset symptoms of STEMI with novel platelet inhibitors and bivalirudin. A multi vessel diseased STEMI patient population receiving contemporary treatment with novel antiplatelet inhibitors has been associated with an increased risk of bleeding in patients undergoing non-emergent PCI for ACS. Hitherto it remains unclarified whether staged complete revascularization in STEMI patients with multi vessel disease, causes an increased risk of bleeding and subsequent mortality.

**Results:** From March 2011 to February 2014 627 patients were randomized in the trial. A total of 314 patients were randomized to complete revascularization while 313 patients were randomized to culprit-PCI only. 90.4% of the patients randomized to complete revascularization underwent a second in-hospital procedure, either coronary angiography or FFR alone, FFR guided PCI or patient artery bypass grafting.

**Conclusion:** Data will be analyzed in March 2015, when the last included patient has been followed clinically for 1 year. Baseline and randomization data will be collected in patients, 30-days and 1-year bleeding episodes as well as short- and long-term mortality will be ready for presentation at the ESC meeting.

### 4002 | BEDSIDE

**The effect of cangrelor and access site on ischemic and bleeding events: insights from CHAMPION-PHOENIX**

J.A. Gutierrez1, R.A. Harrington2, G.W. Stone3, P.G. Steg4, C.M. Gibson5, C.W. Hamm6, M.J. Price7, K.W. Mahaffey2, H.D. White8, D.L. Bhatt1, L. D’Agostino and Women’s Hospital, Cardiovascular Medicine, Boston, United States of America;2 Stanford University Medical Center, Stanford, United States of America;3 Columbia University Medical Center, New York, United States of America;4 Hospital Bichat-Claude Bernard, Paris, France;5 Beth Israel Deaconess Medical Center, Boston, United States of America;6 Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany;7 Scripps Clinic, La Jolla, United States of America;8 Auckland City Hospital, Auckland, New Zealand

**Background:** In CHAMPION-PHOENIX, cangrelor reduced ischemic events with no significant increase in severe/moderate bleeding or in transfusions regardless of PCI access site.

**Conclusion:** In CHAMPION-PHOENIX, cangrelor reduced ischemic events with no significant increase in severe/moderate bleeding or in transfusions regardless of PCI access site.

### WHAT'S NEW IN MICROCIRCULATION AND COLLATERALS

#### 4002 | BEDSIDE

**Index of microvascular resistance in real-world practice in patients with stable ischemic heart disease: insight from the international imr registry**

J.M. Lee1, A.S. Yong2, J.H. Doh3, C.W. Nam4, E.S. Shin5, B.K. Koo6, M.K. Ng6, M. Esebeck7, W. Fearon8, K. Oldroyd9, 1 Seoul National University Hospital, Cardiovascular Center, Department of Internal Medicine, Seoul, Korea, Republic of;2 Stanford University Medical Center, Stanford, United States of America;3 Inje University Ilsan Paik Hospital, Goyang, Korea, Republic of;4 Keimyung University Hospital Dongsan Medical Center, Daegu, Korea, Republic of;5 Ulsan University Hospital, Ulsan, Korea, Republic of;6 Royal Prince Alfred Hospital, Sydney, Australia;7 Hospital Clinic San Carlos, Madrid, Spain;8 Golden Jubilee National Hospital, Clydebank, United Kingdom

**Background:** The index of microcirculatory resistance (IMR) is a quantitative and specific index for coronary microcirculation. However, the distribution, optimal cut-off values, and independent determinants for high IMR have not been fully investigated in patients with stable ischemic heart disease (IHD).

**Methods:** 1,096 patients with 1,452 coronary stenoses who underwent elective measurement of both FFR and IMR were enrolled from 8 centers in 5 countries. Patients with acute MI were excluded. IMR values were corrected with Yong’s formula (IMRcorr) to adjust for the influence of collateral flow. High-IMRcorr was defined as greater than the 75th percentile. FFR<0.80 was defined as an ischemic value.

**Results:** Among patients (mean age 61.1, male 71.2%), 57.9% and 42.1% were from Asian and Western populations, respectively. Mean FFR was 0.84 and median IMRcorr was 16.6 (IQR 12.4–23.0). IMRcorr was significantly different among the 3 main coronary arteries (median values 15.7U, 16.9U and 19.1U for LAD, LCX and RCA, respectively, p<0.001). The categorical agreement of FFR and IMRcorr was very low (kappa value = 0.042, p=0.102). Among patients with FFR<0.80, 26.3% had high IMRcorr. Independent determinants for high IMRcorr were obesity (OR 1.88 [1.32–2.68], p=0.001), female gender (OR 1.85 [1.26–2.71], p=0.002), and age (OR 1.023 [1.003–1.044], p=0.025).

**Conclusion:** The distribution of IMRcorr was significantly different among the coronary arteries and approximately 25% of stenoses with non-ischaemic FFR values had evidence of abnormally high microvascular resistance. The independent predictors of high IMRcorr values were different from those for ischemic FFR values. Integration of IMR and FFR measurements may improve the stratification of patients without evidence of MI.
Conclusions: both groups, though less markedly in patients pretreated with prasugrel compared to patients with coronary artery disease.

Related microvascular impairment and myocardial damage in patients with stable angina pectoris. Glasgow, United Kingdom; 2 University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom; 3 Golden Jubilee National Hospital, Cardiology, Glasgow, United Kingdom

Background: Invasive assessment of coronary physiology provides prognostic insights in STElevation myocardial infarction patients.

Purpose: To assess the clinical significance of the index of microvascular resistance (IMR) versus coronary flow reserve (CFR) measured at the time of primary PCI, in patients with stable coronary artery disease.

Methods and results: Forty thienopyridine-naive patients were randomized to a loading dose of either prasugrel 60 mg (n=20) or clopidogrel 600 mg (n=20) at least 12 hours before PCI. At baseline and post-PCI, we assessed the index of microvascular resistance (IMR) in the treated artery, and adenosine diphosphate (ADP)-induced platelet reactivity with the Multiplate Analyzer. High sensitive troponin T (Hs-TnT) was measured before and at 24 hours after PCI. Baseline IMR was not significantly different between the two groups (15.7±10.1 in prasugrel group vs. 20.2±1.1 in clopidogrel group, p=0.148). Post-PCI IMR was significantly lower in the prasugrel as compared with clopidogrel group (17.3±3.8 vs. 26.1±11.0, p=0.007). A significant post-procedural IMR increase was observed in the clopidogrel group (Delta: 29%, p=0.001), while no significant changes were observed in the prasugrel group (Delta: 10%, p=0.299). ADP-induced platelet reactivity was significantly lower in the prasugrel compared with clopidogrel group at both baseline (16.0±8.7 vs. 33.9±16.0 aggregation units [AU], p<0.001) and post-PCI (16.2±9.0 vs. 39.0±18.6 AU, p<0.001). Hs-TnT increased post-PCI in both groups, though less markedly in patients pretreated with prasugrel compared with clopidogrel group (Delta: 10%, p=0.299) vs. 15.8±9.4% (p=0.033).

Conclusions: Unlike with clopidogrel, prasugrel pretreatment prevents from PCI-related microvascular impairment and myocardial damage in patients with stable coronary artery disease.

4024 | BEDSIDE
The comparative clinical utility of the index of microvascular resistance versus coronary flow reserve for acute risk assessment in reperfused STElevation myocardial infarction patients.

D.J.A. Carrick1, C. Haig1, J. Layland1, M. Petrie3, M. McEntegart1, S. Hood3, N. Ahmed1, A. Radjenovic1, K.G. Oldroyd1, C. Berry1. Cardiovascular Research Centre of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom; 2University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom; 3Golden Jubilee National Hospital, Cardiology, Glasgow, United Kingdom

Background: Invasive assessment of coronary physiology provides prognostic insights in STElevation myocardial infarction (STEMI) patients, but it is unclear which is the most clinically useful physiological parameter.

Purpose: To assess the clinical significance of the index of microvascular resistance (IMR) versus coronary flow reserve (CFR) measured at the time of primary percutaneous coronary intervention (PCI) in a large unsellected cohort of reperfused STEMI survivors.

Methods: We performed a single centre cohort study in near-consecutive reperfused STEMI patients. CFR and IMR were measured at the end of PCI using guidewire-based thermolumination. Contrast-enhanced cardiac magnetic resonance (CMR) imaging was used to assess left ventricular (LV) function and infarct pathology 2 days and 6 months post-PCI. Intramyocardial haemorrhage (IMH) was defined as a hypointense infarct core with a T2* value <20 ms. Infarct size and microvascular obstruction (MVO) were assessed with late gadolinium enhancement (LGE) imaging. Adverse remodelling was defined as an increase in left ventricular end-diastolic volume (LVEDV) >20% at 6 months.

Results: CFR was performed in 245 patients at day 2 and in 228 patients (93%) at 6-months post-MI. The median IMR (IQR) was 25 [15–48] and median CFR was 1.6 [1.1–2.1]. 101 patients (41%) had IMH and 133 patients (54%) had MVO. All of the patients with IMH had MVO, but 32 patients had MVO (13%) without IMH. IMR was higher in patients with IMH (37 [21–63] vs. 17 [12–35]), including those that had MVO in the absence of IMH (17 [13–29]; p<0.001). The corresponding CFR values were 1.4 [1.0–1.8] vs. 1.7 [1.4–2.5] vs. 1.5 [1.1–1.8]; respectively. p<0.001. Both IMR and CFR were associated with LVEF at 6-months, after adjustment for baseline LVEF (p<0.001 and p=0.029, respectively). In matched patients (>70% 1.0–10.0 vs. 15.8–30.0 rpm/μM; p=0.037); only IMR was associated with LVEF at 6-months (correlation coefficient -0.05 [95% CI -0.08, -0.01]; p=0.02). IMR was associated with adverse LV remodelling at 6-months (1.01 [1.00, 1.03]; p=0.015) whereas CFR was not (p=0.117).

Conclusions: IMR and CFR are associated with severe microvascular injury post-STEMI. In the longer term, IMR is independently associated with LVEF and LVEDV at 6-months, whereas CFR is not. Compared with CFR, IMR has prognostic importance and greater potential clinical utility for risk assessment post-STEMI.
Patient demographics

<table>
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<th>Variables</th>
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<td>0.03</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>75.15</td>
<td>70.01</td>
<td>0.05</td>
</tr>
<tr>
<td>Radiotherapy involving the heart (%)</td>
<td>30</td>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: ALVD was prevalent in LS after auto-HCT. However, exercise capacity was preserved and comparable to LS without ALVD.

Acknowledgement/Funding: Extrastitelsen

4049 | BEDSIDE

High-sensitivity T tropinin for early detection of cardiotoxicity among patients on chemotherapy


Introduction: Left ventricular dysfunction as a result of anticancer-drug therapy is an important issue in cancer survivors. Tools for an early detection of cardiotoxicity are needed. Cardiac biomarkers can detect myocardial injury and thus may play an important role in subclinical detection of drug-related toxicity. The aim of this study is to evaluate if cardiac biomarkers can detect patients who will develop cardiotoxicity after chemotherapy.

Methods: GECAME study (Grupo de Estudio de Cardiotoxicidad por MEDicina-mentos) is an unicentric registry of patients treated with cardiotoxic anticancer drugs. Transthoracic echocardiography (TTE) was performed before starting treatment and at 3, 6 and 12 months from the start of treatment, between August 2011 and January 2014. Cardiotoxicity was defined as a relative decrease in LVEF >10% from the basal and below 55% or clinical signs or symptoms of heart failure. Blood samples were drawn at baseline, 21 days, 3 months, 6 months and one year after starting chemotherapy, hs-cTnT-cTn, NT-proBNP and Galectin-3 were measured. We used 99 percentile as cut-offs for Roche Elecsys hs-cTnT (14 ng/L CV = 10%) and Siemens Vista cTnL (27 ng/L CV = 7.7%) assays for Gal-3 27.5 ng/mL, NT-proBNP (125 (-7.5 years) -480 mg/mL (-75 years).

Results: 222 consecutive patients were included. The mean age was 58.8, 11.4 years and 76.7% were women. 59.5% had been diagnosed breast cancer, 34.7% leukemia or lymphoma, and 5.8% other tumor. Mean basal LVEF was 64.3±5.6%. NT-proBNP and 3-Galectine concentrations did not vary significantly during follow-up. Increased hs-cTnT and cTnL concentrations occurred with a maximum concentration at third month, being hs-cTnT the one with more patients above the threshold. 120 patients had hs-cTnL plasma levels above p99, 20 of which developed cardiotoxicity during follow-up. From the 102 patients with hs-cTnT below p99, 7 developed cardiotoxicity. These findings show a sensitivity of hs-cTnT at 3-month in our setting.

4050 | BEDSIDE

Coronary high-intensity plaque on t1-weighted magnetic resonance imaging and its association with percutaneous coronary intervention related myocardial injury

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Aims: Non-contrast T1-weighted imaging (T1WI) has emerged as a novel non-invasive method for characterizing vulnerable coronary plaques, exhibiting a signal of high-intensity plaque (HIP). However, the impact of HIP for percutaneous coronary intervention (PCI) has not been fully evaluated. We investigated the association between the presence of HIP and the incidence of PCI-related myocardial injury.

Methods: A total of 100 lesions from 77 patients with stable angina were imaged with non-contrast T1WI with a 1.5-T MRI before PCI. We defined HIP as a signal intensity of coronary plaque to muscle ratio (PMI) ≥1.4. Cardiac troponin-T (cTnT) was measured before PCI and ≤60 min after PCI. Results: HIP was identified in 36% of plaque. In the IVUS assessment, vessel and plaque volume were significantly greater in HIP group than in non-HIP. The ultrasound attenuation was identified more in HIP group as compared to non-HIP (72% vs 5%, P<0.001).

Conclusions: HIP was an independent predictor of the incidence of PMI. The presence of HIP is a significant predictor of the incidence of PMI (odds ratio 4.65, 95% confidence interval 1.06-20.4, P=0.042).

4051 | BEDSIDE

Computed tomography coronary angiography versus stress cardiac magnetic resonance for the management of symptomatic revascularized patients: a cost-effectiveness study

G. Pontone1, D. Andreins1, C. Rota1, M. Guglielmo1, A. Baggiolo1, V. Beltrame1, A. Solbiasi1, A.J. Guaricci2, M. Peps1,1 Centro Cardiologico Monzino, IRCCS, Milan, Italy; 2University of Foggia, Foggia, Italy

Background: Computed tomography coronary angiography (CTCA) and stress cardiac magnetic resonance (stress-CMR) are both suitable for diagnosing obstructive coronary artery disease (CAD) in symptomatic patients for chest pain with previous history of revascularization. However, the evaluation of performance of non-invasive imaging tests has failed to account the subsequent diagnostic testing and medical procedures derived, clinical outcomes and cumulative costs and radiation exposure rather than their diagnostic accuracy alone. The aim of this study is to compare the clinical and economic outcomes of using anatomical (CTCA) versus functional strategy (stress-CMR) in revascularized symptomatic patients for chest pain.

Methods and materials: Four hundred revascularized symptomatic patients for chest pain were addressed to CTCA (n=200, mean age 68±10 y, male 168) or stress-CMR (n=200, mean age 66±9 y, male 177) and followed-up in terms of downstream non invasive tests, invasive coronary angiography (ICA) and revascularization procedure, medical costs for CAD management, cumulative effective radiation dose and major adverse cardiac events (MACEs) defined as composite endpoints of non fatal myocardial infarction and cardiac death.

Conclusion: HIP on non-contrast T1WI was characterized as vulnerable coronary plaque on IVUS and was associated with the incidence of PMI.
Conclusion: We enrolled 69 (controls: 33, intervention: 36) overweight and obese patients with paroxysmal AF (in sinus rhythm) at the time of CMR scanning) into either an structured physician-directed weight management program, or general lifestyle advice. Patients were followed up at 3 month intervals for a total of 12 months. All patients underwent CMR at baseline and 12 months follow-up. Offline blinded volumetric analysis was performed using the disc summation method by a CMR reference laboratory.

Methods: (Table) Structural changes between groups were independent of body surface area. No significant changes were observed in ventricular volumes between the groups.

Conclusion: Structured weight loss program with cardiometabolic risk management results in favorable changes in atrial volumes, myocardial mass, systolic blood pressure, serum CRP and pericardial fat volume, as compared to aggressive risk factor management alone. These changes may account for the observed reduction in AF arrhythmia burden.

Acknowledgement/Funding: Australian Post Graduate Award

4054 | BEDSIDE
Impact of long-term steroid therapy on epi- and pericardial fat deposition - a cardiac MRI study

Background: The success of emergency coronary reperfusion therapy in ST-elevation myocardial infarction (STEMI) is commonly limited by failed tissue perfusion. Adverse remodeling was defined as an increase in left ventricular end-diastolic volume (LVEDV) ≥20% at 6 months.

Methods: We performed a prospective single centre cohort study in repertused STEMI patients who underwent CMR 2 days (n=286) and 6 months post-MI. IMH was taken to represent a hypointense infarct core with a T2* value < 20 ms. 30 STEMI patients underwent serial CMR at 4 time points: 4 to 12 days, 3 days, 10 days and 7 months respectively. The amount of MVO was greatest ≥4–12 hours post-reperfusion, then fell progressively over time. In contrast, the amount of IMH increased dynamically from 4–12 hours with a peak at 3 days and then a decrease at 10 days. MVO resolved by day 10 in 8 patients (44%), 2 (5%) of which had evidence of IMH. Whereas MVO persisted in 10 patients (56%), all (100%) of which had evidence of IMH.

Conclusion: IMH is independently associated with adverse remodeling at 6-months and CV death or heart failure hospitalisation post-discharge. The severity of MVO affects its degree of persistence and T2* imaging differentiates persistent, structural microvascular injury from functional, potentially reversible MVO. Haemorrhage occurs in primary and secondary phases within the first 5 days post-MI. IMH is a biomarker with potential to reflect the efficacy of therapeutic interventions in STEMI patients.

4055 | BEDSIDE
Comparison of transthoracic echocardiography versus cardiac magnetic resonance imaging to estimate magnetic defibrillator therapy in primary prevention strategy dialted cardiomyopathy patients
G. Pontone1, D. Andreini1, A. Solbiati1, M. Guglielmo1, S. Mushtag1, A. Baggiano1, V. Beltrama1, C. Rota1, A.I. Guaracci1, M. Pepli1, Centro Cardiologico Monzino, IRCCS, Milan, Italy; 2University of Foggia, Foggia, Italy

Background: Implantable cardioverter-defibrillators (ICDs) has been proved as a valid primary prevention strategy to reduce mortality in patients with dilated cardiomyopathy (DCM) with reduced left ventricular ejection function (LVEF) <35%. This LVEF threshold is largely based on studies using trans-thoracic echocardiography (TTE). Magnetic resonance imaging (MRI) is now considered the gold standard technique for LVEF assessment and it provides important information on tissue characterization such as late gadolinium enhancement (LGE). Several studies have shown differences between CMR and TTE evaluation. The aim of this study is to determine whether LV evaluation and LGE detection by CMR are superior to conventional TTE measurements for risk stratification of DCM patients evaluated for ICD implantation in primary prevention strategy.

Methods and materials: Two hundred and seventy consecutive DCM patients (Mean age 63±13 yo, male 220 patients) referred to our Institution to be evaluated for ICD implantation in primary prevention were enrolled. All patients underwent both TTE and CMR left ventricle end-diastolic (LVEDV) and end-systolic (LVESV) volumes and LVEF estimation. Additionally, LGE, presence was also detected by CMR. All patients were followed-up for the major adverse cardiac events (MACE) defined as a combined endpoint of ventricular tachycardia, ventricular fibrillation and sudden cardiac death.

Results: All patients performed both tests successfully. The mean follow-up was 850±330 days. TTE showed a lower LVEDV (86±28 vs. 131±41 ml/m2) and a higher LVEF (57±21 vs. 93±40 ml/m2) and a higher LVEF (35±10 vs. 31±9%) as compared to CMR (LVEF <35% in 68 patients (29%), MACE occurred in 68 patients (29%). Patients experienced MACE showed a higher LVEDV-LTE (94±28 vs. 84±28 ml/m2, p = 0.01), LVESV-TTE (64±27 vs. 55±23 ml/m2, p = 0.003), LVEF-CMR (141±43 vs. 128±41 mln/m2, p = 0.01), LVEF-CMR (105±42 vs. 90±39 mln/m2, p = 0.003), lower LVEF-
Results: were retrospectively included and divided into two groups (i) patients with appro-
vable value as previously reported heterogeneity algorithms. The purpose was to determine 1) if the extent and heterogeneity of LGE
areas predicts appropriate ICD-therapy in ischemic and dilated cardiomyopathy

Purpose:

Background:

Patients at risk for malignant ventricular arrhythmias receive pri-
mary percutaneous coronary intervention (PCI). Therefore, aim of this study was

Methods: Cardiac magnetic resonance can predict appropriate primary prevention
of future major cardiac ischemic events. These impair-
ments may be related to remodeling the myocardial extracellular matrix.

Purpose:

Background: Myocardial extracellular matrix remodeling is associated with diffuse
myocardial fibrosis and collateral function in coronary chronic total

Methods:

Purpose: Myocardial extracellular matrix remodeling is associated with diffuse
myocardial fibrosis and collateral function in coronary chronic total

Purpose: Single-center studies suggest an association of infarct tissue het-
erogeneity assessed by cardiac MR might provide additional prog-
ducts that could be useful for risk stratification and moni-
toring target treatment.

Conclusion: Patients with CTO and 15 age- and sex-matched volun-
teers undergoing cardiac MR were recruited to the study. Global ECV was calcu-
lated from pre- and post-contrast T1 map around the entire LV myocardium and
calibrated by hematocrit. ECV of remote myocardium was calculated from the my-
ocardium without late gadolinium enhancement. Segmental ECV was obtained from
myocardial segments within the perfusion territory of a CTO. The function of
collateral vessels was assessed using the Rentrop classification as the reference
standard. ECV of remote myocardium was significantly higher in CTO patients than in normal subjects (26.6±5.6% vs. 23.3±2.0%, P<0.05). Other factors asso-
ciated with an elevated ECV were an older age (r=0.33, P<0.05), a longer course of
disease (r=0.39, P=0.02), a larger left atrial diameter (r=0.37, P<0.05) and the presence of diabetes and hypertension (r=0.38, P=0.03). Global EF significantly correlated with LV ejection fraction (EF) (r=−0.56, P<0.001) and with the grade of
EF impairment (P<0.001). The lower segmental ECV was associated with the presence of well-developed collaterals (P<0.004), and multivariate binary logistic analysis demonstrated that mean segmental ECV and course of disease were the independent discriminators of collateral formation with overall diagnostic accuracy of 74.4%.

Conclusion: In patients with CTO, diffuse myocardial fibrosis and collateral function can be non-invasively assessed by ECV measurements. ECV measured by cardiac MR may serve as a useful alternative for risk stratification and moni-
toring target treatment.

CMR for clinical diagnosis and prognostication

Conclusion: In patients with single ventricular physiology, LGE identified by cMRI before shunt procedure may be associated with the pathogenesis of de-
creased cardiac elastance and increased myocardial stiffness, leading to the de-
velopment of right ventricular dysfunction. Although latent heart failure could be predicted in these patients after palliations, adjunctive CDT therapy may have a potential to reverse cardiac dysfunction by direct conversion of the extent and severity of myocardial fibrosis.

Purpose: The aim of this study was to quantify extracellular volume fraction (ECV) in CTO patients and to investigate its relationship with diffuse myocardial fibrosis and collateral function.

Methods: A total of 50 patients with CTO and 15 age- and sex-matched volun-
teers undergoing cardiac MR were recruited to the study. Global ECV was calcu-
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calibrated by hematocrit. ECV of remote myocardium was calculated from the my-
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infarction using a standardized protocol. Analysis of tissue heterogeneity of peri-
infarct zones was performed using commercially available CMR post-processing
software (CMR42, Circle Insc. Calgary, Canada). A computer-assisted, semiauto-
matic algorithm quantified the total infarct size and divided it into the core and peri-
infarct regions based on signal-intensity thresholds (5 SDs and 3 SDs above
remote normal myocardium, respectively). The peri-infarct zone was normalized
as a percentage of the total infarct size. The association of peri-infarct tissue
heterogeneity and occurrence of major adverse cardiac events (all cause death,
reinfarction, and new congestive heart failure within 1 year after infarction) was
evaluated.

Results: The median peri-infarct zone was 23.4% LV (interquartile range 15.6
to 29.9). Patients with cardiovascular events had significantly larger peri-infarct zones (28% versus 13%, p < 0.01). In a multivariate model that included clinical and
tissue heterogeneity variables, the extent of the peri-infarct zone was an independent predictor of the combined clinical endpoint (1.45, 95% CI, 1.15 to 1.84; p = 0.002).

Conclusion: In this CMR study of acutely reperfused STEMI patients, peri-infarct
tissue heterogeneity was associated with adverse cardiac events. These results indicate
that peri-infarct tissue heterogeneity might be useful for acute risk strat-
ification of the postinfarction patient. Further studies are warranted to determine potential early ICD indications.

Atrial fibrillation in patients admitted to coronary care units in western Sweden. Focus on obesity and lipotoxicity

P4063 | BENCH
Introduction: Atrial fibrillation (AF) is the most common form of arrhythmia in hu-
mans and is associated with substantial morbidity and mortality. We hypothesized
that obesity and diabetes are involved in the pathophysiology of AF by means of promoting lipidotoxicity and adipose tissue
hypertrophy in cardiac muscle, and that AF is predictive of obesity in cardiac care patients.

Methods: Our study consists of two parts. The first part is a case-control study based on prospective data obtained through the Register of Information and Knowledge about Swedish Hospital Admissions (Riks-IA) from five hospitals in western Sweden. All consecutive patients between 2006–2011 ad-
mitted to coronary care unit (CCU) with sinus rhythm (SR) or AF were included in the analysis. Multivariate logistic regression and Cox proportional-hazards re-
gression were used to test whether diabetes and obesity were independent pre-
dictors of AF at admission to CCU and whether AF was associated with increased one-year mortality. In the second part we obtained atrial biopsies from 54 patients undergoing cardiac surgery and performed lipidomics analysis for a detailed qual-
litative and quantitative analysis of lipid species including triglycerides (TG), cer-
eramides (CER), phosphatidylcholines (PC), lysophosphatidylcholines (LPC), phos-
phatidylethanolamine (PE), sphingomyelins (SM), free cholesterol (FC), choles-
terol esters (CE) and diacylglycerols (DAG).

Results: Between 2006–2011, 35232 patients were admitted to CCUs in western Sweden, mostly due to ischemic heart disease, heart failure, arrhythmia, syncope and chest pain. The mean age was 66 years and 58.7% were male. There was a high prevalence of obesity (20.3%) and diabetes (16.8%). Obesity (OR 1.35, 95%
CI 1.17–1.56, P<0.001) and severe obesity (1.6, 95% CI 1.29–1.99, P<0.001)
and diabetes (OR 0.97, 95% CI 0.94–1.00, P=0.001) were independent predictors of AF. AF incidence increased with age (7.1% ±2.7% 1.2 hours to 2.7% (p=0.004) in women >75 years and delay >12 hours.

Conclusion: Older patients are at high risk for complications and failure of car-
dioversion of acute AF. The risk of TEC rises substantially in both sexes and particularly in women >65 years when delay to cardioversion exceeds 12 hours. This should be taken into account when considering the treatment strategy of this increasing patient population.

Atrial fibrillation and hypertrophic cardiomyopathy: a propensity score analysis from a multicenter Portuguese study

P4062 | BENCH
Introduction: Atrial fibrillation (AF) is a frequent reported complication of hyper-
trophic cardiomyopathy (HCM), but its prognostic impact remains unresolved.

Purpose: To study the prognostic influence of AF in a cohort of HCM patients.

Methods: We enrolled 461 HCM patients from a Portuguese multicenter registry – the Sunshine project. We created two groups based on a propensity score
(PS) matching between AF and sinus rhythm (SR) patients. The adjustment was performed for 7 clinical variables, with a score range of 0.01. For cases with a similar score range, the selection was performed randomly. Our final sample was: Group A (AF) N=69 and Group B (SR) N=69. The clinical endpoints of interest were cardiovascular mortality and all cause mortality.

Results: Both groups were similar regarding age (65±13 vs 65±12 years, P=0.85) and gender. Groups were also homogenous regarding symptomatic status
(NYHA and CCS class), and family history of sudden cardiac death (15.9 vs 14.5%, P=0.81). The interventricular septum was similar (18±5 vs 18±4 mm, P=0.98). AF was the left ventricular ejection fraction (LVEF) <50% (15±8 vs 17±10%, P=0.22). The phenotypic type of HCM, the presence of left ventricular obstruction and the evidence of late gadolinium enhancement were also indistinguishable between the groups. Non-sustained ventricular arrhythmia (23.2 and 20.3%, P=0.68) and his-
teria was more common in women (1.9% vs. 0.4%, P=0.02) and severe obesity
(1.6, 95% CI 1.29–1.99, P<0.001) than those without AF . Patients with AF had a higher rate of an implantable defibrillator (19.7 vs 7.7%, P=0.046). Cardiovascular mor-
tality was the same (4.3 vs 1.4%, p=0.31) and all cause mortality was statistically similar for both groups (7.2 vs 1.4%, p=0.10).

Conclusions: According to our matched groups, AF was not significantly associ-
ated with mortality in HCM patients.
Methods: LLC, Titusville, United States of America

Purpose: (NVAF), may increase the risk of major bleeding (MB).

Conclusions: AF was common and was associated with a substantial risk for stroke and mortality in patients with ApHCM. As AF was observed in most ApHCM patients with strokes, AF should be carefully managed in ApHCM.

P4065 | BEDSIDE
Evaluation of safety and efficacy of perioperative use of rivaroxaban and apixaban in catheter ablation for atrial fibrillation

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Background: Uninterrupted perioperative use of warfarin was reported to decrease cerebral thromboembolic events in catheter ablation for atrial fibrillation (AF) without increasing bleeding complications in some studies. We previously reported that dabigatran increased the risk of both micro-thromboembolism and hemopericardium compared with warfarin, but controversy exists in the safety of non-vitamin-K-antagonist oral anticoagulants (NOAC) in the perioperative use of AF ablation.

Purpose: To investigate the incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium treated with pericardiocentesis in AF ablation with perioperative use of rivaroxaban, apixaban, or warfarin.

Methods: This prospective randomized study was performed from March 2013 to December 2014. Patients taking NOAC on visiting our hospital were randomly assigned into two groups; rivaroxaban and apixaban. Warfarin was not changed in the patients taking warfarin. Rivaroxaban was given in the evening and continued, and apixaban was interrupted only on the morning of the procedure. Heparin was used to keep activated clotting time >300 sec. Asymptomatic cerebral micro-thromboembolism was evaluated by magnetic resonance imaging (MRI) at the day after procedure.

Results: In 176 consecutive patients (101 paroxysmal, and 75 persistent AF), rivaroxaban was used in 55, apixaban in 51, and warfarin in 70. The average of total heparin dose was 11400 units in patients with warfarin, 19500 with rivaroxaban (P<0.001), and 14240 with apixaban (P=0.017). Two patients with paroxysmal AF (1 with apixaban, 1 with warfarin) were not underwent MRI due to the patients’ condition. There were no symptomatic cerebral infarction, and asymptomatic cerebral micro-thromboembolism was detected in 32 (18.4%); 9 (16.4%) with rivaroxaban, 10 (20, P=0.80) with apixaban, and 13 (18.8%, P=0.81) with warfarin. The hemopericardium was occurred in 5 (2.8%) patients; 2 with rivaroxaban, 1 with apixaban (P=1.0), and 2 with warfarin (P=1.0). In monovariate analysis, brachial-ankle pulse wave velocity (p=0.015), left ventricular mass estimated with echocardiography (p=0.004), comorbidity with coronary angiography (CAG, p=0.05), hypertension (HT, p=0.003), and diabetes mellitus (p=0.025), were predictors of micro-thromboembolism in AF ablation. In multivariate analysis, HT (p=0.008, odds ratio 4.0) and CAG (p=0.015, odds ratio 5.0) were predictors. Conclusion: The incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium in AF ablation was similar between the perioperative use of rivaroxaban, apixaban, and warfarin.

P4066 | SPOTLIGHT
Major bleeding in a post-marketing assessment of 39,052 non-valvular atrial fibrillation patients on rivaroxaban


Methods: Nearly 10 million electronic medical records from the Department of Defense healthcare system were queried to identify MB-related hospitalizations among rivaroxaban users with NVAF as part of an ongoing 5-year pharmacovigilance study. MB was defined by a validated case-finding algorithm (Cunningham 2011), which uses a MB definition that is similar to the clinical trial definition. Data were collected on demographics, comorbidities, concomitant medications, MB management, and fatalities.

Results: During the first 2 years of the study, 970 of 39,052 rivaroxaban patients had at least one MB event, with an incidence rate of 2.89 [95% CI 2.71–3.08] per person-years. The most common MB site was gastrointestinal (GI) with 87.2% (846/970), followed by intracranial (IC) with 8.1% (79/970). In the MB group, 42.3% (410/970) were transferred to the ICU, and 51.5% (500/970) received a blood transfusion. The average (SD) length of hospitalization was 4.0 (3.4) days. Mean (SD) age of MB cases was 78.7 (7.9), versus 76.0 (9.9) years in the non-MB group. Patients represented 50.9% of the MB cases, versus 55.8% in the non-MB group. Comparing MB to non-MB patients, comorbidities were more frequent in the MB group, as was a history of AF (94.8% versus 87.4%), coronary heart disease (60.8% versus 31.4%), and heart failure (47.0% versus 19.7%), respectively. Mean (SD) CHA2DS2-Vasc score was 4.8 (1.5) for MB, versus 3.5 (1.6) for non-MB patients. Thirty-five MB patients died, yielding a fatal bleeding rate of 0.10 (95% CI 0.07–0.15) per 100 person-years. Of those who died, 26 (74.3%) experienced ICH, and 9 (25.7%) had GI bleeding. Mean (SD) age at death was 80.3 (8.3) years.

Conclusion: The rates and pattern of major bleeding among rivaroxaban users with non-valvular atrial fibrillation in this study are low and similar to that of the registration trial.

P4067 | BEDSIDE
Clinical evaluation of laboratory methods to monitor rivaroxaban treatment in patients with atrial fibrillation

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Introduction: New oral anticoagulants (NOACs) effectively reduce the risk of ischemic stroke and systemic embolism in atrial fibrillation (AF). The Xa-inhibitor rivaroxaban is dosed once daily. That could cause a more pronounced variability in plasma concentration and effect of the drug and a deeper knowledge of these variables are needed in certain clinical situations.

Purpose: This study aimed to evaluate the plasma concentration and effect of the direct Xa-inhibitor rivaroxaban in a cohort of well characterized ‘real-life’ AF-patients.

Material and methods: Fifty-one AF patients (74±13 years, 53% men) treated with rivaroxaban 15 mg (n=10) or 20 mg (n=41) once daily. Trough (n=51) and peak (n=30) plasma rivaroxaban concentrations determined by liquid chromatography-tandem mass-spectrometry (LC-MS/MS) were compared to the coagulation assays Anti-factor Xa for rivaroxaban, PT-INR (venous samples and point-of-care assay (POC) CoaguChek XS Pro) and aPTT.

Results: The rivaroxaban plasma concentration determined by LC-MS/MS showed a pronounced variation in both trough (median 33.9; range 4.9–83.9 ng/mL) and peak samples (median 232.5; range 120–375 ng/mL); A strong correlation between LC-MS/MS and the anti-Xa-FAA-assay was found (r2=0.80) for both trough and peak values. Peak (k=0.99) samples. Between LC-MS/MS and aPTT or PT-INR in venous samples there were no significant correlation at trough or peak while there was a significant correlation between plasma concentration and PT INR with the POC assay (r2=0.41, p<0.001) in peak samples. There was a significant but weak correlation between trough and peak drug concentration (r2=0.27, p<0.01, n=30). There were no significant correlations between gender, creatinine clearance, body weight or age and rivaroxaban exposure either at trough or peak.

Conclusions: In a cohort of ‘real-life’ AF-patients treated with rivaroxaban, we observed a pronounced variability in plasma concentrations both at trough and at peak measured by LC-MS/MS. The anti-Xa-FXa assay performed well upon rivaroxaban levels in a normal exposure range. Both methods could be of clinical value to measure rivaroxaban in certain situations. Interestingly the POC assay for PT INR might be useful for ruling out overexposure to rivaroxaban in emergency situations, e.g. in acute coronary syndromes when an invasive procedure is required.

PRE-HOSPITAL PHASE OF STEMI

P4068 | BEDSIDE
Does prehospital ECG transmission reduce false activations of the cardiac catheterization lab compared to paramedic ECG interpretation in a primary PCI program?

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Background: Prehospital diagnosis of STEMI reduces first medical contact to reperfusion time by allowing bypass of (i) non PCI-capable hospitals and (ii) the emergency department of PPCI centres. This is at the expense of increased rates

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of false activations of the cardiac catheterization laboratory (CCL) however. Prehospital diagnosis can be made in the field by onsite paramedics or by a physician using wireless ECG transmission. To date, no study has directly compared the accuracy of these 2 modes of diagnosis. In a regional primary PCI programme served by a sole ambulance provider, ECG transmission capability in only selected ambulances (determined geographically) allowed comparison of these 2 diagnostic modes.

**Purpose:** The purpose of this study was to determine whether prehospital ECG transmission in STEMI was associated with lower rates of false positive ECG activation than paramedic CCL activation.

**Methods:** This was a retrospective observational study. All “Code STEMI” admitted directly from the field to the CCL over a 3 year period were included and divided into two groups depending on mode of prehospital diagnosis. Patients who died before reaching the CCL were excluded. A false activation was defined as lack of a culprit lesion by coronary angiography or lack of ECG or biomarker evidence of STEMI. ECG findings in false activations were compared between the two groups.

**Results:** Of 748 “Code STEMI”s over a 3 year period, 362 (48.4%) were transferred directly from the field to the CCL, 214 of these (59.1%) by ambulance and 148 (40.9%) by helicopter. In total, 128 (35.4%) had prior ECG transmission, 108 (50.5%) of ambulance transfers and 20 (13.5%) of helicopter transfers. Overall, 71 were false positive activations (19.6%); 14 (10.9%) of those with transmission time > 20 min. Out of 108 patients transferred to the HH. We compared the two with regard to achieving the optimal Door-balloon time (DBT) of 90 min for those transferred to Primary PCI facility (HH), versus those transferred to the HH. We compared the two with regard to achieving the optimal Door-balloon time (DBT) of 90 min for those transferred to Primary PCI facility (HH), versus those transferred to the HH. It also alerts the Primary PCI teams to be ready even before the patient arrives, and avoids delays in Emergency rooms.

**Methods:** Patients who had Primary PCI for STEMI, 605 (55%) were transferred directly to the Heart Hospital (HH). These were compared with 488 patients (45%) who went to Other Hospitals first (OH) and subsequently transferred to the HH. We compared the two with regard to achieving the optimal Door-balloon time (DBT) of 90 min for those transferred to PPCLI facility (HH), versus 120 min for those going to OH, as per guidelines.

**Results:** Age was similar 49 vs 50 years and there was no Ethnic difference (73% Asians and 23% Arabs) in both groups. The DBT was 58±26 min for HH group vs 117±75 min in OH group (p<0.001). Furthermore, while 89% achieved <90 min in HH group, only 64% achieved ≤ 120 min in OH group, p<0.01. Out of Hospital Delay (OHD i.e delay from symptoms until arrival to hospital) was also different. Patients who had W-ECG arrived faster to HH and thus had shorter OHD (279±375 min) than those using own transport to HH (309±334 min). The combined OHD+DBT (Total delay from symptoms to Balloon) was also shorter in HH (W-ECG group) (337 min) than similar group going to OH (426 min), thus saving 89 vital minutes in the whole process from symptoms to ballooning. Initial TIMI-0 flow was similar (HH 52% vs OH 46%), but TIMI-III flow was achieved significantly more in HH (95%) than in OH group (92%), p=NS. Peak Troponin (ng/ml) was higher in OH group (7934 vs (7669) in HH, p<0.05. While Ejection fraction was similar (HH 46.7% vs OH 46.2%), there was a trend towards higher in-hospital mortality in OH group (3%) vs (2.8%) in HH, p=NS. Finally, length of stay was also longer in OH (3.9±3.3) compared to 3.4±3.1 in HH group, p=0.05.

**Conclusions:** Pre-hospital Trans-satellite wireless ECG from the ambulance to Primary PCI facility results in significantly shorter DBT, total symptoms to balloon time, and length of stay, as well lower peak Troponin and a trend towards lower in-hospital mortality. More efforts are required to make the public aware of cardiac symptoms and to report early, thus reducing the out of hospital delay.

**P4069 | BEDSIDE**

Pre-hospital trans-satellite wireless 12 lead ECG transmission from the ambulance to primary PCI centre

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**Introduction:** In Primary PCI, time is recognized as a crucial factor. To speed up diagnosis and timely intervention, we installed a “Nationwide” Trans-Satellite Wireless ECG (T-Sat-WECG) network. This enables swift Pre-hospital identification of STEMI and transfer of patients directly to the PPCLI facility in Heart Hospital (HH), thus preventing the extra step of transfer to other non-Primary PCI facilities first (OH). It also alerts the Primary PCI teams to be ready even before the patient arrives, and avoids delays in Emergency rooms.

**Methods:** Patients who had Primary PCI for STEMI, 605 (55%) were transferred directly to the Heart Hospital (HH). These were compared with 488 patients (45%) who went to Other Hospitals first (OH) and subsequently transferred to the HH. We compared the two with regard to achieving the optimal Door-balloon time (DBT) of 90 min for those transferred to PPCLI facility (HH), versus 120 min for those going to OH, as per guidelines.

**Results:** Age was similar 49 vs 50 years and there was no Ethnic difference (73% Asians and 23% Arabs) in both groups. The DBT was 58±26 min for HH group vs 117±75 min in OH group (p<0.001). Furthermore, while 89% achieved <90 min in HH group, only 64% achieved ≤ 120 min in OH group, p<0.01. Out of Hospital Delay (OHD i.e delay from symptoms until arrival to hospital) was also different. Patients who had W-ECG arrived faster to HH and thus had shorter OHD (279±375 min) than those using own transport to HH (309±334 min). The combined OHD+DBT (Total delay from symptoms to Balloon) was also shorter in HH (W-ECG group) (337 min) than similar group going to OH (426 min), thus saving 89 vital minutes in the whole process from symptoms to ballooning. Initial TIMI-0 flow was similar (HH 52% vs OH 46%), but TIMI-III flow was achieved slightly more often in HH (95%) than in OH group (92%), p=NS. Peak Troponin (ng/ml) was higher in OH group (7934 vs (7669) in HH, p<0.05. While Ejection fraction was similar (HH 46.7% vs OH 46.2%), there was a trend towards higher in-hospital mortality in OH group (3%) vs (2.8%) in HH, p=NS. Finally, length of stay was also longer in OH (3.9±3.3) compared to 3.4±3.1 in HH group, p=0.05.

**Conclusions:** Pre-hospital Trans-satellite wireless ECG from the ambulance to Primary PCI facility results in significantly shorter DBT, total symptoms to balloon time, and length of stay, as well lower peak Troponin and a trend towards lower in-hospital mortality. More efforts are required to make the public aware of cardiac symptoms and to report early, thus reducing the out of hospital delay.

**P4070 | BEDSIDE**

The importance of a qualified pre-hospital ECG and subsequent triage of patients with STEMI to the catheterization laboratory to minimize the door-to-balloon time

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**Background:** Timely reperfusion therapy is recommended for patients with ST-segment elevation myocardial infarction (STEMI), and door-to-balloon delay has been proposed as a performance measure.

**Purpose:** The first-medical-contact-(FMC)-trial of a city-wide registry of 20 hospitals with primary PCI facilities investigated the reliability of the ECG diagnosis by the emergency physicians.

**Methods:** Retrospective assessment of parameters of first medical care of all 1038 patients with an acute coronary syndrome, who were enrolled in the year 2012 by the EMS and retrospective evaluation of the pre-hospital and hospital ECGs in adherence with the guidelines of the European Society of Cardiology by three experienced cardiologists. Merging and analysis of the data of the FMC-trial and the registry-dataset were performed.

**Results:** From a total of 1038 patients with a pre-hospital ECG, 756 had an unambiguous ST-elevation, 282 patients did not show any ST-segment deviation. In 26% of a total of 756 Patienten with ST-segment elevation the EMS-physicians failed to diagnose a STEMI (see figure), 17% of the patients were discharged with the diagnosis NSTEMI. The medical care of 756 patients with a definite STEMI diagnosis was different from those with ambiguous findings in the pre-hospital ECG assessed by the physician in the field. An unambiguous "STEMI diagnosis led to shorter door-to-balloon times (53 min, median) in comparison to patients with ambiguous readings (142 mm, median)".

**Acknowledgement/Funding:** None
P4072 | BEDSIDE
Increased dissemination of registered AEDs is associated with higher rate of bystander defibrillation in public locations but not in residential areas - a nationwide study
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Introduction: Public automated external defibrillators (AEDs) allow bystanders to defibrillate out-of-hospital cardiac arrest (OHCA) patients prior to arrival of emergency medical services (EMS) and improve survival markedly. We examined by-stander use of AEDs according to public or private home location of arrest, before and after the implementation of a nationwide AED registry besides uncontrolled AED dissemination.

Methods: We identified first-time OHCA cases from 2001–2012 and included 25,287 non-EMS witnessed arrests with known location of arrest (private/public) and whether the patient was defibrillated prior to EMS arrival.

Results: In total, 18,818 (74.4%) and 6,469 (25.6%) patients had an OHCA in a private or public location, respectively (P < 0.001). The number of registered AEDs increased from 141 in 2007 to 7,800 in 2012 and 17.5% of all AEDs were available near residential areas. As the number of AEDs increased, the rate of patients defibrillated by bystanders prior to EMS arrival in public locations, increased from 1.4% in 2001 to 11.8% in 2012 (Figure). The rate of patients defibrillated in private locations remained unchanged from 2001 to 2012. Thirty-day survival increased 1.4% in 2001 to 11.8% in 2012 (Figure). The rate of patients defibrillated in private or public location, respectively (P < 0.001) if adjusted for the GRACE score risk variables by one standard deviation after adjustment for age and gender and of 1.57-fold (95% CI: 1.13–2.19, p=0.008) if adjusted for the GRACE score risk variables.

Conclusion: Public dissemination of AEDs improves bystander defibrillation and may increase overall survival. In residential areas this effect was not observed.

P4074 | BEDSIDE
GDF-15 is a predictor of cardiovascular events in patients presenting with suspicion of acute coronary syndrome
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Background: The appropriate treatment for patients presenting with acute chest pain is based on timely diagnosis and proper risk stratification aided by biomarkers. Growth-differentiation factor-15 (GDF-15) is a member of the transforming growth factor β family proteins induced in the heart after ischemia and reperfusion injury. We aimed at evaluating the predictive value of GDF-15 in an unselected “real world” cohort of patients presenting with acute chest pain.

Methods: Consecutive patients presenting with acute chest pain were enrolled at three chest pain units in Germany. Cardiovascular events were assessed during a follow-up period of 6 months. As combined primary endpoint death or myocardial infarction (MI) was considered. GDF-15 was measured in blood drawn at admission.

Results: From the 1818 patients (m/f=1208/610), 413 (22.7%) had an acute MI; Patients with MI had significantly higher GDF-15 compared with non-ACS patients (967.1pg/mL vs. 692.2 pg/L, p<0.001). 63 patients reached the primary endpoint. Cox regression analysis revealed a 2.1-fold risk for death or MI (95% CI: 1.67–2.65, p<0.001) for an increment of the log transformed GDF-15 concentration by one standard deviation after adjustment for age and gender and of 1.57-fold risk (95% CI: 1.13–2.19, p<0.008) if adjusted for the GRACE score risk variables.

Conclusion: GDF-15 is a predictor of cardiovascular events in patients presenting with suspicion of acute coronary syndrome.

P4073 | BEDSIDE
Epidemiology and outcomes of poisoning-induced out-of-hospital cardiac arrest
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Background: There is very few literature about cardiac arrest from poisoning by therapeutic or recreational drugs. The lack of prehospital data for severe poisonings is a major obstacle to the performance of high-quality clinical research.

Purpose: We aimed to compare the epidemiological features and outcomes among adult patients with poisoning-induced out-of-hospital cardiac arrests (POHCA) and other causes of OHCA.

Methods: We identified OHCA patients managed by advanced cardiac life support (ACLS) emergency medical services (EMS) systems from an exhaustive OHCA registry between 15 May 2011 and 15 May 2014. Data were derived from EMS run sheets and followed by hospital record review. Utstein elements were collected and survival at hospital discharge was measured. We compared patient’s characteristics using Student or Chi2 square tests, as appropriate. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for hospital discharge survival were calculated from a multivariate logistic regression model.

Results: Among the 11,071 OHCA, 84 (0.8%) POHCA were identified. Compared with OHCA patients from other causes, patients with POHCA were often young female patients with unwitnessed cardiac arrest occurring at home. Resuscitation was attempted in 63 (75%) POHCA patients and 6891 (63%) OHCA patients from other causes. For EMS-treated POHCA, a shockable rhythm in the initial electrocardiogram was less likely to occur. Early resuscitative measures recommended in standard ACLS resuscitation guidelines were performed in all patients. Extraordinary resuscitative measures such as extra-corporal membrane oxygenation (ECMO) was used more often in POHCA patients (9 (14%) vs 262 (4%), p<0.0001) while hypothermia was used similarly in the two groups. The survival to hospital admission and discharge rates of POHCA patients were 40% and 11% respectively. In the multivariate model, POHCA versus other causes of OHCA was independently associated with hospital discharge survival (adjusted OR 4.3 (1.8–10.5), p<0.001). Other independent predictors of hospital discharge survival were bystander cardiopulmonary resuscitation, shockable rhythm and hypothermia while increased age, OHCA at home and ECMO were associated with hospital discharge mortality.

Conclusion: Using an exhaustive OHCA registry, poisoning was a relatively infrequent cause of cardiac arrest but occurred often in young female patients with unwitnessed cardiac arrest occurring at home. Extraordinary resuscitative measures were more often used in POHCA compared to EMS-treated OHCA of other causes even after accounting for independent predictors.
compared to a 1.94-fold (1.45–2.60, p < 0.001) and 1.45-fold (95% CI: 1.06–1.98, p = 0.021) for BNP.

**Conclusion:** GDF-15 is a significant predictors of future cardiovascular events in patients presenting with acute chest pain. GDF-15 levels correlate with the severity of CAD and can risk stratify patients in need for coronary revascularisation, possibly facilitating the choice of treatment in those patients.

**INFORMATION TECHNOLOGY APPLICATIONS IN CARDIOLOGY**

**P4076 | BEDSIDE**

Monitoring of day by day fluctuations of different cardiac resynchronization therapy (CRT) device parameters allows to predict device interventions


**Medical University of Silesia, 1st Dept of Cardiology, Congenital Heart Diseases & Electrotherapy, Zabrze, Poland**

**Aim:** To assess the value of day by day variations of different cardiac resynchronization therapy (CRT) device parameters in early prediction of both adequate (AT) and inadequate (IAT) therapies.

**Methods:** A single-center, prospective registry encompassed 305 consecutive heart failure (HF) patients (pts) who were implanted with CRT-D devices. Every pt was monitored on a daily basis via remote monitoring for the median follow-up period (FU) of 20.5 months. Every transmission was screened for potential therapy triggers such as: atrial burden, mean and max. heart rate during atrial fibrillation, mean ventricular heart rate, mean ventricular heart rate at rest, patient activity, mean PVC/h and CRT pacing percentage (CRT%). All pts were assigned to one out of three groups, depending on the presence and/or adequacy of delivered therapy at the end of FU: adequate therapy (ATG), inadequate therapy (IATG) and control group (no therapies during FU).

**Results:** During the FU at least one AT and IAT occurred in 21.3 and 12.8% of pts and the mean time to the first AT and IAT was 328 (79–982) and 212 (58–491) days respectively. Triggers for both AT and IAT were depicted in Table 1. The independent risk factor for AT was mean ventricular heart rate at rest (HR 1.07, 95% CI 1.05–1.09, p < 0.001), while in IAT it was max. heart rate during atrial fibrillation (HR 1.03, 95% CI 1.01–1.04, p = 0.004).

**Conclusion:** Continuous day by day monitoring of variations of different CRT parameters facilitates early detection of therapy triggers which may help in interventions aiming at avoiding both AT and IAT.

**P4076 | BEDSIDE**

The Utilization and Clinical Feasibility of 24-Hour Hand-Carry Remote ECG Recording Device in Cardiac Arrhythmias and Atrial Fibrillation: A Pilot Study

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**Aim:** To determine the diagnostic accuracy of Q-waves on 12 lead ECG to identify myocardial scarring using CMR as gold standard.

**Background:** Traditional, the presence of Q-waves on 12 lead ECG is considered a marker of a large and/or transmural myocardial infarction (MI). Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) accurately identifies myocardial infarction and has become the gold standard for the assessment of myocardial viability. However, CMR is not universally available and clinicians often have to make assumptions on myocardial scarring based solely on the 12 lead ECG.

**Aim:** To determine the diagnostic accuracy of Q-waves on 12 lead ECG to identify myocardial scarring using CMR as gold standard.

**Methods:** Aortic stenosis (AS) or aortic regurgitation (AR) comprised 50.9% among them. Subjects with history of heart failure (OR: 3.37, 95% CI: 1.69 to 6.74), diabetes (OR: 3.03, 95% CI: 1.53–5.93), ischaemic heart disease (OR: 3.38, 95% CI: 1.97–5.80) and/or atrial fibrillation (OR: 1.94, 95% CI: 1.06–1.98, p = 0.021) for BNP.

**Conclusion:** GDF-15 is a significant predictors of future cardiovascular events in patients presenting with acute chest pain. GDF-15 levels correlate with the severity of CAD and can risk stratify patients in need for coronary revascularisation, possibly facilitating the choice of treatment in those patients.

**INFORMATION TECHNOLOGY APPLICATIONS IN CARDIOLOGY**

**P4076 | BEDSIDE**

Monitoring of day by day fluctuations of different cardiac resynchronization therapy (CRT) device parameters allows to predict device interventions


**Medical University of Silesia, 1st Dept of Cardiology, Congenital Heart Diseases & Electrotherapy, Zabrze, Poland**

**Aim:** To assess the value of day by day variations of different cardiac resynchronization therapy (CRT) device parameters in early prediction of both adequate (AT) and inadequate (IAT) therapies.

**Methods:** A single-center, prospective registry encompassed 305 consecutive heart failure (HF) patients (pts) who were implanted with CRT-D devices. Every pt was monitored on a daily basis via remote monitoring for the median follow-up period (FU) of 20.5 months. Every transmission was screened for potential therapy triggers such as: atrial burden, mean and max. heart rate during atrial fibrillation, mean ventricular heart rate, mean ventricular heart rate at rest, patient activity, mean PVC/h and CRT pacing percentage (CRT%). All pts were assigned to one out of three groups, depending on the presence and/or adequacy of delivered therapy at the end of FU: adequate therapy (ATG), inadequate therapy (IATG) and control group (no therapies during FU).

**Results:** During the FU at least one AT and IAT occurred in 21.3 and 12.8% of pts and the mean time to the first AT and IAT was 328 (79–982) and 212 (58–491) days respectively. Triggers for both AT and IAT were depicted in Table 1. The independent risk factor for AT was mean ventricular heart rate at rest (HR 1.07, 95% CI 1.05–1.09, p < 0.001), while in IAT it was max. heart rate during atrial fibrillation (HR 1.03, 95% CI 1.01–1.04, p = 0.004).

**Conclusion:** Continuous day by day monitoring of variations of different CRT parameters facilitates early detection of therapy triggers which may help in interventions aiming at avoiding both AT and IAT.
Methods: Data was collected on consecutive patients referred for a stress CMR with suspected ischaemic heart disease (April 2013 to Mar 2014). Exclusion criteria: non-ischaemic heart disease that may cause Q-wave. Pathological Q-waves: deflection $>25\%$ of the subsequent R wave, or being $>40\text{ms}$ in width and $>2\text{mm}$ in amplitude in $>1$ corresponding lead. Q-waves in any 2 or more precordial leads from V1-V4 reflected LAD territory. Transmural infarction was defined as $>50\%$ LGE.

Results: 498 patients were included (mean age of 64±12 years, 71% males). 290 patients demonstrated MI, 157 were transmural and 133 sub-endocardial based on CMR LGE. 126 patients had pathological Q-waves on 12 lead ECG. The overall diagnostic accuracy of Q-wave as a marker of transmural MI was 66% and the diagnostic accuracy of Q waves as a predictor of previous MI (composite of sub-endocardial and transmural) was only 55%. Table 1. In patients with pathological Q-waves, 40% had LAD territory LGE, 55% non-LAD and 5% a combination. Of those with LAD Q waves, 68% demonstrated LAD territory LGE and in non-LAD Q waves, 67% demonstrated a non-LAD territory infarct by LGE.

Conclusion: Our study demonstrates that the presence of pathological Q-waves on 12 lead ECG is not only a poor marker of myocardial scar, but also a poor predictor of viability when compared to CMR. Our study also demonstrates the limitation of Q-wave in identifying the affected coronary artery territory. Clinicians needs to be aware of the limitations of ECG Q-waves during their clinical decision making process.

P4079 | BEDSIDE
Assessment of deceleration capacity from short-term recordings predicts mortality after myocardial infarction
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Background: Deceleration capacity (DC) of heart rate is a strong predictor of mortality after MI. DC is a measure of deceleration-related oscillations of heart rate and is usually assessed from 24-hour Holter recordings. As yet, there is no data on the predictive power of DC assessed from short-term recordings.

Methods: We included 908 survivors of acute MI in sinus rhythm aged $>80$ years. All patients underwent a 30-min ECG recording (1,600 Hz) in Frank leads configuration within the 2nd after MI. The primary endpoint was all-cause mortality. DC was calculated using previously established technologies. In addition to DC followed risk predictors were considered: reduced LVEF, the Global Registry of Acute Coronary Events (GRACE) score, presence of diabetes mellitus, elevated mean heart rate (HR), impaired standard deviation of all normal-to-normal RR-intervals (SDNN), and increased QT variability index (QTVI). Established cut-off values were used for dichotomization: $<2.5\text{ms}$ for DC, $<35\%$ for LVEF, $>0.47$ for GRACE score, $>150\text{bpm}$ for mean heart rate, $<70\text{ms}$ for SDNN, and $>120$ for the GRACE score. Uni- and multivariable Cox regression analyses were used to test the association of DC with mortality.

Results: 69 patients died within the first 5 years of follow-up. Short-term DC with a cut-off value of 2.5 ms was a strong and independent predictor of 5-year total mortality after adjustment for various predictors including LVEF, GRACE score, mean HR, SDNN and QTVI (Table). Cox regression analyses

<table>
<thead>
<tr>
<th>Risk variable</th>
<th>Univariable Cox regression</th>
<th>Multivariable Cox regression</th>
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<tr>
<td>Hazard ratio</td>
<td>p-value</td>
<td>Hazard ratio</td>
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<tr>
<td>LVEF $&lt;35%$</td>
<td>5.81 (2.23–16.51)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>GRACE score $&gt;120$</td>
<td>5.54 (3.24–9.46)</td>
<td>$&lt;0.001$</td>
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<tr>
<td>Diabetes mellitus</td>
<td>2.61 (1.61–4.23)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Mean HR 75 bpm</td>
<td>1.98 (1.11–3.55)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>SDNN $&lt;70$ ms</td>
<td>2.01 (1.22–3.33)</td>
<td>$&lt;0.001$</td>
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<tr>
<td>QTVI $&gt;0.47$</td>
<td>2.54 (1.55–4.19)</td>
<td>$&lt;0.001$</td>
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<tr>
<td>DC $&gt;2.5$ ms</td>
<td>6.13 (3.80–9.88)</td>
<td>$&lt;0.001$</td>
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</tbody>
</table>

Conclusion: DC assessed from short-term recordings is a strong and independent predictor of 5-year mortality after myocardial infarction.

P4080 | BEDSIDE
How low can we go? Performing EP-Procedures at a low radiation dose level
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Introduction: Fluoroscopy is the standard imaging modality for EP-Procedures. Since fluoroscopic systems are technically optimized for high-resolution angiography, there may be potential for dose reduction when these systems are used for EP interventions not requiring detailed resolution. Aim of this study was to test if a new low dose X-Ray program with 8nGy/pulse could provide adequate imaging quality in EP procedures. Therefore it was compared to the current low dose program using 23nGy/pulse.

Materials and methods: The new program (8nGy/pulse) was installed on an AX-IOM Artis biplane system in August 2014. 214 patients (Group A) treated with the standard 23 nGy program from 08/2014 to 11/2014 were compared to 195 patients (Group B) treated with the 23 nGy program pulse from 08/2013 to 11/2013. To avoid inter-operator effects the interventions performed by each of the three involved physicians in Group A were compared to the corresponding procedures in Group B. Furthermore we divided both groups into five procedures (Atrial fibrillation (Afib), Atrial flutter (Aflut), atrioventricular nodal reentrant tachycardia (AVNRT), atrioventricular reentrant tachycardia (AVRT), premature ventricular contractions (PVC)) because different fluoroscopy times yield different dose area products (DAP). In both groups physician’s directive was to choose a higher x-ray dose program if better image quality could provide necessary information. This happened in one out of 409 patients due to the patients BMI (40).

Results: A significant DAP reduction of 60% could be achieved using the 8 nGy/pulse program (9.06 Gy cm$^2$ (in Group B) vs 3.66 Gy cm$^2$ (in Group A), p<0.001, student-t). The two group’s BMI (27±6.54 (B) vs 27±9.47 (A); p=0.25), age (56±18.4y (B) vs 57±17.3y (A); p=0.30) and fluoroscopy time (17.5±13.0 min (B) vs 17.3±13.3 min (A); p=0.43) were insignificantly different. The average procedure duration of Afib (160±42 min (B) vs 156±35 min (A); p=0.21), Aflut (147±37 min (B) vs 140±35 min (A); p=0.45), PVC (95±40 min (B) vs 96±39 min (A); p=0.42) and AVRT (124±24 min (B) vs 102±52 min (A); p=0.1) was not affected by the dose reduction. No difference between acute success rates (98% (210/214) (A) vs 97% (190/195) (B); p=0.54) were observed.

Conclusions: The use of low dose pulsed fluoroscopy (8 nGy/pulse) can yield a significant reduction (60%; p<0.001) in radiation exposure. Neither procedure success, nor procedure duration was significantly affected (p<0.05).

Information technology applications in cardiology 691

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EXTRACELLULAR MATRIX, REMODELLING AND INFLAMMATION

P4082 | BENCH

Glycoproteomics analysis of cardiac extracellular matrix reveals the presence of decorin fragments with anti-myostatin and anti-fibrotic activity
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Background: Using proteomics, we characterize the glycoproteins of human hearts to study extracellular matrix (ECM) remodelling in the context of atrial fibrosis and cardiomyocyte hypertrophy.
Methods: Left and right matched atrial tissues were obtained from patients during cardiopulmonary bypass. ECM proteins were enriched using a sequential extraction procedure. The glycoprotein- enriched fraction, the flow-through and the input were analyzed by mass spectrometry (MS).

Results: Among ECM glycoproteins, lumican, fibrulin-2, latent TGF-β1-binding protein 4 were differentially expressed in left and right atria. Surprisingly, one glycoprotein, decorin, a member of the small leucine-rich proteoglycans, was consistently identified in the non-glycosylated, flow-through fraction. Decorin is glycosylated at its C-terminus, but only N-terminal peptides were detected in the flow-through, suggesting that decorin might be fragmented. Using MS, we identified 18 different fragmentation sites for decorin, whereas no fragmentation was observed for the closely related biglycan. The proteomic findings were validated by western blot analysis.

Conclusion: The presence of decorin cleavage products may regulate the local environment of the atrial myocardium from patients with atrial fibrillation and sinus rhythm showing structural remodelling in atrial fibrillation.
treated over 10 months with Rosuvastatin. Rac1 activity was reduced and 11β-HSD2 expression decreased compared to untreated RacET mice (324±94% vs. 185±25%, p < 0.05). In H9c2 cardiomyocytes, the expression of 11β-HSD2 was increased by L-buthionine sulfoximine (BSO) (174±47%, p < 0.05), an inhibitor of glutathione synthesis increasing reactive oxygen species and Rac1 activity. NCS-23766, a selective Rac1 inhibitor, decreased 11β-HSD2 expression (21±7%, p < 0.05). In cultured neonatal cardiac fibroblasts, aldosterone increased nuclear translocation of the MR (nuclear to cytoplasm MR localisation ratio, 0.004±0.123 vs. 0.840±0.689, p < 0.001). The translocation was prevented by the addition of racemate 11β-hydroxysteroid dehydrogenase (11βHSD) as well as by spironolactone (0.239±0.266, p < 0.01 vs. aldosterone). NCS-23766 prevented the aldosterone induced CTGF up-regulation in cardiac fibroblasts (183±55% vs. 39±5%, p < 0.01). CTGF increased fibronectin expression in cardiac fibroblasts (368±111%, p < 0.01). Aldosterone and angiotensin II exerted an additive effect on CTGF expression (aldosterone, 141±32%, p < 0.05 vs. control; aldosterone+angiotensin II, 175±67%, p < 0.001 vs. control). Telmisartan completely prevented the aldosterone effect on CTGF expression (97±11%, p < 0.05 vs. aldosterone).

Conclusion: Rac1 increases 11β-HSD2 expression enhancing MR fibrotic signalling, and regulates nuclear translocation of MR and CTGF expression. Therefore, Rac1 may represent a target for the prevention of fibrotic atrial and ventricular remodelling.

P4086 | BENCH
A CD31-derived peptide favors M2 macrophage polarization and arterial repair following Angiotensin II-induced dissection

The loss of the trans-homophilic homeostatic receptor CD31 (PECAM-1), which is constitutively expressed by the cells at the blood-vessel interface, has previously been associated with propagation of the occurrence of atherosclerotic complications, such as abdominal aortic aneurysms/dissemination, in patients and experimental mouse models. Using a synthetic CD31 agonist peptide that is able to sustain the CD31 inhibitory signaling, we analyzed its therapeutic potential in a mouse model of accelerated atherosclerosis and aortic dissection/aneurysm formation. Two weeks after male apolipoprotein E knockout mice were subjected to chronic angiotensin II infusion. Treatment by subcutaneous administration with either the CD31 peptide (2.5mg/kg) or the vehicle (n=10) started 15 days later, after the occurrence of aortic dissection, and continued until day 28. The aortic wall of CD31-treated mice was significantly richer in collagen (picrossirius red staining). Furthermore, the intramural hematoma was consistently reduced in size and infiltrated with M2-like (arginase I+) rather than M1-like (iNOS+) macrophages (CD68+). Indeed, in vitro studies suggested that CD31 signaling favors M2 rather than M1 macrophage polarization based on the analysis of iNOS, IL-6 (M1) and Arginase I, IL-10, (M2) in bone marrow-derived macrophages polarized with either LPS+IFNg (M1) or IL-4 (M2) in the presence or not of the CD31 agonist.

Conclusion: The administration of the CD31 peptide can attenuate the progression of atherosclerosis-associated arterial wall injury through its pro-M2 macrophage polarization potential, likely involved in the acceleration of arterial tissue repair processes.

P4087 | BENCH
Interleukin-1 receptor antagonist contributes to the suppression of both angiotensin II-induced hypertension and organ damage
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Introduction: The interleukin-1 receptor antagonist (IL-1Ra) is one of the most important anti-inflammatory cytokines and plays an important role in inflammation. However, the role of IL-1Ra in angiotensin II (Ang II)-induced hypertension and organ damage remains unknown.

Methods and results: To determine a possible contribution of IL-1Ra to hypertension, we examined responses to Ang II in IL-1Ra deficient (IL-1Ra−/−) mice. We used anesthetized paraplegic mice to continuously infused IL-1Ra−/− (n=18) and wild-type (WT) (n=18) mice with either Ang II or saline for 14 days. On day 14 of Ang II infusion, systolic blood pressure increased significantly in IL-1Ra−/− mice compared with WT mice (178±21 versus 135±21 mmHg, p < 0.001). Furthermore, on day 7 of Ang II infusion, blood pressure in IL-1Ra−/− mice developed higher in IL-1Ra−/− mice compared with WT mice (p<0.01), and renal preproendothelin (preproET)-1 mRNA expression was also significantly higher in IL-1Ra−/− mice compared with WT mice (p<0.05). Renal histological findings (e.g. glomerular injury and fibrosis of the tubulointerstitial area) revealed greater damage in IL-1Ra−/− mice compared with WT mice on day 14 days of Ang II infusion. Furthermore 7 days after infusion, real-time PCR of abdominal aorta in IL-1Ra−/− mice revealed significantly increased mRNA levels of IL-6 (2.1-fold, p<0.01), TNF-a (4.1-fold, p<0.01), and Arginase I (2.0-fold, p<0.05 vs. control). Histological analyses revealed there were numerous inflammatory cells around the abdominal aorta in IL-1Ra−/− mice, but not in WT mice. Furthermore, elastin staining showed destruction of the elastic lamina of abdominal aorta in IL-1Ra−/− mice. These findings suggest that deficiency of IL-1Ra promotes AngII-induced hypertension and organ damage by continuing inflammation and pro-inflammatory cytokine production.

Conclusions: The present study definitively demonstrates that deficiency of endogenous IL-1Ra significantly increases systolic blood pressure and promotes renal damage after Ang II infusion via increased expression of ET-1. Furthermore, our results also show that IL-1Ra deficiency in mice led to increased inflammation and the development of aortic aneurysm after AngII infusion.

P4088 | BEDSIDE
The synergistic effect of -174G/C polymorphism on interleukin-6 gene promoter with tobacco smoking on endothelial function, inflammatory and thrombotic processes in coronary artery disease patients
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Background: Smoking is a well known risk factor for coronary artery disease (CAD). Moreover, controversial data suggest that the -174 G/C polymorphism on IL-6 gene promoter (rs1800795) may represent a genetic risk factor for inflammatory activation, closely related to the initiation and evolution of atherosclerosis.

Purpose: In lack of relevant appropriate data the purpose of this study was to detect a possible synergistic effect of smoking with this polymorphism on several atherogenic inflammation and thrombosis, endothelial function as well as on the incidence of CAD.

Methods: 646 subjects (361 non-smokers) submitted to our department for suspected angina, were subjected to appropriate genotyping. Endothelial function was assessed by flow mediated dilatation (FMD) of the brachial artery. IL-6 (pg/ml), Tumor Necrosis Factor-α (TNF-α) (pg/ml), high sensitivity CRP (hsCRP) (mg/l) and D-dimers (µg/l) were measured with appropriate methods. The diagnosis of CAD was confirmed angiographically.

Results: An increased incidence of CAD was found among the carriers of the allele C, compared to the allele G homozygotes, OR: 1.59, CI: 1.26–2.93, p=0.032 in smokers, while a decreased incidence was observed in non smokers (OR: 0.42, CI: 0.26–0.68, p<0.001), after adjustment for CAD risk factors. The C allele carriers were more likely to be smokers than their GG homozygotes, and the development of aortic aneurysm after AngII infusion. The present study definitively demonstrates that deficiency of endogenous IL-1Ra significantly increases systolic blood pressure and promotes renal damage after Ang II infusion via increased expression of ET-1. Furthermore, our results also show that IL-1Ra deficiency in mice led to increased inflammation and the development of aortic aneurysm after AngII infusion.

AORTIC STENOSIS – FROM BASICS TO PROGNOSIS
P4089 | BEDSIDE
Calcification of aortic valve and coronary atherosclerosis: differences in bispecific and tricuspid valves
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Background: Calcific aortic valve stenosis and atherosclerosis share some underlyng pathophysiological processes. Although statins slow the progression of coronary atherosclerosis, this therapy has been shown ineffective to slow the progression of calcific aortic stenosis suggesting important differences in the pathophysiology of coronary artery disease and calcific aortic stenosis. Bicuspid aortic valves (BAV) develop calcific stenosis two decades earlier than tricuspid aortic valves (TAV) and this process may occur in these patients independent from coronary atherosclerosis development.

Purpose: In a propensity-score matched population, the calcification burden of the aortic valve and coronary atherosclerosis were analyzed with multi-detector computed tomography (MDCT) and compared between patients with BAV versus TAV. The T-test of calcific aortic stenosis suggesting important differences in the pathophysiology of coronary artery disease and calcific aortic stenosis.

Methods: From an ongoing registry of patients who underwent MDCT, patients with BAV were matched with patients with TAV in a 1:3 fashion. Aortic valve calcification and the presence of CAD were determined and propensity matched-scoring was based on age, sex, cardiovascular risk factors and chest pain symptoms.

Results: Patients with BAV (n=60) were comparable to patients with TAV (n=180) for age, sex, cardiovascular risk factors and the presence of chest pain symptoms. In addition, the median Agatston coronary artery score (0 [0–46.8] vs. 0 [0–46.6], p<0.001) compared with WT mice. Furthermore, elastin staining showed destruction of the elastic lamina of abdominal aorta in IL-1Ra−/− mice. These findings suggest that deficiency of IL-1Ra promotes AngII-induced hypertension and organ damage by continuing inflammation and pro-inflammatory cytokine production.

Conclusions: The present study definitively demonstrates that deficiency of endogenous IL-1Ra significantly increases systolic blood pressure and promotes renal damage after Ang II infusion via increased expression of ET-1. Furthermore, our results also show that IL-1Ra deficiency in mice led to increased inflammation and the development of aortic aneurysm after AngII infusion.
Aortic stenosis – from basics to prognosis

Abstract P4089 – Table 1. Calcium analysis per age quintile

<table>
<thead>
<tr>
<th>Bicuspid aortic valves</th>
<th>Tricuspid aortic valves</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quintile 1 (15–40 years)</td>
</tr>
<tr>
<td>Calcium valve volume &lt;0 ml, n (%)</td>
<td>3 (50.0)</td>
</tr>
<tr>
<td>Coronary Agatston score &gt;0, n (%)</td>
<td>0</td>
</tr>
</tbody>
</table>

p=0.673) and the presence of significant CAD (11.7% vs. 19.8%, p=0.155) did not differ between groups. In contrast, patients with BAV had a significantly larger calcium volume of the aortic valve than those with TAV (267 [46.5–1202] mm³ vs. 0 [0–0] mm³, p<0.001). Presence of aortic valve and coronary artery calcium per age quintile type of valve is displayed in Table 1.

Conclusions: Independently from coronary atherosclerosis, the aortic valve calcium load is significantly larger in patients with BAV than in patients with TAV.

P4090 | BEDSIDE
Shorter leukocyte telomere length is associated with the risk of calcific aortic stenosis

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Background: Calcific aortic stenosis (CAS), a common cause for morbidity and mortality, is more prevalent later in life. However, why some individuals develop it and others do not is unclear. We hypothesised that the risk may relate to faster biological ageing. Shorter leukocyte telomere length (LTL) which serves as a biomarker for biological ageing has been linked to a number of age-related conditions including coronary artery disease (CAD). Here we examined the association of LTL with CAS controlling for factors associated with LTL including age, gender, and CAD.

Method: 254 patients with a confirmed diagnosis of CAS were matched one-to-one on age and sex with a group of controls without CAS. All cases and controls had CAD and were of Caucasian origin. LTL was measured using a quantitative PCR-based technique, in which LTL is expressed as a ratio of telomere repeat length to copy number of a single copy gene. Telomere length was standardized using a Z-transformation approach. Conditional logistic regression, to account for the matching, was performed to test the relationship between LTL and CAS.

Results: The baseline characteristics for CAS cases and controls were similar (Table 1). There was an inverse relationship between LTL and risk of CAS. For each 1 SD shorter LTL there was a 54% higher risk of CAS (OR 1.54; 95% CI, 1.15 to 2.06, P=0.0037). In an analysis adjusted for cardiovascular risk factors subjects in the shortest LTL tertile had 2.57 times (1.29 to 5.14; P=0.007) higher CAS risk compared to subjects in the longest LTL tertile.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CAS (n=254)</th>
<th>Controls (n=254)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68±6 (4.4)</td>
<td>68±6 (4.4)</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>193 (76.0)</td>
<td>193 (76.0)</td>
</tr>
<tr>
<td>BMI*</td>
<td>29 (4.9)</td>
<td>28 (4.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>183 (72.0)</td>
<td>196 (77.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>73 (28.7)</td>
<td>59 (23.2)</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>198 (78.0)</td>
<td>205 (82.7)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>16 (6.3)</td>
<td>18 (7.1)</td>
</tr>
</tbody>
</table>

*Variable expressed as mean (SD), other parameters as frequency (%).

Conclusion: Shorter telomere length is significantly associated with risk of calcific aortic stenosis independent of age, gender, and CAD status. Our finding supports the hypothesis that CAS is partly a disease of premature biological ageing.

P4091 | BEDSIDE
Myocardial fibrosis and microRNA-21 expression in patients with severe aortic valve stenosis and preserved ejection fraction: a 2D speckle tracking echocardiography, tissueal and plasmatudy


Background: Myocardial fibrosis (MF) is an adverse correlate of severe aortic valve stenosis (SAVS), microRNA expression modulates different pathophysiological pathways in cardiovascular disease. In particular miRNA-21, has been associated to MF due to pressure overload. Non-invasive estimation of MF, using speckle-tracking echocardiography (2D-STE), could be useful in determining early myocardial damage.

Purpose: To analyze the correlation between 2D-STE parameters, MF, plasmatudy and miRNA miRNA-21 in SAVS.

Methods: We evaluated 36 consecutive patients (75±28 y.o., 63% F) with SAVS and preserved ejection fraction (EF), undergoing to surgical aortic valve replacement (AVR; Euroscore II 2.28±1.13%; Logistic Euroscore 6±4.1%). Clinical, ECG, biohumoral evaluation (including plasma miRNA-21) and a complete echocardiography, including 2D-STE, was performed before AVR. 28 patients eventually underwent AVR and, in 23 of them, a basal interventricular septum biopsy was performed. MF and tissue miRNA-21 expression (micro-dissection) was evaluated in each sample.

Results: All patients with SAVS (AVAI 0.33±0.1 cm²/m²; V max 4.4±0.4 m/sec; Mean Grad. 50±9 mmHg) showed concentric hypertrophy (LVM 147±20.7 g/m², RWT 0.51±0.07), diastolic dysfunction and increased Valvulo-Arterial Resistance (2VA: 5.9±2.3 mmHg/m²).

Despite a preserved EF (65±11%), an altered global and septal deformation (Global longitudinal strain, GLS –13±6.1; Global longitudinal strain rate, GLSR –0.8±0.2 1/sec; Global early diastolic Sr, GLSe 1±0.3 1/sec; Septal longitudinal strain, SLS –8.6±2.8; SL-Sr –0.6±1.1/sec; SL-Sr 0.6±2.9 1/sec) were observed.

We found a significant association between MF and 2D-STE parameters, stroke volume and end-diastolic pressure (all p<0.05).

Tissue miRNA-21 was mainly expressed in fibrous tissue than in myocardium (p=0.0001). Myocardial miRNA-21 was associated with AVAI (r=0.46; p=0.043) and cardiac index (r=0.5; p=0.02) while fibrous tissue miRNA-21 was associated to GLS (r=0.8; p=0.0003), GLSe (r=−0.72; p=0.005), SLS (r=0.6; p=0.01), SL-Sr (r=-0.5; p=0.03), SL-Se (r=0.2; p=0.04) and PAPa (r=0.66; p=0.04). Plasma miRNA-21 was associated to MF (r=0.5; p=0.02) and sepltal longitudinal strain (r=−0.38; p=0.037).

Conclusions: In SAVS with preserved EF, MF is associated to impaired myocardial deformation. miRNA-21 has a potential pathophysiological role in fibrogenesis. Non-invasive evaluation of plasmatic miRNA-21 and 2D-STE could be useful in risk stratification, to optimize the timing of surgery in SAVS patients.

P4092 | BEDSIDE
Combining tumor marker carbohydrate antigen 125 and the logistic EuroSCORE improves risk stratification in patients undergoing transcatheter aortic valve implantation


Introduction: Conventional risk scores are inaccurate in patients undergoing transcatheter aortic valve implantation (TAVI). Elevated tumor marker Carbohydrate Antigen 125 (CA125) is known to be associated with adverse outcome after TAVI.

Purpose: We investigated the additional value of CA125 to that of the EuroSCORE for predicting long-term mortality after TAVI.

Methods: CA125 was determined in 422 patients undergoing TAVI for severe aortic stenosis. Elevated levels of CA125 were regarded according to the manufacturers recommendations and as previously published (>30 U/ml) while elevated EuroScore was regarded as > median.

Results: Median follow-up was 59 weeks. 272% of patients (115/422) died after TAVI (1.95, 95% CI [1.63–2.34] per 10 person-year). If CA125 and EuroSCORE were elevated, mortality (and in per 10 person-year) was higher (CA125: 47%, 4.05 95% CI [3.09–5.31] vs. EuroSCORE: 20%; 1.37 [1.09–1.75], P=0.001 and CA125: 38%, 3.13 95% CI [2.52–3.89] vs. EuroSCORE: 16%, 1.03 95% CI [0.74–1.44], P<0.001, respectively) with a comparable Harrell’s C-statistic (CA125: 0.657 vs. EuroSCORE: 0.684). After adjustment for EuroScore, atrial fibrillation, previous coronary artery disease and NYHA class III/IV, elevated CA125 and EuroScore were low, mortality was low, too (14%, 0.9 95% CI [0.62–1.33]; if either variable was elevated, mortality was moderate (28%, 2.1 95% CI [1.56–2.81]); when both CA125 and EuroScore were elevated, mortality was high (43%, 5.1 95% CI [3.8–6.6]) and as value trend for >0.001.

Conclusion: CA125 offers additional prognostic information to that obtained by the EuroSCORE alone. Elevation of both CA125 and EuroSCORE was associated with poor prognosis.
**P4093 | BEDSIDE**

New-onset midwall dysfunction predicts impaired prognosis in aortic valve stenosis with normal ejection fraction (the SEAS study)

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**Background:** In hypertension, low left ventricular (LV) midwall function is associated with impaired prognosis independent of normal ejection fraction (EF).

**Purpose:** To test the prognostic value of new-onset low LV midwall shortening (MWS) during follow-up of patients with asymptomatic aortic stenosis (AS) and normal EF.

**Methods:** 1107 patients with AS, normal EF and MWS at baseline in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study were followed for a median of 4.0 years. LV systolic function was assessed by biplane EF (low if <50%) and MWS (low if <14%/16% in men/women) at baseline and annual echocardiograms. New-onset low MWS was identified at follow-up visits before any clinical event.

**Results:** 574 patients (52%) developed low MWS during follow-up. They included a higher proportion of elderly women with higher blood pressure and abnormal LV geometry (all p < 0.05). In time-varying Cox analyses new-onset low MWS predicted 45% increase in major CV events and a 2-fold increase in heart failure and CV death (Table, Figure).

**Conclusion:** In patients with mild-moderate AS, suPAR is a strong independent predictor for adverse cardiovascular events and mortality.

**P4094 | BEDSIDE**

SuPAR is associated with cardiovascular events and mortality in patients with asymptomatic aortic stenosis

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**Introduction:** Soluble uric acid plasmogen activator receptor (suPAR) is an inflammatory marker associated with cardiovascular disease. Whether suPAR is of prognostic value for asymptomatic patients with aortic stenosis (AS) remains unknown.

**Methods:** Serum suPAR levels were measured in 1,504 patients aged 28–86 years (mean age 76.7), recruited in the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trial. Cox regression analyses were performed for baseline suPAR, adjusted for traditional cardiovascular risk factors, C-reactive protein (CRP) and statin treatment. Primary outcomes were incidence of cardiovascular events (composite of non-fatal myocardial infarction, non-hemorrhagic stroke and cardiovascular death [n=135]), cardiovascular [n=80] and all-cause mortality [n=150].

**Results:** Significantly elevated suPAR levels were found in women, smokers and older patients (p < 0.01). SuPAR levels positively correlated with CRP (p < 0.001). SuPAR was significantly associated with cardiovascular events (HR=1.22 [95% CI: 1.08–1.37], p=0.001) and cardiovascular (HR=1.23 [95% CI: 1.05–1.44], p=0.009) and all-cause mortality (HR 1.21 [95% CI: 1.07–1.35], p<0.002), in fully-adjusted multivariate models.

**Conclusion:** In patients with severe AS, a global PLAS <21% is a strong independent predictor of MACEs (HR 2.88, p<0.04), as was CAD (HR 2.68, p=0.004) and the NYHA functional class (HR 2.08, p<0.03).
Differerntiating physiological adaptation from cardiac pathology in athletes

P4096 | BEDSIDE
Athletic cardiac adaptation is secondary to increased myocyte mass

Background: Cardiac remodelling occurs in response to regular athletic training, and the degree of remodelling is associated with fitness. Understanding the myocellular changes in athlete’s heart (AH) is important to develop tools that differentiate athletic from cardiomyopathic change.

Purpose: We hypothesised that athletic LV hypertrophy is a consequence of increased myocardial cellular rather than extracellular mass and measured this with cardiovascular magnetic resonance (CMR).

Methods: 34 athletes underwent cycle ergometer maximal exercise test and CMR including native and post-contrast T1 mapping allowing extracellular volume (ECV) calculation.

Results: Subjects were divided into tertiles by VO2max (n=11, n=12, n=11): 50±3; 60±5; 68±6 mlO2/min/kg (p=0.01 by definition). Indexed LV end diastolic volume (LVEDVi) and mass (LVMI) correlated with VO2max (r=0.455, P=0.01; r=0.34, P=0.05). CMR derived measures of tissue composition (T1, ECV) differed significantly by VO2max tertile, P=0.05, -0.01 respectively, and were significantly correlated: Native T1 (r=−0.40, P=0.02); ECV (r=−0.55, P=0.01). An inverse relationship was seen between LVMI and ECV (r=−0.56, P<0.01). Extracellular mass (28±4; 30±5; 30±5 g; P=0.56) in AH was similar between tertiles not significantly correlated: Native T1 (r=−0.40, P=0.02); ECV (r=−0.55, P=0.01). An inverse relationship was seen between LVMi and ECV (r=−0.56, P=0.01). A similar inverse relationship was observed between TIMP-2 and LVMI and also TIMP-2 and RVMi (r=-0.38, P=0.001; r=-0.24, P=0.039). MMP-9 showed a significant positive correlation with the LV end-diastolic volume (LVEDVi: r=0.27, P=0.019). In the control group, we did not notice these relationships.

Discussion: Athlete pathological LV hypertrophies, serum levels of MMP-2 showed an inverse relationship to the ventricular volumes and masses in the elite athlete group. The dissimilar correlations of MMP-2 and MMP-9 also imply a different regulation of these enzymes in the athlete’s heart. MMP-2 may be a useful biomarker in clinical practice to distinguish between physiological and pathological hypertrophies and to recognize overlapping cardiac diseases.

Remodelling by performance tertile

Conclusions: Increased LV mass in AH occurs as a consequence of increased myocyte mass, whilst the extra-cellular mass remains constant. Athletic remodelling, both on a macroscopic and cellular level, is associated with the degree of an individual’s fitness. ECV mapping may have a future role in differentiating AH from change secondary to cardiomyopathy.

P4098 | BEDSIDE
Impact of exaggerated blood pressure response on parameters of cardiac remodelling in amateur endurance athletes
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Background: Extensive endurance training and arterial hypertension are established risk factors for atrial fibrillation (AF). The impact of exaggerated blood pressure responses (EBPR) on cardiac remodelling in athletes is unknown.

Purpose: The aim of the study was to assess the proportion of exaggerated blood pressure response (EBPR) during an exercise test in amateur endurance athletes and the impact on cardiac function, morphology and atrial ectopy.

Methods: 34 athletes who participated in the Grand Prix of Bern, a popular Swiss 10 mile race, were included. Cardiopulmonary exercise test (CPET) was performed and athletes were stratified into an exaggerated blood pressure response (EBPR, peak systolic BP >200 mmHg in males and >190 mmHg in females) group and a normal (NBPR) group. Left atrial volume index (LAVI), left ventricular mass index (LVMi), tissue Doppler annular early (Ea), and signal averaged P wave duration (SAPWD) were measured. 24-hour Holter monitoring was performed and premature atrial contractions (PAC) were recorded. Data was adjusted for age, gender, lifetime training hours, and BP at baseline.

Results: 119 runners (51% male) were included in the final analysis, and 16 athletes (13%) fulfilled the criteria for EBPR. Mean age was comparable in both groups (45±10 years in the EBPR and 42±7 years in NBPR). EBPR and NBPR did not differ with respect to anthropometric data, lifetime training hours, and peak oxygen uptake (51.5 vs 52.2 ml/kg respectively, p=0.68). Mean systolic and diastolic BPs at rest and at peak exercise were significantly higher in EBPR (123±11/75±8 vs. 116±11/72±8 mmHg, respectively, P=0.001; and 207±12/98±8 vs. 170±13/77±7 mmHg, respectively, P=0.001). Compared to athletes in NBPR, athletes in EBPR had a higher LVMi (1.08±0.26 vs. 0.94±0.19 g/ml, P=0.006), a lower Ea (11.6±1.4 vs. 13.5±1.7 cm/s, P=0.002), and a longer SAPWD (135±16 vs. 127±12 ms, p=0.044), while LAVI showed no significant differences between the groups. In logistic regression models presence of EBPR was an independent predictor for LVMi (beta=−0.203, P=0.001), Ea (beta=−0.253, P=0.006), SAPWD (beta=0.179, P=0.044), and PAC (beta=0.199, P=0.033), but not for LAVI (beta=0.112, P=0.186).

Conclusion: In our study, 13% of athletes fulfilled the criteria of EBPR. EBPR was associated with alteration of LV structure, diastolic function, atrial remodelling and atrial ectopy.

P4099 | BEDSIDE
Differerntiation of arrhythmogenic right ventricular cardiomyopathy and athlete’s heart using cardiac magnetic resonance imaging
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The diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is based on the revised Task Force Criteria defined in 2010, which includes right ventricular end-diastolic volume (LVEDVi: RVEDVi), right ventricular mass (RVMi), and wall motion abnormalities evaluated using cardiac magnetic resonance (CMR) imaging. However, the elevated RVEDVi can be a result of sport adaptation as well, the revised Task Force guideline contains no criteria for professional athletes.

Our goal was to determine the CMR parameters which can help to distinguish ARVC and athlete’s heart.

Between 2010 and 2014 CMR examination was performed on 436 patients between the two groups. In 34 patients (41±11±22 years, 15±8±6 g/m² soft imaging), revised Task Force criteria showed major criteria, and fulfilled revised Task Force Criteria. Additionally 54 professional athletes free of complaint (25±5±36 male) and 56 healthy volunteers (28±5±36 male) were examined by CMR. Left (LV) and right ventricular...
Methods: We performed a retrospective analysis of 274,468 digitally recorded 12-lead ECGs acquired during military conscription between 2008 and 2013. The Seattle Criteria were directly implemented into automated resting ECG measurement and interpretation software ETM. The percentage of detection of abnormal vs. normal ECG’s as well as of each specific abnormal subtype on all ECG’s was assessed.

Results: We detected 17,765 abnormal ECGs (6.47%). The largest abnormality subgroup identified was “pathologic Q waves” (5,947/2.17%) followed by the groups “ST segment depression” (3,080/1.12%), “Left axis deviation” (2,800/1.02%), “left atrial enlargement” (1,799/0.62%), “Atrial tachyarrhythmias” (1,599/0.58%), “Long QT interval” (1,412/0.51%), “T-wave inversion” (1,193/0.43%), “Right ventricular hypertrophy pattern” (991/0.36%), “Premature ventricular contractions” (416/0.15%) and “Intraventricular conduction delay” (282/0.10%).

Conclusions: The 6.47% of automatically detected abnormal ECGs correspond to 288,149 male individuals per year which would warrant more profound clinical, and/or electrophysiological and genetic investigation to confirm or exclude the presence of an acquired or familial cardiac disease.

P4101 | BENCH

Graz CLI Score: a risk score for critical limb ischemia in peripheral arterial occlusive disease patients

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Background: Critical limb ischemia is a frequent entity associated with a high rate of limb amputation and mortality. To highlight patients at high risk for CLI we developed a risk score that can be applied easily in patients with peripheral arterial occlusive disease (PAOD).

Methods and findings: We evaluated 1000 consecutive PAOD patients treated at our institution from 2005 to 2007. Clinical symptoms, comorbidities, and concomitant medication were documented. We calculated odds ratios (OR) in a binary logistic regression model and determined possible risk factors for CLI. In a second step a total of 1124 PAOD patients treated at our institution between 2007 and 2011 were included to verify the score.

Conclusion: The data confirms that the incidence of ankle pressure during exercise stress testing is low, even in patients with abnormal serum potassium. Patients with a potassium range between 3 and 6 mEq/L are not at a significantly increased risk of rhythm disturbance.

PREDICTION MODELS IN CLINICAL PRACTICE
P4104 | BEDSIDE
Usefulness of the Platelet- to- lymphocyte ratio in predicting long term cardiovascular mortality in patients with peripheral arterial occlusive disease

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Background: Peripheral arterial occlusive disease (PAOD) is related with increased cardiovascular mortality and morbidity. Platelet to lymphocyte ratio (PLR) has recently been reported as a new independent predictor for major adverse cardiovascular events including mortality in various cardiovascular diseases.

Purpose: The aim of this study was to investigate the association between PLR and long-term cardiovascular mortality both in patients with intermittent claudication and critical limb ischemia.

Methods: In a retrospective study, 602 consecutive patients who had been admitted to the inpatient ward of the vascular department of a large tertiary training and research hospital with diagnosis of symptomatic PAOD between May 2009 and September 2013 were included. Patients were divided into two groups according to their PLR as follows: high PLR (PLR>142) and low PLR (PLR<142) groups

Results: During the course of the present study (median follow-up period of 33.8 months (interquartile range, 21–45)), 131 death occurred out of 602 patients (21.8%). Cardiovascular mortality was found to be significantly higher in patients with high PLR score (Score >4), intermediate (Score 2–4), and low PLR score (Score <2).

Conclusions: We developed a simple risk stratification scheme, which is based on conditions that can be assessed easily from the medical history, without need of laboratory parameters. This score might help to identify PAOD patients at high risk for CLI.

P4105 | BEDSIDE
Gender-related differences in carotid inflammation in patients with coronary artery disease

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Background: Carotid atherosclerosis is a major cause of stroke. Controversy exists regarding the gender related differences in carotid plaque vulnerability. Although men exhibit higher inflammatory infiltration in carotid endarterectomy specimens, women show in vivo more intense intraplaque neovascularization. Microwave Radiometry (MWR) allows the non-invasive in-vivo measurement of internal temperature of tissues, reflecting local inflammation. The aim of the present study was to evaluate the impact of gender on carotid plaque temperatures, as evaluated by MWR.

Methods: Consecutive patients with significant coronary artery disease (CAD), as documented by coronary angiography (≥50% stenosis in at least one major epicardial vessel) underwent ultrasound echo-color Doppler (US-ECD) study and MWR measurements, of both carotid arteries. During the ultrasound study, carotid plaque thickness of each carotid artery was determined. Temperature difference (ΔT) by MWR was assigned as maximal temperature along the carotid artery minus minimum. ΔTmax was assigned as the maximal value of ΔT of both carotid arteries. Vessel- and patient-based analysis were performed to determine the impact of gender on morphological and functional carotid artery characteristics.

Results: From 359 patients, 306 (85%) were men and 54 (15%) were women. Women had similar IMTmax compared to men in both vessel- and patient-based analysis (2.04±1.03 vs 2.00±1.08 mm, p=0.69 and 2.46±1.12 vs 2.39±1.18 mm, p=0.66, respectively). On the contrary, carotid arteries of women showed higher ΔT values in both vessel and patient-based analysis (0.98±0.51 vs 0.70±0.43°C, p<0.001 and 1.16±0.48 vs 0.87±0.45°C, p<0.001, respectively). Univariate analysis showed a statistically significant association between gender and ΔTmax values (coefficient β =-0.29, p<0.001). After adjustment for possible covariates this association remained significant (β=0.28, p<0.001).

Conclusions: Women with CAD exhibited a more vulnerable carotid atherosclerotic plaque phenotype. Whether this is associated with worse prognosis, remains to be elucidated in prospective studies.
The peak rate of arterial dilatation during measurement of flow-mediated dilation

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Background: Measures of flow-mediated dilation (FMD) are used in the assessment of endothelial function. Traditionally, this is a single, time-based measure of maximal conduit artery dilatation. To date, little attention has been given to more integrated measures addressing the rate of change in vessel diameter over time.

Purpose: To examine the rate of change in radial artery diameter (dD/dt) after the ischemic stimulus used in the assessment of FMD.

Methods: We examined the peak rate of radial artery diameter dilatation (peak +dD/dt) following the FMD stimulus. A total of 223 patients (62±5 yrs, 167 males) with known coronary artery disease and 99 normal volunteers (24±3 yrs, 91 males) were studied.

Results: Although FMD was significantly blunted in the patient group as compared to the normal volunteers (4.1±3.7 vs. 8.3±3.3%, 10% peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (4.1±3.7 vs. 0.015 mm/sec; P<0.001; figure). The hyperemic flow response was similar in both groups. There was no correlation between peak +dD/dt and age, baseline or peak vessel diameter, FMD, or peak hyperemic flow.

Conclusions: Therefore, there are significant differences in the rate of radial arterial dilatation in patients with coronary artery disease as compared to a group of normal volunteers following the ischemic stimulus used in FMD. The mechanism of the greater rate of arterial dilatation remains uncertain, however this measure ment may provide further insight into vascular function as it assessed by FMD.

Acknowledgement/Funding: Canadian Institutes of Health Research

Ankle brachial index predicts two year mortality in sub-saharan adults

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Background: Ankle-brachial index (ABI) is a simple, non-invasive test that is used to determine the presence and extent of peripheral arterial disease (PAD). ABI may provide further insight into vascular function as it is assessed by FMD.

Purpose: To examine the rate of change in radial artery diameter (dD/dt) after the ischemic stimulus used in the assessment of FMD.

Methods: We examined the peak rate of radial artery diameter dilatation (peak +dD/dt) following the FMD stimulus. A total of 223 patients (62±5 yrs, 167 males) with known coronary artery disease and 99 normal volunteers (24±3 yrs, 91 males) were studied.

Results: Although FMD was significantly blunted in the patient group as compared to the normal volunteers (4.1±3.7 vs. 8.3±3.3%, P<0.001; figure), peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (4.1±3.7 vs. 0.015 mm/sec; P<0.001; figure). The hyperemic flow response was similar in both groups. There was no correlation between peak +dD/dt and age, baseline or peak vessel diameter, FMD, or peak hyperemic flow.

Conclusions: Therefore, there are significant differences in the rate of radial arterial dilatation in patients with coronary artery disease as compared to a group of normal volunteers following the ischemic stimulus used in FMD. The mechanism of the greater rate of arterial dilatation remains uncertain, however this measurement may provide further insight into vascular function as it assessed by FMD.

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P4109 | BEDSIDE

Ankle brachial index predicts two year mortality in sub-saharan adults

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Background: Ankle-brachial index (ABI) is a simple, non-invasive test that is used to determine the presence and extent of peripheral arterial disease (PAD). ABI may provide further insight into vascular function as it is assessed by FMD.

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Conclusions: Therefore, there are significant differences in the rate of radial arterial dilatation in patients with coronary artery disease as compared to a group of normal volunteers following the ischemic stimulus used in FMD. The mechanism of the greater rate of arterial dilatation remains uncertain, however this measurement may provide further insight into vascular function as it assessed by FMD.

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P4110 | BEDSIDE

Ankle brachial index predicts two year mortality in sub-saharan adults

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Background: Ankle-brachial index (ABI) is a simple, non-invasive test that is used to determine the presence and extent of peripheral arterial disease (PAD). ABI may provide further insight into vascular function as it is assessed by FMD.

Purpose: To examine the rate of change in radial artery diameter (dD/dt) after the ischemic stimulus used in the assessment of FMD.

Methods: We examined the peak rate of radial artery diameter dilatation (peak +dD/dt) following the FMD stimulus. A total of 223 patients (62±5 yrs, 167 males) with known coronary artery disease and 99 normal volunteers (24±3 yrs, 91 males) were studied.

Results: Although FMD was significantly blunted in the patient group as compared to the normal volunteers (4.1±3.7 vs. 8.3±3.3%, P<0.001; figure), peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (4.1±3.7 vs. 0.015 mm/sec; P<0.001; figure). The hyperemic flow response was similar in both groups. There was no correlation between peak +dD/dt and age, baseline or peak vessel diameter, FMD, or peak hyperemic flow.

Conclusions: Therefore, there are significant differences in the rate of radial arterial dilatation in patients with coronary artery disease as compared to a group of normal volunteers following the ischemic stimulus used in FMD. The mechanism of the greater rate of arterial dilatation remains uncertain, however this measurement may provide further insight into vascular function as it assessed by FMD.

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Prediction models in clinical practice / Heart failure: diversity of phenotyping 699

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Background: Hemococoncentration (HC) was known to be related with improved cardio or renal function. More attention should be paid to HC in patients with chronic heart failure (CHF). However, the relationship between HC and renal function variability (RFV) in CHF remains unknown until now.

Methods: We analyzed 5,660 AHFS pts (3,019 males, 68±14 years of age) and used Cox multivariate analysis model to identify significant predictors for RFV.

Results: Declined GNRI which reflect PEW or malnutrition state strongly predicted worsened renal function outcome as well as mortality and hospitalization for lower extremity revascularization in chronic heart failure patients. More attention should be paid to pre-procedural PEW or malnutrition control in this high-risk population.

HEART FAILURE: DIVERSITY OF PHENOTYPING

P4110 | BEDSIDE

The relationship between hemococoncentration and renal function variability in patients with acute heart failure syndrome: data from the Korean Acute Heart Failure (KorAHF) registry

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Background: Hemococoncentration (HC) was known to be related with improved clinical outcomes in patients (pts) with acute heart failure syndrome (AHFS). Generally, variable rise and fall in renal indices was observed during hospitalization in pts with AHFS. However, the relationship between HC and renal function variability (RFV) in AHFS remains unknown until now.

Methods and results: We analyzed 5,660 AHFS pts (3,019 males, 68±14 years of age) and used Cox multivariate analysis model to identify significant predictors for RFV. Declined GNRI which reflect PEW or malnutrition state strongly predicted worsened renal function outcome as well as mortality and hospitalization for lower extremity revascularization in chronic heart failure patients. More attention should be paid to pre-procedural PEW or malnutrition control in this high-risk population.
old, 37.4% ischemic origin, left ventricular ejection fraction 38±5.16%, 1% from Korean Acute Heart Failure (KoAHE) Registry. We defined HC as an increased hemoglobin level between admission and discharge and RFV as standard deviation of serum creatinine at admission, maximum, minimum and discharge. There were 270 cases of all-cause in-hospital mortality (4.6%). Mean hemoglobin levels at admission and discharge were 12.4±2.3 and 12.6±2.2 g/dL, respectively and HC was presented in 2,603 AHFS patients (46.1%). Mean creatinine at admission was 1.48±1.46mg/dL and mean RFV was 0.36±0.78 (n=5,655), respectively. The AHFS group with HC had significantly lower RFV compared to those without HC (0.33±0.56 vs. 0.39±0.58, p<0.005). In correlation analysis, RFV was significantly associated with B-type Natriuretic Peptide (BNP, r=0.238, p<0.001), N-terminal pro-BNP (r=0.233, p<0.001) and high sensitive c-reactive protein (r=0.116, p<0.001). In multivariate logistic regression analysis for in-hospital mortality in the AHFS patients, RFV was confirmed as a significant predictor after adjusting other risk factors including baseline BUN, creatinine level and hemoglobin concentration (hazard ratio 5.374, 95% confidence interval 4.083–7.073, p<0.001).

Conclusion: Our study demonstrated that higher RFV was related to higher in-hospital mortality in large cohort of AHFS for the first time. Therefore, the further prospective research regarding the prognostic value of RFV during hospitalization should be warranted and it may provide a new information in the risk stratification of AHFS.

P4111 | SPOTLIGHT
Prevalence of hereditary transthyretin cardiac amyloidosis in patients with Hypertrophic Cardiomyopathy. A multicenter study
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Background: Hereditary transthyretin cardiac amyloidosis (mTTR-CA) is a rare progressive disease with challenging diagnosis and poor prognosis. Patients show increase in LV wall thickness (LWT) mimicking sarcomeric hypertrophic cardiomyopathy. The prevalence of m-TTR in patients with increase LWT is unknown.

Methods: Screen systematically for TTR genotype patients with LWT ≥15mm in 9 French primary cardiology centres.

Results: 298 patients were prospectively genotyped of whom 23% were African descendant. The median (IQR) age was 62 (50,74), 74% were men and 36% were non-white. The median maximum LWT was 28mm (16, 21). Of the 298, 17 were identified as having an mTTR mutation of which 15 had CA. The prevalence of mTTR-CA in the overall population was 5.0% and 8.3% in patients ≥55 years old. Of the 15 with mTTR-CA, 8 were Africans and 6 Caucasians. In Africans ≥55 years old the prevalence was 22% and 35% in ≥65 years old. The most frequent mutations in CA were V142I (8), V50M (2) and I127V (2). The patients with mTTR-CA were older (all of them ≥55 years old), had more frequently neuropathy (53%), carpal tunnel syndrome (46%), EKG low voltage (36%), symmetric hypertrophy (92%), impaired LVEF, increase in filling pressure and late gadolinium enhancement more than the patients without mTTR. Both groups had similar increase in maximal LV wall thickness.

Conclusions: mTTR-CA is frequent in patients older than 55 years old with hypertrophic cardiomyopathy and particularly in African descendant. mTTR genetic screening may be warranted for patients characterized by hypertrophic cardiomyopathy especially with neuropathy or carpal tunnel syndrome.

P4112 | BEDSIDE
Clinical impact of quantitative and qualitative alterations in the extracellular matrix (ECM) in human cardiomyopathy
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Background: Cardiac fibrosis is a key pathological feature in left ventricular (LV) remodeling. Quantitative and qualitative alterations in the extracellular matrix (ECM) in human cardiomyopathy have not been clarified.

Purpose: This study aimed to analyze the relationships between pathologically determined fibrosis, markers of collagen turnover and LV remodeling.

Methods: In the pathological analysis, 113 patients of non-ischemic cardiomyopathy (CM) who underwent LV endomyocardial biopsy (EMB) were retrospectively analyzed. EMB were performed in pre-transplantation patients; mild fibrosis area ranged from 0 to 11% in the mild fibrosis group, 12 to 30% in the moderate fibrosis group and 30 to 99% in the severe fibrosis group. Ejection fraction (EF) was lower in the severe fibrosis group compared with the mild fibrosis group (43.8±13.4% vs. 33.7±14.0%, P <0.01). LV end-diastolic volume index was larger in the severe fibrosis group compared with the moderate fibrosis group (128.5±43.9 ml/m 2 vs. 107.3±42.1 ml/m 2, p<0.001). Reverse remodeling defined as an absolute increase of EF ≥10% to a final value of ≥45% was more observed in the mild fibrosis group compared with the severe fibrosis group (71.4% vs. 35.0%, P<0.05). Among the markers of collagen turnover, ICTP and PINP were higher in the patients with CM as compared with controls (ICTP: 3.3 mg/ml vs. 11.4 mg/ml, p<0.0001, PINP: 0.57 U/ml vs. 0.91 U/ml, p<0.005), ICTP but not PINP were correlated with BNP (r=0.30, p<0.01). Neither LV nor aortic wall thickness (WT) were correlated with collagen turnover. ICITP and PINP were higher in the patients with CM as compared with controls (ICTP: 3.3 mg/ml vs. 11.4 mg/ml, p<0.0001, PINP: 0.57 U/ml vs. 0.91 U/ml, p<0.005), ICTP but not PINP were correlated with BNP (r=0.30, p<0.01). Neither LV nor aortic wall thickness (WT) were correlated with collagen turnover. ICITP and PINP were higher in the patients with CM as compared with controls (ICTP: 3.3 mg/ml vs. 11.4 mg/ml, p<0.0001, PINP: 0.57 U/ml vs. 0.91 U/ml, p<0.005), ICTP but not PINP were correlated with BNP (r=0.30, p<0.01). Neither LV nor aortic wall thickness (WT) were correlated with collagen turnover. ICITP and PINP were higher in the patients with CM as compared with controls (ICTP: 3.3 mg/ml vs. 11.4 mg/ml, p<0.0001, PINP: 0.57 U/ml vs. 0.91 U/ml, p<0.005), ICTP but not PINP were correlated with BNP (r=0.30, p<0.01). Neither LV nor aortic wall thickness (WT) were correlated with collagen turnover. ICITP and PINP were higher in the patients with CM as compared with controls (ICTP: 3.3 mg/ml vs. 11.4 mg/ml, p<0.0001, PINP: 0.57 U/ml vs. 0.91 U/ml, p<0.005), ICTP but not PINP were correlated with BNP (r=0.30, p<0.01).
MiR-21, -30c, and -133a are correlated to the progression of TAC, miR-21 is increased and miR-30c is decreased. MiR-133a is decreased in ure). A broad range of interstitial fibrosis is histologically observed in 8W-TAC. Methods: Mice were subjected to transverse aortic constriction (TAC) or sham surgery (sham) and sacrificed 1, 4, and 8 weeks thereafter (1W - 4W - 8W; n=5 per group). Gene expression of collagen type I and III (coll1A1 and coll1A2, and coll3A1 respectively), and miR-expression were analysed by TaqMan assays. Picrosirius red staining was used to determine cardiac fibrosis. Results: Col1A1, col1A2, and col3A1 are upregulated in 4W- and 8W-TAC (Figure, left). Patients with abnormal breathing have breath-by-breath changes in ISs and therefore have high IQR score. Results: IQR score increased through NYHA classes 1 to 4 (Figure, right), and significantly correlated with BNP (r=0.58, p<0.01) and cardiac index (r=−0.42, p<0.01).

**Conclusion:** This novel method effectively quantified respiratory instability in HF patients. IQR score of ISs well correlated with the functional and hemodynamic severity of HF, thus it can be utilized as one of the key tools in the diagnosis and guidance of HF therapy.

**P4115 | BENCH**

**MicroRNAs as a quantitative and prognostic biomarker of interstitial cardiac fibrosis in pressure overloaded mice**

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**Background:** Detecting interstitial fibrosis in cardiac diseases is of particular interest for clinical evaluation. It has been shown that microRNA (miR) -21, -29b, -30c, and -133a over time and to assess the relation between these miR-levels and the amount of interstitial fibrosis during pressure overload in mice.

**Methods:** Mice were subjected to transverse aortic constriction (TAC) or sham surgery (sham) and sacrificed 1, 4, and 8 weeks thereafter (1W - 4W - 8W; n=5 per group). Gene expression of collagen type I and III (coll1A1 and coll1A2, and coll3A1 respectively), and miR-expression were analysed by TaqMan assays. Picrosirius red staining was used to determine cardiac fibrosis.

**Results:** Col1A1, col1A2, and col3A1 are upregulated in 4W- and 8W-TAC (Figure, left). A broad range of interstitial fibrosis is histologically observed in 8W-TAC (sham 0.35± 0.03 vs TAC 2.56± 1.07; p<0.01). In both 4W-TAC and 8W-TAC, miR-21 is increased and miR-30c is decreased. MiR-133a is decreased in 4W-TAC. (Figure) MiR-21, -30c, and -133a are correlated to the progression of fibrosis (r=0.63, r=−0.45, and r=−0.42 respectively; p<0.05).

**Conclusion:** Increased collagen gene expression correlates to changes in cardiac miR-21, -30c, and -133a levels. In addition, these miR-levels correlate to the amount of fibrosis. Therefore, these miRs may serve as a quantitative and prognostic marker for cardiac fibrosis. Further studies are required to examine whether these miRs are detectable in circulation and herewith valuable as a non-invasive biomarker of interstitial fibrosis.

**P4117 | BEDSIDE**

**Hemodynamic correlates of abnormal aortic root dimension in an adult population: the strong heart study**


**Background:** We analyzed aortic root dimension (ARD) in 1207 multiethnic non-obese, normotensive subjects, free of CV or aortic valve disease, to predict sex-specific ARD at a given age and body height.

**Purpose:** We applied this equation to evaluate impact of flow output and other hemodynamic parameters on ARD.

**Methods:** In 3160 adult participants from the Strong Heart Study, echocardiographic ARD was measured at the Valvula sinuses and compared with the value predicted (ARDp) for age, sex and height: ARDp = 1.52 × (age[ys] × 0.03) + (Height[m]) − (sex [1=M, 2=F] × 0.25) + [sex-specific Z-score] × (Height[m]) − (sex [1=M, 2=F] × 0.25) + [sex-specific Z-score]. Significant differences of eGFR and CVP were observed between VF patterns (eGFR, 72.5±24.3, 60.8±30.8, 45.2±23.6 ml/min/1.73m², p<0.001; CVP, 4.6±3.2, 7.4±3.1, 14.2±6.6 mmHg, p<0.001). During follow up period 192±118 days, 24 patients met the end-point (11 cardiac deaths and 13 unplanned CHF hospitalizations). Discontinuous VF pattern was associated with the endpoints independently of ejection fraction, BNP, eGFR, and RI (Figure).

**Conclusion:** IRD profile was associated with CVP and eGFR, which were related with RC. In particular, VF patterns at pre-discharge significantly associated with clinical courses of CHF.

**P4116 | BEDSIDE**

**Respiratory waveform analysis method**

**P4116 | BENCH**

**MicroRNAs as a quantitative and prognostic biomarker of interstitial cardiac fibrosis in pressure overloaded mice**

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**Conclusion:** Increased collagen gene expression correlates to changes in cardiac miR-21, -30c, and -133a levels. In addition, these miR-levels correlate to the amount of fibrosis. Therefore, these miRs may serve as a quantitative and prognostic marker for cardiac fibrosis. Further studies are required to examine whether these miRs are detectable in circulation and herewith valuable as a non-invasive biomarker of interstitial fibrosis.

**P4117 | BEDSIDE**

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**Conclusion:** IRD profile was associated with CVP and eGFR, which were related with RC. In particular, VF patterns at pre-discharge significantly associated with clinical courses of CHF.
flow volume distending proximal aorta; 3) pulse pressure (PP, measure of aortic capacitance); 4) heart rate (marker of frequency of aortic distension).

**Results:** Variance of ARDz was evaluated, controlling for age, sex, body composition (by BIA), waist circumference (WC), white blood cell count and % neutrophils, C-reactive protein, fibrinogen, PAI-1, lipid profile, SV, cuff diastolic BP (fitted vs current), DBP variability, and DBP and PWV. ARDz was also positively and independently related to ARDz, but PP exhibited negative correlation (all p < 0.0001). ARDz was also positively related to WC, PAI-1 and neutrophils (all p < 0.01). Using estimates of central BP instead of cuff BP did not change the regression model.

**Conclusions:** At a given age, gender and height, larger ARD is associated with high DBP and SV, central fat distribution and inflammatory status. In contrast, at a given DBP and SV, AR dilatation is associated with lower PP.

P4118 | BEDSIDE

**Association of plasma testosterone with central hemodynamics in hypertensive men**

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**Background:** There is evidence for an inverse association between plasma testosterone and blood pressure. Recently, low plasma testosterone was associated with increased risk of major cardiovascular events in middle-aged hypertensive men. Central (aortic) blood pressures predict cardiovascular mortality with equal, if not increased, precision compared to peripheral (brachial) blood pressures. The aim of the present study was to assess the relationship of plasma total testosterone (TT) with peripheral and central hemodynamics in hypertensive men.

**Methods:** We studied 70 non-diabetic, hypertensive men (mean age = 60 years old). Central blood pressures (cSBP and cDBP) were measured according to the ESH guidelines. Pulse pressure (PP) was calculated as SBP minus DBP. All patients were subject to measurement of aortic systolic (aoSBP), diastolic (aoDBP) and pulse pressures (aoPP) by pulse wave analysis using the SphygmoCor device. Wave reflections were assessed by the measurement of heart-rate corrected augmentation index (Aix75). Plasma TT was measured in all subjects by enzyme immunoassay.

**Results:** The mean value of TT in the whole population was 4.6 ng/ml (hypogonadism was defined as TT < 3.4 ng/ml). Plasma TT was inversely and significantly related to aoSBP (β = −0.26, p < 0.03), aoPP (β = −0.30, p < 0.01) and Aix75 (β = −0.31, p < 0.01) but only marginally related to cSBP (β = −0.22, p = 0.07) and cPP (β = −0.23, p < 0.06). In linear regression analysis, after adjustment for age, smoking, BMI, plasma glucose, total cholesterol and presence of antihypertensive treatment, aoSBP (β = −0.29, p < 0.03), aoPP (β = −0.31, p < 0.02) and Aix75 (β = −0.30, p = 0.03) were independently associated with TT but the relationship of TT with cSBP (β = −0.25, p < 0.06) and cPP (β = −0.23, p < 0.07) remained weak.

**Conclusions:** In hypertensive men, plasma TT is independently associated with central blood pressures and wave reflections. Considering the adverse prognostic role of central blood pressures on cardiovascular outcomes, the present finding might explain part of the increased cardiovascular risk associated with low testosterone. Whether measurement of central hemodynamics may improve risk stratification in men with low testosterone warrants further investigation.

P4119 | BEDSIDE

**Relationship between cognitive dysfunction, clinic and 24-h blood pressure, and blood pressure variability**

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**Background and aims:** The relation between blood pressure (BP) and cognitive function was reviewed growing interest in recent years. Some cross-sectional studies have shown an inverse association between BP and cognitive dysfunction, while longitudinal studies yield mixed results.

**Methods:** In the PAMELA study cognitive function was assessed via minimenentation, while longitudinal studies yield mixed results in the present paper. The present study aimed to assess the impact of central blood pressure (cSBP) on cognitive function in a large, community-based population with normal kidney function (estimated GFR ≥ 60 ml/min/1.73 m²).

**Results:** Mean age of the subjects enrolled was 63.0 ± 5.7 yrs (mean ± SD) at the evaluation performed in 2001–2002, taking as reference clinic data of the Italian National Health Service. In the PAMELA study cognitive function was assessed via minimenentation, while longitudinal studies yield mixed results.

**Conclusions:** The relation between blood pressure (BP) and cognitive function was reviewed growing interest in recent years. Some cross-sectional studies have shown an inverse association between BP and cognitive dysfunction, while longitudinal studies yield mixed results.

P4121 | BEDSIDE

**Association of hypertension with the incidence of adverse events in patients with atrial fibrillation:** 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. Hypertension is considered a major risk factor of stroke and systemic embolism (SE) in patients with AF, and is one of the components of CHADS2 score. The purpose of this study was to investigate the relation between hypertension and the incidence of adverse events including stroke and SE in Japanese AF patients.

**Methods:** The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients who visited the participating medical institutions in Fushimi-ku, Kyoto City. Fushimi is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. Follow-up data were available for 3,390 patients, and the median follow-up period was 777 days.

**Findings:** Among 3,390 patients, 2,087 patients were diagnosed as hypertension (HT: 61.6% of total). HT group was older (HT vs. non-HT: 74.4 ± 72.5 years; p < 0.01), had more co-morbidities (diabetes mellitus, dyslipidemia, coronary artery disease, and vascular disease), and thus had higher CHADS2 score (HT vs. non-HT: 2.49 ± 1.28 vs. 2.24 ± 0.9, p < 0.01). They received more oral anticoagulation (OAC) prescription (54.7% vs. 50.3%; p < 0.01), but the proportion of patients with previous stroke or SE was comparable (21.5% vs. 19.1%; p = 0.097).

During this follow-up period, the incidence rate of hospitalization for heart failure was higher in HT group than in non-HT group (8.48% vs. 6.45%, log-rank p = 0.04).

However, the incidence rates of major bleeding and all-cause death were not different between the two groups. Moreover, the incidence of stroke or SE was also equivalent (5.03% vs. 4.76%, log-rank p = 0.80).

Despite the higher overall risk of OAC in the HT group, the incidence of stroke or SE was equivalent between HT and non-HT among patients with OAC (5.69% vs. 5.04%, p = 0.55) and those without OAC (4.23% vs. 4.48%, p = 0.82).

Multiple logistic regression analysis including components of CHA2DS2-VASc score and OAC revealed that age and previous stroke were independent determinants of stroke or SE, but hypertension was not an independent determinant of stroke or SE [odds ratio: 0.98, 95% CI: 0.71–1.37, p = 0.91].

**Conclusion:** Hypertension was associated with the incidence of hospitalization for heart failure, but not with other adverse events such as stroke/SE, major bleeding and all-cause death.
Results: Subjects were 56.6±8.5 years old. 36% were male and 49.3% had hypertension. Mean (SD) baseline eGFR was 101.2±10.6 ml/min/1.73 m². Mean (SD) baseline cSBP was 133.1±18.5 mmHg. After 2.2 years follow-up, the incidence of rapid decline and CKD was 7.3% and 0.7%, respectively. In multivariable logistic-regression analyses, cSBP was associated with both rapid decline (crude OR [95% CI], 1.02, 1.01–1.02) and incident CKD (OR, 95% CI, 1.03, 1.00–1.05) after adjustment for demographic variables, comorbidities, antihypertensive medications and baseline eGFR. This relationship remained (rapid decline, OR, 95% CI, 1.02, 1.01–1.02; incident CKD, OR, 95% CI, 1.03, 1.00–1.06) even after further adjustment for peripheral SBP. However, peripheral SBP was not associated with either rapid decline or incident CKD after adjustment for confounders including cSBP.

Conclusion(s): cSBP is an independent risk factor related to early kidney function decline in a Chinese community-based population with normal kidney function. Future research should focus on the mechanisms of central as opposed to peripheral haemodynamics on kidney function decline.

4149 | BEDSIDE
Associations between serum uric acid levels and the incidence of hypertension and atrial fibrillation

Objective: Serum uric acid (SUA) is associated with many traditional cardiovascular risk factors (CVRF) as well as with HTN. Our aim was to investigate the relationship of SUA with HTN and atrial fibrillation as also the correlation of SUA with pulse wave velocity and specific diastolic echocardiographic parameters in hypertensive patients.

Methods: We prospectively enrolled 678 hypertensive patients (mean age 61.9) and 143 controls (mean age 68.3). In all subjects routine blood chemistry, including SUA determination, echocardiographic examination and 24 h ambulatory blood pressure (BP) monitoring were obtained. The group of hypertensives was divided into two subgroups: subgroup A (N=47): hypertensives with atrial fibrillation and subgroup B (N=631): hypertensives in sinus rhythm. We investigated the differences of SUA levels among group A, group B and the control group. In the second part we studied the correlation of SUA with left atrial diameter (LA), left ventricular mass (LVM) and pulse wave velocity (PWV) in the overall hypertensive population (N=678).

Results: Logistic regression analysis showed that increased SUA levels were significantly and positively associated with the incidence of hypertension and atrial fibrillation (group A: 9.9±1.8 mg/dl vs group B: 5.2±0.9 mg/dl vs control group: 4.8±1mg/dl, p<0.001), Furthermore the ANOVA regression analysis revealed that SUA levels are significantly associated with LVM (p<0.001) and LA (p<0.001), while there was no significant correlation between SUA and PWV (p=NS). For a 100 mg and 10 mm increase in the LVM and LA respectively, an 0.4 and 0.6 mg/dl on average increase in SUA was observed.

Conclusion: Increased SUA levels were significantly associated with the incidence of hypertension and atrial fibrillation, while there was also a strong positive association between SUA, LVM and LA, implicating that hyperuricemia might be a novel risk factor for the LA and LV remodelling and finally for the development of atrial fibrillation.

KILLING THE HEART

4151 | BENCH
Folic acid reduces doxorubicin-induced cardiomyopathy by modulating endothelial nitric oxide synthase and mitochondrial integrity
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1 Erasmus Medical Center, Division of Experimental Cardiology, Department of Cardiology, Thoraxcenter, Rotterdam, Netherlands; 2 Charite University Hospital, Institute of Gender in Medicine and Center for Cardiovascular Research, Berlin, Germany; 3 Maastricht University, CARIM, Department of Cardiology, Maastricht, Netherlands; 4 KU Leuven, Department of Cell Sciences, Leuven, Belgium; 5 Maastricht University, Electron Microscopy Unit, Department of Molecular Cell Biology, Maastricht, Netherlands

Purpose: Endothelial nitric oxide synthase (eNOS) plays an important role in the pathogenesis of doxorubcin (DOXO)-induced cardiomyopathy. Here we tested the hypothesis that folic acid (FA), as an eNOS modulator, attenuates DOXO-induced cardiomyopathy and improves mitochondrial integrity.

Methods: Male C57BL/6J mice (n=265) received DOXO (1x 20 mg/kg, ip) or saline (FA). (10 mg/d po) or placebo was administered from 7d before DOXO administration until the end of the experiment (10d). Left ventricular (LV)

stress) -2 mm ST depression during stress test, Lown 3 VA. All the pts with suspected TOX underwent a stress test - 10 days after withdrawing FP and without additional cardiologic therapy; ECHO and Holter were repeated in those with LVD or VA. The TOX group comprised the pts with signs/symptoms of TOX during FP, and with normal exames after wash out. The control group was represented by the pts who did not have any TOX at rest or under effort.

Results: We examined 372 pts: 42 cases and 330 controls. Age, obesity, smoking habit, diabetes, dyslipidemia, hypertension, number of CVRF, number of cardiovascular drugs taken, anemia were similar in both groups. IHD was present in 9.5% of cases and in 3.3% of controls (p=0.06). Atypical symptoms (gastric or chest discomfort, sore throat, jaw pain, mild dyspepsia) before stress test were present in 33% of cases and 3.9% of controls (Odds Ratio 12.15 with 95% CI 5.2–28.4; chi-square test p=0.01).

Conclusions: The risk of cardiotoxicity seems to be independent from the common CVRF and the presence of IHD does not increase significantly the risk. A possibly life-saving CT with FP should not be denied to pts with IHD. During CT, patients should be asked for even atypical symptoms, which might reveal cardiotoxicity.
function was measured by echocardiography; fibrosis and apoptosis by Picrosirius Red and TUNEL staining, respectively; eNOS uncoupling, activity and S-glutathionylation by co-immunoprecipitation and immunoblotting; superoxide (O2−) production by lucigenin-enhanced chemiluminescence; cardiac NO by Griess reaction. Mitochondrial oxygen consumption measurements and electron mi-
roscopy were performed at day 6.

**Results:** DOXO produced 70% mortality (P < 0.01 vs sham), while mice receiv-
ing DOXO and FA (DOXOFA) had significantly lower mortality (45%; P = 0.01).

FA ameliorated DOXO-induced LV dysfunction, fibrosis, and apoptosis (Table). Uncoupling, activity and glutathionylation levels of eNOS were restored in DOX-
OFA, and subsequently lead to a reduction in O2− generation and an increase in cardiac NO. Furthermore, FA attenuated mitochondrial dysfunction and morpho-
logical changes.

**Conclusion:** Targeting eNOS with FA might be a new and immediate therapeutic approach to reduce DOXO-induced cardiomyopathy.

### 4152 | BENCH
Cardio-Oncology: the cardioprotective role of NACA in reducing oxidative stress due to doxorubicin and trastuzumab


**Introduction:** Despite the clear therapeutic benefits of the anti-cancer drugs Doxorubicin (DOX) and Trastuzumab (TRZ) on improving the overall survival in women with breast cancer, the risk of developing heart failure cannot be ig-
nored. Amongst the potential mechanisms of DOX+TRZ mediated cardiotoxicity, increased oxidative stress (OS) and apoptosis has gained recent attention.

**Purpose:** To investigate whether a novel anti-oxidant, N-acetylcysteine amide (NACA), can attenuate DOX+TRZ mediated cardiac dysfunction in a murine model.

**Methods:** A total of 65 wild-type C57Bl/6 female mice received one of the following drug regimens: i) 0.9% saline (n=5); ii) DOX (20 mg/kg; n=15); iii) DOX+TRZ (20 mg/kg; 10 mg/kg; n=15); iv) NACA+DOX (250 mg/kg; n=15); or v) NACA+DOX+TRZ (n=15) and were followed for 10 days. In vivo cardiac function was assessed daily. At day 10, cardiac tissue was used to measure superoxide dismutase (marker of OS) and the Bax:Bcl-xL ratio (marker of apoptosis).

**Results:** In mice receiving DOX+TRZ, left ventricular ejection fraction (LVEF) de-
creased from 72±3% at baseline to 32±2% at day 10 (P < 0.05 vs corr. sham; §P < 0.05 vs corr. DOXO).

**Conclusion:** The antioxidant NACA partially attenuates the cardiotoxic side ef-
fects of DOX+TRZ in an acute murine model of chemotherapy induced cardiac dysfunction.

### 4153 | BENCH
Cardioprotective effects of Ecklonia cava polyphenol on doxorubicin-induced cardiomyopathy in rats

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**Background:** Long-term therapy with doxorubicin is associated with a high inci-
dence of a cumulative and irreversible dilated cardiomyopathy, despite of its broad anti-neoplastic effectiveness. Seapolyphenol (polyphenol purified from Ecklonia cava,brown algae) have strong antioxidant and antiinflammatory properties.

**Purpose:** The goal of this study was to evaluate the cardioprotective effects and safety of seapolyphenol against doxorubicin-induced cardiotoxicity in an animal model.

**Methods:** Of total 42 rats, we divided 21 rats into Group 1 (low-dose seapoly

**Results:** Left ventricular ejection fraction significantly decreased and the left ven-
tricular end diastolic/systolic dimension and LV mass index significantly increased in single doxorubicin group compared to high dose seapolyphenol plus doxorubicin group. Also, electron microscopic finding showed less impaired myofiber and mi-
tochondria in high dose seapolyphenol plus doxorubicin group than in single dox-
oroubicin group.

**Conclusions:** Our data showed that high dose seapolyphenol had cardioprotective effects against doxorubicin-induced cardiotoxicity in an animal rat model with the evidence of electron microscopic finding in addition to echocardiographic results.

### 4154 | BEDSIDE
Galectin-3 and longitudinal global strain predict drug-related cardiotoxicity in patients with breast cancer

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**Purpose:** To assess the role of biomarkers and myocardial deformation analysis in early detection of CTX in pts with breast cancer (BC).

**Methods:** Prospective study of pts newly diagnosed with BC. Clinical, echocar-
diographic and biomarker (Troponin I, NT-proBNP and Galectin-3 (Gal3)) evalu-
ations were performed before and 1, 3, 6, 9 and 12 months after CT. The echocar-
diographic assessment included measurement of left ventricular ejection fraction (EF) and myocardial deformation analysis by speckle tracking. CTX was defined as a decline in initial EF of at least 5% to an absolute value <55%.

**Results:** Progressive decline in EF was detected (68±5% vs. 64±5%; P = 0.008) during the median follow-up of 12 months. Five pts (6.8%) met the end-
point. The pts who developed CTX had lower longitudinal global strain at 3 months (<15.6±0.9 vs. (19±2.2; P = 0.009) and this parameter showed high accuracy in predicting the endpoint (AUC 0.92; P = 0.016).

Gal3 was significantly elevated 3 months after CT (11.9±4.3 vs. 14.3±5.6 ng/mL; P < 0.001), especially in those pts who developed CTX (19.5±5.2 vs. 13.6±1.5 ng/mL; P = 0.023). This biomarker was an accurate predictor of CTX (AUC 0.84; P = 0.037 – figure). The cut-off value of 17.8ng/mL showed the best sensibility-
specificity ratio (S:75%; E:82%). The risk of development of CTX was significantly higher in pts with Gal3 above 17.8 ng/mL (OR 13.3;CI95% 1.2–147.5; P = 0.035).

Neither troponin I or NT-proBNP showed to be predictors of CTX.
4155 | BEDSIDE

Are all heart failure risk factors equal? Comparison of myocardial dysfunction late after chemotherapy with other stage A heart failure in community patients

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Background: Chemotherapy increases the risk of heart failure. Global longitudinal strain (GLS) is a sensitive marker of early LV systolic dysfunction, and has been shown to change acutely in some pts after chemotherapy. However the long-term impact of chemotherapy on GLS in comparison with other cardiac risk factors is unknown.

Methods: We recruited 521 asymptomatic pts from the community aged >65 years with stage A heart failure (SAHF, based on at least one of: diabetes, obesity, hypertension, coronary artery disease or chemotherapy). 228 controls with no cardiac risk factors were recruited for controls. All pts underwent a conventional echocardiographic study and GLS measurement. Reduced GLS was defined as GLS <−16%. This study compared 46 pts with prior chemotherapy (mean duration 7.15 years), matched 2:1 on age and clinical criteria with 92 non-chemotherapy SAHF pts, separately with controls without cardiac risk factors.

Results: SAHF patients previously treated with chemotherapy were more likely to have a clinically significant reduction in GLS compared with healthy controls (36% vs 12%, p=0.04). There were no differences between chemotherapy and non-chemotherapy SAHF patients with respect to GLS, LV ejection fraction or diastolic parameters.

Comparison of LV echocardiographic performance parameters with other SAHF risk factors and with and without prior chemotherapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chemotherapy (n=46)</th>
<th>Other SAHF (N=92)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global longitudinal strain (%)</td>
<td>−16.15±3.35%</td>
<td>−18.71±5.64</td>
<td>0.25</td>
</tr>
<tr>
<td>Abnormal GLS (&lt;−16%)</td>
<td>28%</td>
<td>15.2%</td>
<td>0.18</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>63.51±11.3</td>
<td>63.11±12.1</td>
<td>0.57</td>
</tr>
<tr>
<td>E (cm/sec)</td>
<td>0.067±0.023</td>
<td>0.065±0.031</td>
<td>0.21</td>
</tr>
<tr>
<td>Indexed LA volume (mL/m²)</td>
<td>29.3±12.1</td>
<td>29.9±11.8</td>
<td>0.92</td>
</tr>
<tr>
<td>Abnormal e' (&lt;−8 mm/s)</td>
<td>78.3%</td>
<td>83.7%</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Conclusion: Prior chemotherapy is a significantly associated with reduced GLS, late after treatment. This effect is analogous to that of other SAHF risk factors.

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4156 | BEDSIDE

Global longitudinal strain to detect cardiotoxicity in adult survivors of childhood leukemia

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Background: Global longitudinal strain has been recommended for screening of cardiotoxicity in cancer survivors. However, there are limited study data supporting this recommendation, in particular in adult survivors of childhood cancer.

Aim: To compare global longitudinal strain (GLS) in adult survivors of childhood leukemia with apparently normal left ventricular (LV) function, to a matched control group.

Methods: From a cross-sectional study of survivors of childhood acute lymphoblastic leukemia, we identified 62 survivors without known heart disease or hypertension, and with both normal LV ejection fraction and fractional shortening. GLS was measured off-line in all participants with semi-automatic software (EchoPAC v. 112, GE Healthcare). The effects of CT cardiotoxicity in cancer survivors. However, there are limited study data supporting this recommendation, in particular in adult survivors of childhood cancer.

Results: The survivors were examined mean 18.5±5.3 years after diagnosis. Pre-dating chemotherapy, the mean group I (n=33) and group II (n=33) GLS were −22.0±2.6% and −19.9±3.0% respectively. Arterial stiffness and oxidative stress were increased in group I (p:<0.0005). Killian index for arterial stiffness; oxidant stress from carbonyl concentration into the plasma proteins (CCPP); and genetic variation from genotypes rs28371759, rs2032582, and rs1056836.

Conclusions: We detected subclinical LV dysfunction assessed by GLS. This supports the use of GLS in follow-up after treatment for childhood cancer.

4157 | BEDSIDE

New mechanisms of taxanes-related cardiotoxicity in women with breast cancer

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Background: Chemotherapy increases the risk of heart failure. Global longitudinal strain (GLS) is a sensitive marker of early LV systolic dysfunction, and has been shown to change acutely in some pts after chemotherapy. However the long-term impact of chemotherapy on GLS in comparison with other cardiac risk factors is unknown.

Methods: We recruited 35 women with HER2- breast cancer (45±7 years) that were evaluated at baseline, after the 1st cycle, immediately after taxanes, and 2 years after therapy, in order to assess LVEF and deformation (by 4D echo): radial (RS), longitudinal (LS), circumferential (CS), and area strain (AS); R-index for arterial stiffness; oxidant stress from carbon content into the plasma proteins (CCPP); and genetic variation from genotypes rs28371759, rs2032582, and rs1056836.

Results: 13 patients developed cardiotoxicity (group I), recovered 2 years after therapy, whereas 22 patients did not (group II) (table). LS and AS were reduced after the 1st cycle of taxanes, but normalized at 2 years (table). Arterial stiffness and oxidative stress were increased in group I (p:<0.01) (vs. group II). Homozygote of genotype rs1056836 was related to the decrease of LVEF (p=0.45, p=0.05). A reduction of AS by 16% after the 1st cycle of taxanes was the most powerful predictor of LVEF reduction after therapy.

Conclusions: Taxanes-related cardiotoxicity appears early after completion of treatment, related to increased oxidative stress and genetic variation, but is completely reversible 2 years after therapy.

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4158 | BEDSIDE

Detection of early and late left and right ventricular dysfunction in patients treated with anthracyclines

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Introduction: Cardiotoxicity can be a side effect of chemotherapy (CT) with other drugs used in oncological therapy. Echocardiographic monitoring is recommended for timely detection of left ventricular dysfunction. Myocardial deformation imaging has been suggested to have higher reproducibility and sensitivity compared to conventional echocardiography. The effects of CT in right ventricular function are poorly studied.

Methods: Prospective echocardiographic study of a cohort of patients (pts) referred for CT with anthracyclines. Echocardiography done one week before the beginning of CT (T0), one week after the first cycle (T1), one week after the third cycle (T2), one week after the conclusion of CT (T3) and one year after the conclusion of CT (T4). In each moment, a conventional echocardiographic study was performed (M-mode, 2D and Doppler assessment of the dimensions and systolic and diastolic function of the left and right ventricles), as well as 2D-speckle tracking strain of the left ventricle.

Results: Fifty-one pts (breast cancer, n=32, from which 5<erbB2-positive; lymphoma, n=14; gastric cancer, n=5). Treated with doxorubicin, n=26 or epirubicin, n=25. Age 51±12.4 years, forty (78.4%) females. A significant and progressive decrease of global longitudinal strain (GLS) was noticed, throughout and after CT, T0 (−22.0±2.6%), T1 (−19.3±3.0%), T2 (−17.3±0.2%), T3 (−15.3±0.2%), T4 (−13.2±0.2%), p<0.0005. Left ventricular ejection fraction (LVEF) also decreased significantly throughout CT (66.7±4.0% at T0; 64.1±3.3% at T1; 62.2±2.9% at T3, p<0.0005), but partially recovered in the long term (62.6±6.4% at T4, p=0.005 vs T0 but p=NS vs T1 or T2). At T4, GLS was −19% in 72.4% of the pts and −15% in 10.3%. All pts except one had FE≥55% at T4 and in 10.3% a ≤10% decrease in LVEF was observed between T0 and T4. A GLS at T2 >−17.5% had a sensitivity of 80% and a specificity of 91.5% to predict a ≥10% decrease of LVEF between T0 and T3 (AUC=0.94, p<0.002) with no absolute value or relative change in strain was able to predict a ≤10% decrease in LVEF between T0 and T4. Right ventricular systolic function decreased significantly throughout and after CT (TAPSE 23.3±2.9 mm at T0; 23.6±3.7 mm at T1; 22.3±3.8 mm at T2; 21.2±2.7 mm at T4, p=0.001).

Acknowledgement/Funding: #1584.04.417/G/19 guest on 07 February 2019
Conclusions: Anthrycyclines provoke a significant and progressive decrease of left ventricular function, during and after CT. GLS is a sensitive and early marker of myocardial lesion and was still decreased in the long-term. Right ventricular function also progressively decreases and should be monitored.

RISK STRATIFICATION IN PULMONARY EMBOLISM AND IN PULMONARY HYPERTENSION

4174 | BEDSIDE

Acute pulmonary embolism: external validation of the 2014 risk stratification model of the European Society of Cardiology

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Background: In patients with acute pulmonary embolism (PE), risk stratification for short-term mortality is crucial to drive clinical management. The European Society of Cardiology (ESC) has recently proposed an updated model for risk stratification based on clinical features, right ventricle dysfunction (RVD) and/or troponin levels. Study outcomes were 30-day death and PE-related death (2014-ESC model).

Methods: The aim of this study was to provide an external validation of the 2014-ESC model. Consecutive patients with symptomatic, objectively confirmed PE were included in prospective cohorts that were subsequently merged in a collaborative database. Patients were included in the analysis if full information about their sPESI score, RVD (by either echocardiography or computed tomography) and troponin levels were available. Study outcomes were 30-day death and PE-related death (as adjudicated by the local investigator).

Results: Among 906 patients (mean age 68±16, 489 females), 801 were hemodynamically stable. Death and PE-related death occurred in 7.2% and 4.1% of the patients. Death rates according to risk stratification (2014 and 2008-ESC models) are reported in the Table. One of the 196 low-risk patients died (0.5%). The 2014 and the 2008 ESC models showed similar discriminatory powers for death (c-statistics 0.71; 95% CI 0.65–0.77 versus 0.71; 95% CI 0.65–0.78) as well as for PE-related death (c-statistics 0.77; 95% CI 0.70–0.85 versus 0.79; 95% CI 0.72–0.85).

Conclusions: The 2014-ESC model avoids further testing in about 20% of the patients preserving a high negative predictive value. The 2014-ESC model has a discriminatory power for death and for death due to PE similar to that of the 2008-ESC model. Further studies are required to improve the clinical profile of patients at intermediate-risk to justify a treatment upgrading.

Acknowledgement/Funding: this study was performed without any external support

4175 | BEDSIDE

BNP testing performed after triaging patients with acute PE by standard Hestia decision rule is not needed - a randomised trial

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Background: Traditionally, patients with acute pulmonary embolism (PE) are hospitalised for initial anticoagulant treatment. Out of hospital treatment has in- increased but there is still great uncertainty as to what is the optimal triaging instrument. BNP testing is a promising simple bedside tool in acute PE, which has not been extensively investigated in this setting.

Aims: To investigate the efficacy and safety of selecting PE patients for outpatient treatment by NT-proBNP testing.

Methods: Randomized non-inferiority trial conducted in the Netherlands. Patients with CT pulmonary angiography proven acute PE were first screened for outpatient treatment eligibility based on the Hestia criteria (Zondag et al JTH 2011). Patients without any of the Hestia criteria were randomized to (1) discharge within 24 hours after diagnosis of acute PE, or (2) additional NT-proBNP testing. Patients in the BNP group were only discharged after 24 hours after diagnosis, if NT-proBNP was &lt;500ng/L; they were admitted to the hospital if NT-proBNP was &gt;500ng/L. Primary endpoint was 30-day adverse outcome defined as PE or bleeding-related mortality, cardiopulmonary resuscitation or IC admission. Secondary endpoints were recurrent VTE, major bleeding and all-cause mortality.

Results: Between 2010 and 2013, 550 patients were randomized. In the NT-proBNP group, 34/275 (12%) had elevated NT-proBNP values and were managed as inpatients. The primary endpoint occurred in none of these 275 patients (0%; 95% CI 0–1.3%); versus in 3/275 (1.1%; 95% CI 0.2–3.3%) of the patients in the direct discharge group (p=0.08). These 3 patients had normal NT-proBNP levels measured post-hoc. During 3-month follow-up, recurrent VTE occurred in 2 patients (0.73%; 95% CI 0.1–2.6%) in the NT-proBNP group versus 3 patients (1.1%; 95% CI 0.2–3.3%) in the direct discharge group (p=0.65). The rates of major bleeding were 0.4% vs 1.1% (p=0.62) and of all-cause mortality 1.5% vs 1.1% (p=0.70), respectively.

Conclusion: Prognostic assessment, based on NT-proBNP levels does not affect 30-day prognosis. It changes the acute risk in the majority of patients. It is concluded that additional BNP testing is not needed after applying the Hestia decision rule.

4176 | BEDSIDE

Results: cross a clinical score, cardiac troponin, and echocardiography testing algorithm for risk stratification of normotensive patients with acute symptomatic pulmonary embolism


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Background: For risk stratification of normotensive patients with acute symptomatic pulmonary embolism (PE), the updated guidelines of the European Society of Cardiology (ESC) recommend use of an algorithm that sequentially applies a clinical score, imaging testing assessing right ventricle (RV) function, and cardiac biomarkers. This study aimed to validate the ESC prognostic algorithm.

Methods: We retrospectively examined the cohort of normotensive patients that had low symptomatic PE (categorized in a previous study). Using the baseline data collected at the time of PE diagnosis, the central coordinating center prospectively determined the simplified Pulmonary Embolism Severity Index (sPESI). Patients underwent transthoracic echocardiography within 24 hours after diagnosis of PE, and the core laboratory personnel measured cardiac troponin I levels. This study used a complicated course (i.e., death from any cause, hemodynamic collapse, or adjudicated recurrent PE) through 30 days after the PE diagnosis as the primary outcome.

Results: Of 848 patients, 313 (37%; 95% confidence interval [CI], 34–40%) had a sPESI score of 0 (low-risk ESC group), and 5 (1.6%; 95% CI, 0.5–3.7%) of these patients experienced a complicated course. Of the 63% (535/848) patients with a sPESI score >1 (intermediate-risk ESC group), 478 (89%) had normal RV function on echocardiography and/or normal troponin level (intermediate-low ESC group), and 48 (10%; 95% CI, 7.3–13%) experienced a complicated course. Fifty-seven (11%; 95% CI, 8.0–13.1%) of the 535 patients with a sPESI score >1 had both echocardiographic RV dysfunction and elevated troponin level (intermediate-high ESC group), and 10 (18%; 95% CI, 7.7–27%) experienced a complicated course. Of the 194 patients with tachycardia and/or mild hypotension, 164 (85%; 95% CI, 79–90%) had normal RV function on echocardiography and/or normal troponin level (intermediate-low ESC group), and 18 (11%; 95% CI, 6.2–16%) experienced a complicated course. Thirty (15%, 95% CI, 10–21%) of the 194 patients with both tachycardia and/or mild hypotension had both echocardiographic RV dysfunction and elevated troponin level (intermediate-high ESC group), and 7 (23%; 95% CI, 8.2–38%) experienced a complicated course.

Conclusions: A prognostic strategy that uses a simple clinical rule, echocardiography and cardiac troponin testing in a stepwise fashion effectively risk stratifies normotensive patients with acute symptomatic PE. Compared to the sPESI, tachycardia and/or mild hypotension refine stratification of intermediate-risk PE.

4177 | BEDSIDE

Acute not-high-risk pulmonary embolism: a comparison of risk assessment strategies


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Background and introduction: Based on numerous scores and models for risk

Abstract 4174 – Table 1

<table>
<thead>
<tr>
<th>High risk*</th>
<th>Intermediate risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=108</td>
<td>n=384</td>
<td>n=196</td>
</tr>
<tr>
<td>24 (22%)</td>
<td>7 (7.7%)</td>
<td>1 (0.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RVD or increased troponin</th>
<th>Death PE</th>
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</thead>
<tbody>
<tr>
<td>18 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>12 (4.0%)</td>
<td></td>
</tr>
<tr>
<td>6 (3.0%)</td>
<td></td>
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<tr>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>0 (0%)</td>
<td></td>
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<tr>
<td>3 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

Notes: *Low-risk patients with no Hestia criteria included.

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stratification of normotensive pulmonary embolism (PE) developed and validated during the past years, a new algorithm for risk assessment was introduced by the 2014 ESC guideline.

**Purpose:** To compare the performance of the new algorithm proposed by the 2014 ESC guideline with other scores for risk stratification of not-high-risk PE.

**Methods:** Normotensive patients with confirmed PE were included in an observational cohort study at our university medical center Germany between September 2008 and August 2014. Risk classes were assessed according to the algorithms proposed by the 2008 and 2014 ESC guideline, the sPESI, the Bova score and the FAST score. An age-adjusted cut-off value for hsTnT (>14 pg/ml for <75 years, >45 pg/ml for ≥75 years) was used for calculation of the Bova and the (modified) FAST score.

**Results:** During the first 30 days, 25 of 386 patients (6.4%) had an adverse outcome as defined by the modified FAST score, and in 14 patients (3.6%) died. The sPESI, the 2008 and the 2014 ESC guideline algorithms classified a greater number of patients in the higher risk classes while the Bova and the FAST score classified more patients in the low-risk classes. Regardless of the score or algorithm used, the risk of an adverse 30-day outcome was highest in the high-risk classes while all patients classified in low-risk classes had a favourable 30-day outcome (no PE-related deaths, rate of an adverse outcome 0 to 1.4%). The c-index for prediction of an adverse 30-day outcome was higher for the ESC 2014 algorithm (AUC, 0.71 [0.64–0.78]) compared to the ESC 2008 algorithm (AUC, 0.65 [0.57–0.74]) and highest for the FAST score (AUC, 0.82 [0.75–0.86]). Regardless of the score used, increase in risk classes was associated with an elevated risk of an adverse 30-day outcome with the highest OR for patients classified as “high-risk” in the FAST score (compared to “low-risk”; OR, 15.9 [5.3–47.8]) and in the sPESI (compared to “low-” and “intermediate-risk”; OR, 37.8 [5.1–282.4]; 19.3% adverse outcome).

**Conclusions:** The new algorithm proposed by the ESC 2014 guideline is more suitable for risk stratification of normotensive PE patients compared to the other score algorithms. Prevention of severe thromboembolic complications was observed for the FAST score if an age-adjusted hsTnT cut-off value was used for calculation instead of H-FABP. All available scores and algorithms safely identify low-risk patients while the FAST and the Bova score are more suitable to identify patients at elevated risk.

### 4179 | BEDSIDE

**Investigation of a new pathophysiological axis for risk stratification of normotensive pulmonary embolism: prognostic impact of copeptin**

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**Background:** Vasopressin plays a key role in cardiovascular homeostasis and is released upon stress and hypotension. While previous studies emphasize the value of the vasopressin surrogate marker copeptin in myocardial infarction, heart failure, and pulmonary hypertension, the prognostic value of copeptin in pulmonary embolism (PE) is unknown.

**Purpose:** To assess the prognostic impact of copeptin in normotensive patients with PE.

**Methods:** We prospectively studied 268 consecutive normotensive patients with acute PE at our University Hospital between 09/2008 and 08/2014. Copeptin plasma levels were measured on admission using a commercial sandwich immunoluminometric assay.

**Results:** Copeptin levels ranged between 0.9 and 705.0 pg/ml with a median concentration of 13.8 (IQR, 5.9–44.5) pg/ml. Patients with copeptin levels above the median were older (p = 0.001), had more often cardiopulmonary diseases (p = 0.002) or renal insufficiency (p = 0.001), and presented more frequently with syncope (p < 0.001), tachycardia (p = 0.001) or hypoxemia (p = 0.034). Overall, 15 patients (5.6%) had an adverse 30-day outcome defined as PE-related death, resuscitation, catecholamine administration or intubation. These patients had higher copeptin levels compared to patients with a favourable course (12.0 [5.0–31.3] vs. 18.4 [10.6–48.8] pg/ml, p = 0.020). ROC analysis yielded an AUC of 0.68 (95% CI, 0.52–0.83) for copeptin with regard to an adverse outcome and a concentration of 24 pg/ml was identified as optimal cut-off value (sensitivity, 0.73; specificity, 0.66). Using logistic regression analysis, copeptin ≥24 pg/ml was associated with a 5.3-fold increased risk for an adverse outcome (95% CI, 1.6–17.5; p = 0.006). To further optimize risk stratification of normotensive PE patients, we developed a biomarker-based strategy. Based on the excellent NPV of hsTnT and NT-proBNP (>14 pg/ml for <75 years, ≥45 pg/ml for ≥75 years) used for calculation of the Bova score and (modified) FAST score.

**Conclusions:** Copeptin might be helpful for risk stratification of normotensive patients with acute PE, especially if integrated into a novel biomarker-based algorithm.

### 4179 | BEDSIDE

**Derivation of a new score to predict chronic thromboembolic pulmonary hypertension after acute pulmonary embolism**


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**Introduction:** Validated risk factors for chronic thromboembolic pulmonary hypertension (CTEPH) after acute pulmonary embolism (PE) are currently unknown.

**Methods:** We combined 3 observational cohorts of consecutive PE patients who underwent echocardiography after a median of 1.5 years, if abnormal follow-up by additional diagnostic tests for confirmed CTEPH. Baseline demographics and clinical variables associated with CTEPH were included in a multivariate regression analysis. Independent predictors were combined in a risk stratification score.

**Results:** Of 772 patients with complete follow-up, CTEPH was ruled out in 711 (92%) and confirmed in 22 (2.8%) by right heart catheterization (RHC). CTEPH was "probable" although RHC was not performed in 12 and "unlikely" but not completely ruled out in 27 patients. The former patients with "probable" CTEPH were included in the sensitivity analysis, the latter excluded from further analysis. Unprovoked PE, hypothyroidism, symptom onset -2 weeks before PE diagnosis, right ventricular dysfunction on CT or echocardiography, diabetes mellitus, and thrombotic therapy or embolectomy independently predicted CTEPH (Table 1). The area under the curve (AUC) of ROC curve of the clinical scoring including those variables was 0.89 (95% CI 0.84–0.94). Sensitivity analysis and bootstrap internal validation confirmed this AUC. Seventy-three percent of patients were categorized to low risk category (CTEPH incidence 0.38%, 95% CI 0–1.5%) and 27% to high risk category (CTEPH incidence 10%, 95% CI 6.5–15%).

**Conclusion:** The proposed score is based on previously identified and new clinical variables associated with CTEPH after acute pulmonary PE. If externally validated, the score may guide targeting CTEPH screening to high risk patients.

### 4180 | BEDSIDE

**RV dysynchrony predicts clinical outcomes after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension**

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**Background:** Balloon pulmonary angioplasty (BPA) may improve hemodynamics and exercise tolerance in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Recently, we reported a significant correlation between echocardiographic right ventricle (RV) predictors and right heart catheterization (RHC) in patients with CTEPH, and that BPA could ameliorate RV function. However, long-term follow up of RV function after BPA has not been fully established.

**Purpose:** The objectives of this study were to follow up the RV hemodynamics and function after BPA, using RHC and echocardiography.

**Methods:** We studied 25 consecutive patients with CTEPH who underwent BPA, and assessed RV hemodynamics and function before, immediately after, and at 6 months after the procedure. RV hemodynamic parameters, including mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), and cardiac output were recorded by RHC. RV function was assessed using conventional echocardiographic parameters such as RV diameter (RVD), tricuspid annular plane systolic excursion (TAPSE), RV S', RV index of myocardial performance (RIMP), and RV fractional area change (RVFAC). We also used two-dimensional speckle-tracking echocardiography (2DSTE) and three-dimensional transhauricular echocardiography (3DTEE) to investigate RV strain and RV volumetric parameters including RV ejection fraction (RVEF), RV end diastolic volume (RVEDV), and RV end systolic volume (RVESV). RV dysynchrony was also assessed by...
the standard deviation (SD) of the intervals from QRS onset to peak systolic strain for 6 segments of the RV (SDTTP). Finally, exercise capacity was assessed by the 6-minute walk distance (6MWD) test.

**Results:** Hemodynamic parameters such as mPAP, PVR, and cardiac index were significantly improved immediately after BPA, and the effects of BPA were maintained at 6 months follow up. RVD, RVEDV, and RVESV were significantly reduced after BPA. TAPSE, RVFAC, RVEF, and RV mid free wall longitudinal strain (MFWSLS) were significantly improved after BPA, implicating that RV systolic function was ameliorated. RV dysynchrony was also improved after BPA. Receiver operating characteristic analysis revealed that SDTTP was a good predictor for improvement of 6MWD (sensitivity of 86% and specificity of 56%, area under the curve: 0.78, P=0.03).

**Conclusions:** BPA induced RV reverse remodeling and improved RV function, as assessed successfully by echocardiography. RV dysynchrony could be a useful parameter for assessing exercise tolerance after BPA.

### 4181 | BEDSIDE

**Reduction in NT-proBNP and its correlation with survival in patients with PAH treated with riociguat:** 2-year results from the PATENT-2 long-term extension study

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**Background:** Increased levels of NT-prothrombin propeptide (NT-proBNP), a biomarker of right ventricular dysfunction, are associated with poorer outcomes in pts with pulmonary arterial hypertension (PAH). Riociguat significantly reduced NT-proBNP levels compared with placebo in pts with PAH during the 12-week PATENT-1 study.

**Purpose:** We present the 2-year NT-proBNP data from PATENT-2.

**Methods:** Pts with PAH who were treatment-naïve or pretreated with ERA or prostanooids entered PATENT-2 after completing PATENT-1 without ongoing drug-related SAEs. All pts received riociguat individually adjusted up to 2.5 mg tid. Pts were randomized into 2 treatment arms: 1.5 mg tid or 2.5 mg tid. Primary endpoints were safety and tolerability; change in NT-proBNP was an exploratory efficacy endpoint.

**Results:** Of the 405 pts who completed PATENT-1, 396 (98%) entered PATENT-2. At 2 yrs, mean±SD NT-proBNP had improved by −145±1659 pg/ml (n=198) from PATENT-1 baseline in the overall population. In the treatment-naïve and pretreated subgroups, NT-proBNP changed by −291±1626 pg/ml (n=104) and +19±1553 pg/ml (n=92), respectively, from PATENT-1 baseline. A Cox proportional-hazards analysis showed significant correlation between change from baseline in NT-proBNP levels and both survival (HR=0.91; 95% CI 0.84 to 0.98; p=0.001) and clinical worsening-free survival (HR=0.90; 95% CI 0.85 to 0.95; p<0.001), using −300 pg/ml as the unit of change for HR. Figure 1 shows the difference in survival for pts with NT-proBNP levels above and below the clinically relevant threshold of 1800 pg/ml at baseline and follow-up.

**Conclusion:** Reduction in NT-proBNP in pts with PAH treated with riociguat was sustained for up to 2 yrs in PATENT-2. Change from baseline in NT-proBNP correlated with survival and clinical worsening-free survival.

**Acknowledgement/Funding:** Editorial assistance was provided by Adelphi Communications Ltd (Bollington, UK), supported by Bayer Pharma AG.

### 4182 | BEDSIDE

**Outcome comparison of patients with idiopathic/hereditary pulmonary arterial hypertension, pulmonary hypertension due to left heart disease and pulmonary hypertension due to lung disease**

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**Background:** Despite therapeutic advances for idiopathic/hereditary pulmonary arterial hypertension (PAH) the most common forms of pulmonary hypertension (PH) are due to left heart disease (PH-LHD) and lung disease (PH-LD).

**Purpose:** To compare clinical, functional and hemodynamic characteristics and survival of patients with I/HPAH, PH-LHD and PH-LD.

**Methods:** Consecutive in- and out-patients with I/HPAH, PH-LHD and PH-LD referred to our centre were included; at baseline patients underwent clinical evaluation, six-minute walking distance (6MWD) and right heart catheterization. All patients received a goal oriented therapy (I/HPAH) or a therapy for the underlying disease (PH-LHD and PH-LD). Survival was estimated by Kaplan-Meier curves.

**Results:** 752 pts were enrolled: 304 with I/HPAH (39% males; 65% in NYHA III/IV), 231 with PH-LHD (27% males; 60% in NYHA III/IV) and 217 with PH-LD (65% males; 77% in NYHA III/IV). I/HPAH patients were younger [51 years old vs 69 (PH-LHD) and 70 (PH-LD); p<0.001], with better exercise capacity [405 m vs 347 (PH-LHD) and 300 (PH-LD); p<0.001] and with worst hemodynamic profile [mean pulmonary arterial pressure: 53 mmHg vs 37 (PH-LHD) and 38 (PH-LD); p<0.001; cardiac index: 2.3 l/min/m² vs 2.6 (PH-LHD) and 2.5 (PH-LD); p<0.001; pulmonary vascular resistance: 11.2 WU vs 3.7 (PH-LHD) and 6.5 (PH-LD); p<0.001]. Survival rates are shown in the Figure.

**Conclusions:** Patients with I/HPAH are younger, with better exercise capacity and survival despite a worse hemodynamic profile as compared to patients with PH-LHD or PH-LD. This may be explained by the younger age and/or the availability of effective medication for I/HPAH. The actual lack of effective medications for the underlying LD may explain the worst prognosis of patients with PH-LD in comparison with PH-LHD.

### 4183 | BEDSIDE

**Prognostic value of right heart adaptation to pulmonary arterial hypertension: a prospective cohort study**

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**Background:** Although right ventricular (RV) function is the primary determinant of prognosis in pulmonary arterial hypertension (PAH), ejection fraction is dependent on preload and afterload, and is insensitive to changes in regional function.

**Purpose:** In this study we employed 3D motion analysis of cardiac magnetic resonance (CMR) imaging to understand how RV contraction changes in the remodelled hearts of PAH patients, what features of systolic dysfunction are most strongly related to outcome and whether this enables better discrimination of ventricles which are destined to fail.

**Methods:** A cohort of 271 patients diagnosed with PAH underwent conventional CMR imaging. We used automated segmentation to construct a 3D representation of RV systolic motion. For machine-learning the patients were randomly allocated to training (50%) and testing (50%) cohorts. Patterns of 3D contraction predictive of survival were learnt from the training cohort using supervised principal component analysis (SPCA), and compared with RV ejection fraction (RVEF), pulmonary vascular resistance (PVR) and six-minute walk distance (6MWD) as predictors of survival in the test cohort. Analysis was repeated 1,000 times using randomly allocated cohorts.

**Results:** Patients were followed up for a mean of 3.8 years and 99 (36.5%) patients died. Baseline 3D systolic motion predicted mortality significantly better than RVEF, PVR or 6MWD (all p<0.001) and predicted 5-year mortality significantly better than RVEF (receiver operating characteristics area under curve area: 0.58 vs 0.41, p<0.001). Deterioration in the longitudinal component of function was most strongly related to survival (longitudinal: 60%, circumferential: 24%, radial 16%) whereas all three components of function reflected a deterioration of...
ADVANCES IN CARDIAC REGENERATION

4189 | BENCH
Leukemia inhibitory factor enhances cardiomyocyte regeneration after myocardial infarction from endogenous cell systems and not from circulating bone marrow-derived cells

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Purpose: Cardiac stem cells or precursor cells can regenerate cardiomyocytes, but the mechanism underlying this effect remains unclear. Using a genetic fate-mapping model, we tested the hypothesis that leukemia inhibitory factor (LIF) influences cardiac stem cells and stimulates endogenous cardiomyocyte renewal after myocardial infarction (MI).

Methods: We generated CreLacZ mice in which the cardiomyocytes in the left ventricular field showed positive 5-bromo-4-chloro-3-indolyl-β-D-galactoside (X-gal) staining immediately after tamoxifen injection. We counted the number of X-gal-negative (newly generated) cardiomyocytes in the mice after various interventions, including the administration of the LIF plasmid. Combining this with a label-retaining strategy and a EGFP-bone marrow transplantation technique, we also analyzed the origin of cardiac regeneration.

Results: More than 99.9% of the cardiomyocytes in the CreLacZ mice heart field showed positive X-gal staining after tamoxifen injection. Three months after MI, the MI mice had more X-gal-negative cells than the control mice (3.0±0.3%, LIF; 0.47±0.16%, sham; p<0.05). The cardiac side population (CSP) cell fraction contained label-retaining cells, which differentiated into X-gal-negative cardiomyocytes after MI. We injected the LIF plasmid at the time of MI and found significant functional improvement in the LIF-treated group. At 1 month after MI, in the MI border, and MI scar area, the LIF-injected mice had 31.4±5.83 X-gal-negative cardiomyocytes/mm², whereas control mice had 12.3±4±2.56 X-gal-negative cardiomyocytes/mm² (p<0.05). On 5-ethyl-2'-deoxyuridine (EdU) administration after MI, the percentages of EdU-positive GSP cells in LIF-treated and control mice were 29.4±2.7% and 10.6±3.7%, respectively, suggesting that LIF influenced CSP proliferation. We also showed that LIF activated the JAK-STAT pathway in CSPs, in vivo and in vitro. The results observed in EGFP-bone marrow-chimeric CreLacZ mice indicated that LIF did not stimulate cardiogenesis and survival together with improvement in cardiac remodelling 4 weeks post-infarct compared to mice injected with siRNA-c-treated cells.

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4190 | BENCH
Epigenetic modulation of cardiac progenitor cells through miR-29a/Dnmt3a axis promotes their cardiac differentiation

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Epigenetic programming within the cardiac progenitor cell (CPC) niche controls CPC specification and differentiation, but the identity of putative mediators is poorly characterized.

To dissect these mechanisms, we used primary expanded Sca-1+ CPC from murine adult hearts and stimulated cardiomyocyte differentiation upon culture in a differentiation medium (DIFF) containing 5-Aza-cytidine and TGFβ1 or co-cultured with rat cardiomyocytes. With this model, we previously showed that inducible deletion of β-catenin enhanced CPC differentiation in vitro and in vivo. Accordingly, we detected a constitutive activity of Wnt/β-catenin pathway in undifferentiated CPCs (Axiom 2.3 miR-29a 46.7% p<0.01) together with a reduced β-catenin protein level (62.80±7.5% p<0.05) in DIFF-treated CPC, associated with an upregulation of Wnt antagonist (VtgWnt anti-villin-1 (530±57% p<0.05). Like several Wnt/β-catenin repressor genes, Wnt-1 expression is DNA methylation sensitive and susceptible to be regulated by the de novo DNA methyltransferases Dnmt3. Indeed, Dnmt3a was downregulated in CPC treated with DIFF, while siRNA targeting Dnmt3a decreased Wnt-1 promoter methylation (34.2±21.9%; p<0.05) and increased Wnt-1 gene expression in non-differentiated cells (425±254%; p<0.05). Dnmt3a silencing promoted CPC cardiac differentiation in co-culture assay (assayed by quantitative expression of cTnT; 162±7% vs. siRNA-ctl; p<0.001). In parallel, we found an early upregulation of miR-29a (444±43%; p<0.01), a well-known regulator of Dnmt3a, in DIFF-treated CPC. Indeed, modulation of miR-29a using mimic or anti-miR affected Dnmt3a protein level, promoter methylation of Wnt-1 and Wnt-1 expression (mimic: 839±257%; LNA: 519±9%; p<0.05). Importantly, LNA treatment also significantly decreased CPC differentiation in co-culture assay (63±4% vs. cTn: p<0.001). Altogether, this suggests that miR-29a controls CPC differentiation through Dnmt3a-dependent regulation of Wnt-1. We showed that miR-29a and siRNA-Dnmt3a abrogates the above effect both on Wnt-1 expression and CPC differentiation.

Extending these findings in vivo, transient silencing of Dnmt3a in CPC subsequently injected in the border zone of infarcted mouse hearts improved 4-week survival together with improvement in cardiac remodelling 4 weeks post-infarct compared to mice injected with siRNA-ctl treated cells.

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4191 | BENCH
Arrhythmic risk after transplantation of induced pluripotent stem cell derived cardiomyocytes into infarcted mouse hearts

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Introduction: iPSCM are regarded as promising cell type for cardiac cell replacement therapy. Long-term survival and functional integration of these cells have been demonstrated. However, data on the arrhythmicogenicity of this cell type are missing, and there have been conflicting results on pro- or antiarrhythmic effects of other stem cell-derived cardiomyocytes (CM) after transplantation. Thus, we investigated electrical integration and arrhythmic potential of transplanted iPSCM in infarcted mouse hearts.

Methods: Murine iPSCM expressing EGFP and a puromycin resistance under control of the alpha-MHC promoter were obtained by antibiotic selection. After LAD ligation, iPSCM (500,000 cells/10 μl) were injected into adult mouse hearts. 6 weeks later, electrophysiological catheter examinations were performed. The catheter was placed into the right ventricle for programmed stimulation. ECG recordings revealed number and duration of induced fibrillation episodes. Afterwards, hearts were resected and ventricular tissue slices (150 μm) were prepared. Slices were focally stimulated by an electrode placed in host tissue. Recordings of action potentials (AP) were performed with glass microelectrodes in transplanted iPSCM and in host CM within the slices.

Results: Persistence of ECG and electrical integration of iPSCM in the perifarct zone could be clearly demonstrated. No cells were found within the infarction. Quality of electrical integration was good indicated by a maximal stimulation frequency without conduction blocks of 9.1±0.5 Hz. AP properties of transplanted iPSCM differed significantly from those of host CM (P<0.05 for all parameters); iPSCM had a lower maximum diastolic potential (-64.0±2.8 mV vs. -70.2±2.6 mV), amplitude (70.0±7.8 mV vs. 84.2±2.2 mV) and maximum upstroke velocity (51.3±24.1 V/s vs. 125.7±19.4 V/s). Action potential duration to 50% repolarization (APD50) was longer (18.2±3.3 ms vs. 10.7±2.0 ms). APD90 was shorter (65.1±20.2 ms vs. 101.9±34.5 ms). iPSCM treated mice (n=8) showed a higher sensitivity to induced ventricular tachycardia than sham animals (n=8). Although the number of episodes was similar (6±0.3 ms in iPSCM treated mice vs. 5.5±5.6 in sham animals; P=0.83) the average duration of each episode was longer (727±148 ms vs. 311±85 ms; P=0.03).

Conclusions: Transplanted iPSCM were able to integrate into the perifarct zone, but did not persist within the infarcted tissue. Although quality of electrical integration was good, iPSCM treated mice showed increased risk for induced ventricular tachycardia compared to sham animals.

Acknowledgement/Funding: Hans and Gertie Fischer Foundation
sensus on daily temperature, lag time and snowfall on ST segment elevation myo-
cardial infarction (STEMI). Methods: A retrospective audit of all patients with STEMI within the coldest Cana-
dian city was completed (January 1, 2009 to December 31, 2014). Temperature and snowfall data was collected from Environment Canada. Poisson regression modelling was used to identify the relationship between weather and STEMI. Weather characteristics tested included daily high (DH), low and average tem-
perature on the same day, previous day, and two days before, along with the average temperature for the combined current and previous days, and the current and previous two days. Daily snowfall was analyzed similarly. Results: Over the 6 year study period, there were 1817 STEMIs. The DH was the strongest predictor of STEMI. Of days with a DH < 0°C, STEMI event rates were 0.94/day, compared to 0.79/day when DH = 0°C. Despite yearly variation, the average STEMI rate over the study period has a statistically significant linear trend across temperature (p < 0.001). Temperature (DH) in the preceding 1 or 2 days was also predictive (p < 0.001). Higher temperature groups were not associated with higher STEMI rates. With every drop of 1°C in DH, the risk of STEMI increased by 0.7% (p < 0.001). Snowfall was a univariate predictor but showed no independent association after adjusting for temperature. Conclusion: There is a clear association between daily temperature and STEMI risk with predictability seen 2 to 2 days prior to STEMI. Increased public aware-
ness and or reallocation of health care resources should be considered to re-
spond to the seasonal increased incidence of STEMI.

4195 | BEDSIDE
Pollutant matter and NO2 air pollution trigger ST-elevation myocardial infarction: a case cross over study of Belgium STEMI registry
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Background: Previous studies have shown that air pollution particulate matter (PM) is associated with increased risk of myocardial infarction. Effects of air pol-
lution on the particular subset of transmural myocardial infarction (STEMI), the role of gaseous air pollutants such as NO2 and O3 and the susceptibility of spe-
cific populations are still under debate. Methods: From 2009 to 2013 all patients of the Belgian prospective STEMI reg-
istry were included. National air pollution parameters were extracted from the Bel-
gian Environment Agency and adjusted for population density using a validated spatial interpolation model. A case cross-over analysis of the risk of STEMI was performed and all risks were adjusted for ambient temperature, day of the week and season. Results: 11428 STEMI patients were included in the study. According to W.H.O air quality guidelines, PM2.5 air quality standard was exceeded in 17.5% of days. Each 10 μg/m-3 increase in PM10, PM2.5 and NO2 were respectively associated with an increased relative risk (RR) of STEMI of 1.026 (IC 95%: 1.005–1.048), 1.014 (IC 95%: 1.003–1.025) and 1.059 (IC 95%: 1.018–1.094). No effect of O3 was found (fig.1). These associations between air pollutants and STEMI were only observed in men (p < 0.05). STEMI were associated with PM10 exposure in 75 y.o patient (RR: 1.046, IC 95%: 1.002–1.092), and with NO2 in < 54 y.o. patients (RR: 1.071, IC 95%: 1.010–1.136). No effect of air pollution on cardiac arrest and in-hospital STEMI mortality was found. Conclusion: In Belgium, 10 μg/m-3 increase in PM2.5 and NO2 increase the risk of STEMI of respectively 2.8 and 5.1%. This relation is observed only in men. Older population develop more STEMI in relation to PM exposure, whereas younger population appears more susceptible to NO2.

4196 | SPOTLIGHT
Environmental exposure to beta-hexachlorocyclohexane is associated with higher systolic blood pressure among people living close to an industrial area
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Background: Human contamination by persistent organic pollutants such as pes-
ticides has been associated to a variety of adverse health effects. Health conse-
quences of exposure to β-hexachlorocyclohexane (β-HCH), a lipophylic byproduct of the production of the insecticide lindane, have been poorly studied, and might include systemic alterations.

Purpose: To evaluate the relationship between β-HCH serum concentrations and blood pressure (BP) and electrocardiographic (ECG) variables in a cohort of in-
dividuals living in the Sacco river Valley (Lazio, Italy), close to a chemical plant.
Methods: 331 individuals (age range 5–86 years, mean 46±18 years, 44% hypertensives, 25.1% treated with BP-lowering drugs, 14.5% smokers, BP 126±19/78±11 mmHg, BMI 27.23–31 kg/m²) were recruited in a cross sectional health surveillance study. Blood samples for metabolic profile and β-HCH assays, physical examination, office BP and resting ECG were performed.

Results: β-HCH was 77 (33–177) ng/g/g in the overall population. As expected, lipid-corrected β-HCH concentrations were associated with age (p < 0.001) and BMI (p < 0.001). Serum concentrations of β-HCH were associated with systolic BP in a model in-
cluding only lipids (coefficient 3.8, 95% CI 1.4–6.3, p = 0.003) and in a regression model adjusted for age, sex, smoking status, BMI, lipids, BP-lowering drugs use (coefficient 4.5, 95% CI 1.4–7.5, p = 0.004). A similar association was found for mean BP (p = 0.03 in the fully adjusted model) but not for diastolic BP.

Left ventricular hypertrophy, defined by either Sokolow-lyon or Cornell Product criteria and present in 29 individuals (9%), was not associated to lipid adjusted β-HCH, nor were heart rate and QRS duration. Lipid-corrected serum concen-
trations of β-HCH were associated with QTc (coefficient 7.9, CI95% 4.4–11.4, p < 0.001). However in a model adjusted for age, sex, smoking status, BMI, lipids, BP-lowering drugs use, the association was no longer significant (p = 0.16).

Conclusions: Higher β-HCH concentrations were independently associated with increased systolic BP values in a population living in an area contaminated by a chemical plant.

PREDICTING THE FUTURE: THE ACCURACY OF RISK SCORES

4203 | BEDSIDE
External validation of the biomarker-based ABC-stroke risk score for atrial fibrillation
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Background: The ABC-stroke score is a novel biomarker-based stroke risk score including the variables Age, Biomarkers (troponin-T high sensitivity [TnT] and N-terminal pro-B-type natriuretic peptide [NT-proBNP]), and Cardiovascular disease history (prior stroke). In the derivation cohort of 14701 pts with AF from the ARIS- TOTLE trial the ABC-stroke score outperformed the traditional CHA2DS2-VASc score (C index 0.67 vs. 0.62, p < 0.001).

Purpose: To externally validate the ABC-stroke score risk in pts with AF and compare with the CHA2DS2-VASc score.
Methods: The STABILITY trial, randomising 15828 pts with stable coronary heart disease to darapladib or placebo showed no significant effect on cardiovascular outcomes. 1400 pts had a history of AF (689 on oral anticoagulation) and qualified for external validation of a stroke risk score in AF. Blood was collected at random-
isation, and TnT and NT-proBNP were centrally analysed with high-sensitivity assays.

Results: In the external validation, based on 4751 person-years of follow-up and 48 adjudicated stroke events, ABC-stroke score achieved a C index of 0.66 in
comparison to 0.58 for the CHA2DS2-VASc score (p = 0.001). The incidence rates (events per 100 person-years) were similar in the derivation and validation data within each predefined risk class: 0.69 vs. 0.72, 1.66 vs. 1.58, and 3.31 vs. 3.81. Kaplan-Meier curves within risk classes (Fig) for both the derivation and validation data illustrate that the ABC-stroke score was well calibrated in different cohorts of AF-patients.

Conclusions: The ABC-stroke score was successfully validated and performed better than CHA2DS2-VASc score in several populations with AF. The ABC-stroke score should thereby be ready for implementation as a decision support tool in routine clinical care.

**References:**

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**Background:** The SCORE risk estimation system is used for cardiovascular risk stratification in apparently healthy adults. The purpose of the current study was to evaluate whether exercise capacity can be used to improve the accuracy of the SCORE cardiovascular risk estimation.

**Methods:** We investigated 21,301 asymptomatic men and women who were annually screened in a tertiary medical centre. All subjects were free of ischemic heart disease or diabetes, and had completed maximal exercise stress test according to the Bruce protocol at their first visit. The SCORE risk estimation system was used to evaluate individual cardiovascular risk for all subjects. The primary endpoint of the current analysis was all-cause mortality. The incremental contribution of exercise capacity to the prediction of the risk of death was evaluated by net reclassification improvement (NRI) and area under the receiver operating curve (AUROC).

**Results:** Mean age of the study population was 47.10 and 71% were men. There were 384 (1.80%) deaths during a mean follow up of 9.2±4.0 years. Kaplan-Meier survival analysis showed that both high SCORE and low exercise capacity were associated with poor survival (FIGURE). When added to the SCORE risk prediction, exercise capacity allowed improved risk stratification: NRI analysis showed a significant increase of 13.5% (P < 0.001) and the AUROC increased (0.81 vs. 0.79).

**Conclusion:** Both SCORE and exercise capacity are strong predictors of all-cause mortality. The addition of exercise capacity to the SCORE risk model can significantly improve the accuracy of the model.

**References:**

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**Background:** In 2013, new ACC/AHA guidelines have been issued for the prevention of cardiovascular diseases (CVD), introducing a new algorithm for risk assessment of a first non-fatal or fatal atherosclerotic cardiovascular disease (ASCVD) event within 10 years of follow-up.

**Purpose:** To evaluate the performance of the new ACC/AHA risk score in Germany, we investigated the risk algorithm in two prospective population-based cohorts: the Southern German Cooperative health research in the Region of Augsburg (KORA) and the Heinz Nixdorf Recall (HNR) Study.

**Methods:** We evaluated n=5,238 participants aged 40–75 years from the KORA surveys S3 (1994–1995) and S4 (1999–2001) and 4,208 subjects aged 45–76 from the Heinz Nixdorf Recall (HNR) Study (2000–2003). There were 383 (7.3%) and 271 (6.4%) first ASCVD events within 10 years in KORA and HNR, respectively. We compared the estimated and observed 10-year event rates and determined discrimination and calibration quality of the new risk algorithm.

**Results:** A systematic overestimation of the 10-year ASCVD risk could be observed in both cohorts. In KORA, the estimated event rate was in men 43.4% and in women 25.5% higher than the observed event rate. In HNR, a pronounced overestimation of 62.4% and 69.2% in men and women, respectively, was seen. For both study populations, 10-year risk was consistently overestimated in all risk categories in men and women. These observations were also present in the calibration plot of the ACC/AHA risk score. Discrimination analysis showed area under the curves of 0.78 in KORA and 0.73 in HNR.

**Conclusion:** Our results are in line with recently published reports documenting an overestimation of the true risk for ASCVD by the new AHA/ACC risk score. Nevertheless, results from the ROC analysis indicate reasonable discriminative power. We therefore recommend a re-calibration of the ACC/AHA risk score for the German population.

**ECHO STRAIN IMAGING: WHAT DOES IT TELL EARLY AFTER MYOCARDIAL INFARCTION?**

**References:**

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**Background:** Two-dimensional diastolic speckle tracking echocardiography in the triage of patients with acute chest pain at emergency department.

**Methods:** 101 consecutive patients with acute chest pain and without wall motion abnormality were enrolled and underwent 2D-STE at ED. Left ventricular (LV) longitudinal, circumferential, transverse and radial strain values at aortic valve closure and one-third of diastole duration were measured, and strain imaging diastolic index (SI-DI) was analyzed to assess regional LV delayed relaxation using 2D-STE (Figure). Results: After comprehensive clinical evaluations, ACS was diagnosed in 8 patients. 2D-STE was obtained at a mean of 7.5 hours after chest pain episode. SI-DI of longitudinal, circumferential, transverse and radial strain of ischemic segments were significantly lower than those of non-ischemic segments (44.6±24.2 vs. 59.3±37.0, 51.5±19.5 vs. 69.5±20.1, 56.3±20.0 vs. 81.6±20.6, 59.0±21.3 vs. 83.1±16.5, P < 0.001, respectively), and transverse and radial SI-DI demonstrated high diagnostic accuracy (area under the curve: 0.812, 0.811, respectively). Sensitivity, specificity, positive and negative predictive value for ACS of transverse SI-DI were 65.9%, 88.0%, 15.0% and 98.9%, respectively, using a cut-off value of 60.0 (odds ratio: 14.1, 95% confidence interval: 7.5 to 26.7).

**Conclusion:** In patients with acute chest pain evaluated at ED, normal SI-DI virtually excluded ACS. Detection of regional LV delayed relaxation using 2D-STE is a promising technique for the triage of ACS.
4236 | BEDSIDE
The timeline of changes in regional systolic and diastolic function in patients with stunned myocardium
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Background: The purpose of this study was to evaluate the timeline of changes in regional systolic and diastolic left ventricular function within six months after successful reperfusion therapy of acute myocardial infarction (AMI).

Methods: 97 consecutive patients admitted with AMI and treated with successful percutaneous coronary intervention were included in this study. On days 1, 2, 3, 7, 30 and 180 following admission patients underwent transthoracic echocardiography with subsequent measurement of systolic longitudinal strain (SLS), systolic longitudinal strain rate (SLSR) and early diastolic longitudinal strain rate (DLSR) in left ventricular segments by speckle-tracking technique. 379 segments with systolic dysfunction at baseline, which recovered function after 180 days, were analyzed.

Results: The largest increase in regional SLS and SLSR was observed between day 1 and 2 (from −8.06±3.03 to −15.48±4.29, p<0.0001 and from −6.70±2.28 s−1 to −1.2±0.33 s−1, p<0.0001, respectively). On days 3, 7, 30 and 180 further improvement was noticeable, but the changes were less significant. The most significant improvement in regional DLSR was evenly distributed between days 1, 2, 3 and 7 (0.71±0.24, 0.96±0.26, 1.16±0.30 and 1.42±0.35, respectively with p<0.0001 for all differences). The increase observed on days 30 and 180 was less significant.

Conclusion: The most of regional systolic function recovery after successful reperfusion therapy in patients with AMI occurs within the first 2 days. However, the recovery of regional diastolic function takes longer – the most significant part of improvement occurs within the first 7 days. These observations have clinical implications for diagnosis and treatment of patients with myocardial stunning.

MANAGEMENT OF CARDIOGENIC SHOCK

4254 | BEDSIDE
Temporal trends in the epidemiology, management and outcome of patients with cardiogenic shock complicating acute coronary syndromes
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Background: Despite advances in the management of patients with an acute coronary syndrome (ACS), cardiogenic shock (CS) remains the leading cause of death in these patients.

Purpose: We sought to describe the evolution of clinical characteristics, in-hospital management and outcome of patients with CS complicating ACS.

Methods: We analysed data from five Italian nationwide prospective registries, conducted between 2001 and 2014, including consecutive patients with ACS.

Results: Out of 28,217 patients with ACS enrolled in the 5 registries, 1208 (4.3%) had CS during admission. Over the years, the proportions of CS patients with a history of heart failure declined, whereas those with hypertension, renal dys- function, previous percutaneous coronary intervention (PCI) and atrial fibrillation significantly increased. The use of PCI considerably increased from 2001 to 2014 (19% to 60%; percentage change, 41 [95% CI 29 to 51]), while the rate of bypass surgery remained unchanged (2.3% to 3.3%; percentage change, 1 [95% CI −4 to 6]). In-hospital mortality of CS patients decreased from 68% (95% CI, 59–76) in 2001 to 38% (95% CI, 29–47) in 2014 (percentage change, −30 [95% CI −41 to −18]). After adjustment for the changing baseline characteristics, compared with 2001, the risk of death was significantly lower in all of the following registries with reductions in in adjusted mortality between 45% and 66%.

Conclusions: Over the last 14 years, substantial changes occurred in the clinical characteristics and management of patients with CS complication ACS, with a greater use of PCI and a significant reduction in adjusted mortality rate.

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Modest shock index - a strong predictor of outcome among patients presenting with ST-segment elevation myocardial infarction

Background: Prompt identification of higher risk patients presenting with ST-elevation myocardial infarction (STEMI) and undergoing primary percutaneous coronary intervention will allow a more assertive strategy and approach.

Aim: To evaluate the modest shock index (MSI) - a ratio of heart rate (HR) to mean blood pressure (MAP), as a predictor of in hospital and 6-month mortality among patients (pts) admitted with STEMI.

Methods: We analyzed retrospectively 2389 pts admitted consecutively in our coronary care unit with acute coronary syndrome, from July of 2009 to June 2014 and we admitted those who presented with STEMI (n=1140). The patients were divided in two groups: group 1 – pts with MSI ≥1.3 (n=1076, 94.4%); group 2 – pts with MSI <1.3 (n=64, 5.6%). For each group we compared clinical and laboratory features and adverse events. Primary endpoint was the occurrence of death at 6 months; follow-up was completed in 99% of patients.

Results: Patients of group 2 were older (62±14 vs 67±14 years; p<0.003), more frequent women (19% vs 23%; p<0.001), had higher prevalence of atrial fibrillation (10.3% vs 20.3%; p<0.001) and previous stroke (5.9% vs 14.1%; p<0.016). On admission, group 2 presented more often lower MAP (96±18 vs 71±14; p<0.001) and higher HR values (76±17 vs 108±19; p<0.001); Killip ≥1 (18.0% vs 56.3%; p<0.001). Killip=4 (2.9% vs 28.1%; p<0.001), anaemia (20.9% vs 48.4%; p<0.001) and renal insufficiency (eGFR<60 ml/min) (21.8% vs 46.2%; p<0.001).

They also presented more severe coronary artery disease – left main coronary artery or 3 vessels disease (16.3% vs 31.3%; p<0.005) and higher prevalence of moderate to severe systolic dysfunction (48.3% vs 68.9%; p<0.009). They required more often aminergic support (7.4% vs 50%; p<0.001), intra-aortic balloon pump (2.9% vs 38.3%; p<0.001) and mechanical ventilation (2.7% vs 17.4%; p<0.001). They also had higher prevalence of malignant arrhythmias (8.1% vs 15.6%; p<0.008) and mechanical complications (1.7 vs 6.3%; p<0.031). Compared with 1st group, the 2nd group had 6.42 times higher in-hospital mortality [OR 6.42; 95% CI (4.07–12.67)] (p<0.001) and 7.18 times higher 6-month mortality [OR 7.18; 95% CI (3.39–15.63)] (p<0.001). After adjusting for different base line characteristics in multivariate analysis, MSI ≥1.3 remained as independent predictor of overall 6-month mortality [OR 3.81, 95% CI (1.81–8.03), p<0.001].

Conclusion: Modified shock index ≥1.3 is a stronger predictor of in-hospital and 6-month mortality among patients with STEMI.

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Aetiology of shock or cardiac arrest in patients treated with venoarterial extracorporeal membrane oxygenation
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Background: Venoarterial extracorporeal membrane oxygenation (ECMO) rapidly provides circulatory support for patients complicated with refractory shock or cardiac arrest in emergency situations. However, guidelines for choosing optimal candidates for ECMO remain unknown.

Purpose: We assessed the hypothesis that the outcomes of patients treated with ECMO were different based upon the aetiology of shock or cardiac arrest.

Methods: Patients who were treated with unplanned ECMO in tertiary care hospitals were enrolled in this study. The aetiologies of shock or cardiac arrest, clinical characteristics, weaning from ECMO, and 90-day survival were assessed. P<0.05 was defined as statistically significant.

Results: Among the study patients (N=203), ECMO was initiated during cardiopulmonary resuscitation in 168 (76%) patients and immediate coronary angiography in 152 (69%). Subsequent coronary revascularization was performed in 84 (38%) patients, and pulmonary angiography was performed in 24 (11%). The median age and rates of weaning (P<0.001 and P=0.051, respectively) from ECMO were as follows: 56 years and 46% in patients with acute coronary syndrome (N=104); 57 years and 57% for pulmonary embolism patients (N=23); 47 years and 77% for myocarditis patients (N=22); and 64 years and 49% for patients with all other conditions, respectively. The 90-day survival curves constructed by Kaplan-Meier method were shown in the figure.

Conclusions: The 90-day survival rates in patients treated with ECMO were encouraging; patients with fulminant myocarditis had particularly favourable out-
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logistic EuroSCORE was 28.4±13.3%. NYHA class III/IV was reported in 92.5%.

Between April 2010 and October 2014, 570 consecutive pts (age 80.6±0.34 years) with severe aortic stenosis (pmean 43.1±0.77 mmHg, A VA 0.68±0.02 cm²) and high surgical log (risk Euroscore 18.6±0.82%, pmean 44.2±1.12 mmHg, A VA 0.68±0.02 cm²) underwent TAVI with the MCV and 209 pts (age 81.7±0.41 years, log Euroscore 18.6±0.82%, pmean 44.2±1.12 mmHg, A VA 0.68±0.02 cm²) underwent TAVI with the ESV. Clinical events were evaluated according to the VARC-II criteria.

Conclusion: Transfemoral TAVI using local anesthesia only is feasible and safe in an all-comer TAVI-population using either selfexpandable or balloon-expandable transcatheter heart valves.

**BIOMARKERS: PRESENT AND FUTURE**

**4277 | BEDSIDE**

Soluble Neprilysin compared to NTproBNP for heart failure risk stratification in ambulatory patients

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Introduction: Neprilysin (NEP) breaks down numerous vasoactive peptides. NEP has been identified as a therapeutic target and its inhibition has proven to improve outcomes in patients with chronic heart failure (HF). The soluble form of NEP (sNEP), recently identified in heart failure, (HF) is associated with cardiovascular (CV) outcomes.

We directly compared sNEP and NTproBNP as risk stratifiers.

Methods: sNEP and NTproBNP levels were measured in 1030 consecutive ambulatory HF patients from May 2006 to May 2013. Patients were followed for 4.2 years. Comprehensive multivariable analyses and head-to-head assessments of performance were performed. The composite endpoint of CV death or HF hospitalization and CV death alone were explored.

Results: Median sNEP and NTproBNP concentrations were 0.64 ng/mL and 1302 ng/L, respectively. Both biomarkers significantly correlated with age (both p<0.01). but only NTproBNP significantly correlated with eGFR and BMI. In multivariable Cox regression analyses, both sNEP and NTproBNP were significantly associated with the composite endpoint (hazard ratio [HR] 1.18, 95% confidence interval [CI] 1.07 to 1.30, p<0.001; HR 1.30, 95% CI 1.15 to 1.48, p<0.001) and CV death (HR 1.17, 95% CI 1.05 to 1.32, p<0.007; HR 1.41, 95% CI 1.21 to 1.65, p<0.001). Only sNEP remained independently associated with the composite endpoint and CV death when hs-TnT and ST2 were incorporated in the analysis. The head-to-head sNEP vs. NTproBNP comparison showed good calibration and similar discrimination (figure) and reclassification for both endpoints in all models.

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**4269 | BEDSIDE**

Comparative survival after trans-apical, direct aortic, and subclavian transcatheter aortic valve implantation

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Background: Many patients have ilio-femoral anatomy unsuitable for conventional trans-femoral (TF) trans-catheter aortic valve implantation (TAVI). Safe and practical alternatives to the TF approach are therefore needed.

Objective: This study compared outcomes of alternative non-femoral routes, transapical (TA), direct aortic (DA) and subclavian (SC), with standard femoral access.

Methods: In this retrospective study conducted at 33 sites in the United Kingdom, data from 3,962 patients in the UK TAVI registry was analysed. All patients who received TAVI via a femoral, subclavian, transapical or direct aortic approach were eligible for inclusion. The primary outcome measure was survival up to two years. Secondary endpoints included safety and morality.

Results: Median Logistic EuroSCORE was similar for SC, DA, and TA, but significantly lower in the TF cohort (22.1% vs 20.3% vs 21.2% vs 17.0% respectively, p<0.001). Compared to TF (3.7%), in-hospital mortality was similar in the SC group (4.3%, p=0.69), but was significantly higher in the TA (9.5%, p<0.001) and DA (7.6%, p<0.001) cohorts. Estimated one-year survival was similar for TF (84.6±0.7%) and SC (80.5±3%, p>0.27), but was significantly worse for TA (74.7±1.6%, p<0.001) and DA (84.6±0.7%) respectively. Civity, both significantly worse than with the trans-femoral route. In contrast, subclavian access was not significantly different to trans-femoral, and may represent the safest non-femoral access route for TAVI.

Conclusion: Trans-apical and direct aortic TAVI were associated with similar survival, both significantly worse than with the trans-femoral route. In contrast, subclavian access was not significantly different to trans-femoral, and may represent the safest non-femoral access route for TAVI.
Conclusions: sNEP performed similarly to NTproBNP as a risk stratifier in ambulatory patients with HF, though it was less influenced by comorbidities and retained its prognostic value in multimeter analysis.

4278 | BEDSIDE
Cardiac injury in neoplasia and association with cardiovascular hormones
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Objectives: Patients with malignancies display elevated levels of B-type natriuretic peptide (BNP) and hs-TnT without clinical manifestation of cardiac disease. This study evaluated circulating cardiovascular hormones and hs-TnT and their association with mortality in neoplastic disease.

Methods: We prospectively enrolled 555 consecutive patients with primary diagnosis of neoplastic disease without prior cardiotoxic anticancer therapy. NTproBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin, hs-TnT, IL-6 and CRP were measured. Cox regression analysis was performed to investigate the prognostic values of cardiovascular hormones and hs-TnT on survival. Correlation with inflammatory markers was tested.

Results: During a median follow-up of 25 (IQR 16–31) months 186 (34%) patients died. All cardiovascular hormones and hs-TnT levels rose with progressing tumor stage. All markers were significant predictors of mortality with hazard ratios per IQR of 1.54 (95% CI 1.24–1.90; p=0.001) for NTproBNP, 1.40 (95% CI 1.10–1.79; p<0.001) for MR-proANP, 1.31 (95% CI 1.19–1.44; p<0.001) for MR-proADM, 1.21 (95% CI 1.14–1.30; p<0.001) for CT-proET-1, 1.22 (95% CI 1.04–1.42; p=0.014) for Copeptin and of 1.21 (95% CI 1.13–1.32; p<0.001) for hs-TnT, independent of age, gender, entity of neoplastic disease, tumor stage, and prevalence of cardiac comorbidities. Kaplan-Meier analysis confirmed the discriminatory power of the hormones and hs-TnT (Fig.). NTproBNP, MR-proANP, MR-proADM and hs-TnT displayed significant correlation with IL-6 and CRP.

Conclusions: Circulating cardiovascular peptides like NT-proBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin and hs-TnT are elevated in an unselected population of patients with neoplastic disease and strongly related to all-cause mortality suggesting the presence of subclinical myocardial damage.

4282 | BEDSIDE
One-year mortality in diuretic treated patients with heart failure. A report from the Swedish Heart Failure registry based on a cohort of 27,374 patients
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Background and introduction: Diuretics are recommended in international guidelines for relief of symptoms related to heart failure (HF). However, the prognostic impact of diuretics in HF is unclear. Hospitalization for HF is associated with a poor prognosis. Previous observational data have indicated a worsened prognosis associated with diuretics irrespective of hospitalization or not. Purpose: To analyze the association between diuretics and one-year all-cause mortality in HF patients at hospital discharge and in HF outpatients respectively with data from a nationwide HF registry.

Methods: The Swedish Heart Failure Registry was introduced in 2003. Inclusion criteria are clinician-judged HF. Approximately 80 variables are recorded. Of 45,174 unique patient baseline registrations between 2003 and 2011 27,374 had information on diuretic medication, ejection fraction (EF) and the Heart Association (NYHA) class and were included in this study. Of the included cohort 13,424 were registered at hospital discharge and 13,950 as outpatients. Propensity score (PS) for diuretic treatment was estimated with logistic regression using 44 clinically relevant baseline variables. Matching was made 1:1 on diuretic information and 1:1 on NYHA HF status. The Swedish Heart Failure Registry is a nationwide registry including 45,174 unique patient baseline registrations between 2003 and 2011.

Results: Median admission sNEP levels were 0.67 ng/ml (Q1-Q3 0.37–1.29), and sNEP was significantly associated, in age-adjusted Cox regression analyses, with the composite endpoint at short-term (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.04–1.61, p=0.02) and long-term follow-up (HR 1.23, 95% CI 1.01–1.05, p=0.003). In multivariable Cox analyses that included clinical variables and NTproBNP admission sNEP showed a clear trend towards significance for the composite endpoint at 2 months (HR 1.22, 95% CI 0.97–1.53, p<0.09) and remained significant at the end of follow-up (HR 1.21, 95% CI 1.04–1.40, p=0.01).

At discharge, sNEP levels decreased from 0.70 to 0.52 ng/ml (p=0.06).

Conclusions: Admission sNEP was associated with short- and long-term outcomes in AHF and dynamic sNEP concentrations were observed during hospital admission. These preliminary data may be proof-of-principle for the use of NEP inhibitors in AHF.

MODERN DRUG THERAPY IN HEART FAILURE

4279 | BEDSIDE
Soluble nephrilysin in acute heart failure: prognostic value and kinetics. A pilot study
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Introduction: The soluble form of nephrilysin (sNEP) was recently identified in chronic heart failure (HF) and associated with cardiovascular outcomes.

Purpose: To examine the prognostic value of sNEP in acute HF (AHF) and sNEP kinetics during hospital admission.

Methods: A total of 350 patients (53% women, mean age 72.6±10.7 years) were included in the study. Primary endpoints were a composite of cardiovascular death or heart failure hospitalizations at short-term (2 months) and long-term (mean 1.8±1.2 years) follow-up. sNEP was measured using an ad hoc modified ELISA assay and its prognostic value assessed using Cox regression analyses. In a subgroup of patients sNEP was measured both at admission and discharge (n=92).

Results: Median admission sNEP levels were 0.67 ng/ml (Q1-Q3 0.37–1.29), and sNEP was significantly associated, in age-adjusted Cox regression analyses, with the composite endpoint at short-term (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.04–1.61, p=0.02) and long-term follow-up (HR 1.23, 95% CI 1.01–1.05, p=0.003). In multivariable Cox analyses that included clinical variables and NTproBNP admission sNEP showed a clear trend towards significance for the composite endpoint at 2 months (HR 1.22, 95% CI 0.97–1.53, p<0.09) and remained significant at the end of follow-up (HR 1.21, 95% CI 1.04–1.40, p=0.01). At discharge, sNEP levels decreased from 0.70 to 0.52 ng/ml (p=0.06).

Conclusions: Admission sNEP was associated with short- and long-term outcomes in AHF and dynamic sNEP concentrations were observed during hospital admission. These preliminary data may be proof-of-principle for the use of NEP inhibitors in AHF.
Low-dose aspirin therapy is not associated with reduced cardiovascular morbidity or mortality in heart failure with sinus rhythm: a nationwide propensity score matched study

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Background: Chronic low dose aspirin (75 mg/day) therapy has never been evaluated against placebo in a randomized clinical trial in heart failure (HF). However, aspirin is widely used in HF with sinus rhythm regardless of the etiology of the disease.

Purpose: We aimed to assess safety and efficacy of aspirin therapy in a nationwide cohort of HF patients with sinus rhythm.

Methods: Patients with a first diagnosis of HF in the period 2007–2012 and with sinus rhythm were identified from Danish administrative registries and classified according to ischemic or non-ischemic etiology. Aspirin users and non-users were compared in propensity score matched Cox regression models with respect to a primary composite outcome of all-cause mortality, myocardial infarction and ischemic stroke, and the secondary outcomes all-cause bleeding and HF readmission.

Results: In patients with ischemic HF (3,931 aspirin users and 3,931 non-users; median follow-up 23 months), aspirin therapy was not associated with a significantly altered risk of the primary composite outcome, (hazard ratio [HR]: 0.99, 95% CI: 0.92–1.06). Aspirin therapy was, however, associated with an increased risk of bleeding (HR: 1.29, 95%-CI: 1.08–1.53). In the non-ischemic HF population (3,744 aspirin users and 3,744 non-users; median follow-up 22 months), aspirin therapy was not associated with significantly altered risk of the primary composite outcome, (HR: 0.95, 95%-CI: 0.89–1.02), nor bleeding (HR: 1.01, 95%-CI: 0.84–1.22).

Conclusion: In patients with HF and sinus rhythm, we found no benefit of aspirin therapy, regardless of ischemic or non-ischemic etiology, but aspirin was associated with increased risk of bleeding in patients with ischemic HF. Routine use of aspirin in HF might cause more harm than benefit.

4286 | BEDSIDE
How to make a diagnosis of microvascular angina; the diagnostic potency of rest-stress myocardial perfusion magnetic resonance imaging
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Background: Microvascular Angina (MVA) causes chest pain without significant stenosis and spasm in epicardial coronary artery. Its diagnosis is very difficult because few efficient diagnostic modalities have been reported in the past studies.

Purpose: The purpose of this study is to make a diagnosis of MVA using rest-stress myocardial perfusion magnetic resonance imaging (MRI).

Methods: Clinically suspected patients of MVA with chest pain were examined after coronary angiography revealed no significant stenosis in their epicardial coronary arteries and coronary spasm provocation test by ergonitrate maleate turned out to be negative. Subsequently, contrast-enhanced myocardial perfusion MRI was performed under the rest conditions and the stress conditions with adenosine trisphosphate (ATP). ATP dose was 140 μg/kg/min for 6 minutes. Contrast media was injected 3 minutes after starting ATP-stress. The semi-quantitative analysis of the rest-to-stress ratio index of the maximal slope of the myocardial 12 segments was adopted. The patients were diagnosed as MVA when MRI showed localized endocardial perfusion defect only under ATP-stress and the rest-to-stress index of the endocardial segment in question showed ischemic pattern.

Results: Thirty-nine patients were included in this study. 35 patients were diagnosed as MVA, rest of the patients were diagnosed as non-MVA. Twenty-five patients showed localized endocardial perfusion defect only under ATP-stress in anterior segment, 27 patients in anterolateral, 27 patients in inferolateral, 20 patients in inferior, 21 patients in interoseptal, and 26 patients in anteroesopetal. The average of the rest-to-stress index of the endocardial segment in question and not in question of MVA were 0.81±0.16 and 1.52±0.54, respectively. That of non-MVA was 1.56±0.44. Sensitivity was 89.7%. Subsequently, rest-stress myocardial perfusion scintigraphy was performed to 24 patients of 35 MVA, and only 1 patient showed ischemia.

Conclusion: This study showed efficacy of rest-stress myocardial perfusion MRI in the diagnosis of MVA. Rest-stress myocardial perfusion MRI could cast new light on the diagnostic difficulty of MVA.

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Effect of pre-procedural antiplatelet and anticoagulant therapy on myocardial no-reflow following percutaneous coronary intervention
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Background: No-reflow occurring during percutaneous coronary intervention (PCI) has been associated with poor in-hospital outcomes.

Purpose: The objectives of this study were to evaluate the incidence of no-reflow in PCI and to identify independent predictor of adverse events and to assess whether baseline pre-procedural treatment options may affect clinical outcomes.

Methods: Data were derived from the International Survey of Acute Coronary Syndromes in Transitional Countries (NCT01216776) registry, a prospective survey of patients presenting with ACS over a 5-year period (January 2010 to January 2015). We prospectively collected data from 5997 patients undergoing PCI, identifying those with no-reflow, and analyzed their treatments and clinical outcomes. No-reflow was defined as post-PCI TIMI flow grade 0–1, in the absence of post-procedural significant (>25%) residual stenosis, abrupt vessel closure, dissection, perforation, thrombus of the original target lesion, or epicardial spasm. The outcome measure was in-hospital mortality.

Results: No-reflow was identified in 128 of 5997 patients who have undergone PCI.
to identify CMD. Therefore CAC score cannot be used to identify CMD.

Conclusions: In patients with angina pectoris and NO-CAD suspected for CMD, there is no association between CAC and CFR, suggesting that CFR and CAC provide different information regarding cardiovascular risk and the atherosclerotic process. Therefore CAC score cannot be used to identify CMD.

4290 | BEDSIDE
Decreased shear stress affects vascular clinical outcome in Kawasaki disease patients with coronary artery lesions

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Objectives: Shear stress affects strongly to vascular endothelial cell function. We estimated shear stress at different portions of coronary artery lesions, and compared to shear stress and clinical outcome in patients with Kawasaki disease (KD) patients with coronary artery lesions.

Subjects: 186 of coronary branches in 122 KD children aged 3 to 16 years old who had giant aneurysm (AN) without stenosis (diameter of AN ≥ 10 mm) (n=31, G-An group), AN without stenosis (diameter of AN < 5 mm) (n=26, AN group), >75% coronary stenosis (n=12, S group), <75% coronary stenosis (n=23, s-S group), and children with coronary abnormal findings by 2-D echo but denied normal by CAG (n=94, N group) were subjected and grouped.

Methods: The averaged peak flow velocity (APV) was measured at normal apical two-chamber view or in three-chamber view, to reach optimal alignment with the interventricular sulcus.

Results: A total of 20 patients (20.47%) had DM. The groups were similar in age (66.39±10.65 vs. 66.38±10.92 p=ns). There was no significant difference in LA size between diabetic and non-diabetic patients [AVA (0.81±0.18cm² vs 0.85±0.13cm²), Vmax (4.20±0.56 vs 4.21±0.48m/s); p=ns]. There was also no significant difference in E/E’ between two groups of patients (12.59±4.63 vs 12.76±5.31, p=ns). Mean CFR in diabetic patients was 1.98±0.48, while mean CFR in non-diabetic patients was 2.64±0.54 (P<0.01). The mean LAD basal flow velocity (μAPV/R) was higher in diabetic patients, but not significantly [0.34±0.08 vs. 0.30±0.05; p=0.063]. DM was the best independent predictor of CFR [B=−0.41, CI 95% (−0.0781 to −0.0142), p=0.005].

Conclusion: Diabetes mellitus additionally impairs coronary microvascular function assessed by CFR in patients with asymptomatic severe aortic stenosis and nonobstructed coronary arteries.

4291 | BEDSIDE
In-hospital outcomes associated with radial versus femoral access and initial intervention in acute coronary syndromes: results from the ISACS-TC registry

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Background: Recent randomized studies have suggested that radial access

PSCI (2.1%). On multivariate analysis, patients with no-reflow were more likely to be older (>75 years; OR: 2.78; 95% CI: 1.15-6.71) and to have ST-elevation myocardial infarction (OR: 3.67; 95% CI: 1.57-8.56). No-reflow was highly predictive of inhospital mortality (17.2% vs. 4.2%, P<0.001) and remained a significant independent predictor of death after adjustment for demographic and clinical variables (OR: 4.78; 95% CI: 2.7-8.3). Multivariable regression analysis was also performed to identify independent relationship between pre-procedural treatment regimens and no-reflow phenomenon. A 600 mg loading dose of clopidogrel, showed a strong inverse predictive value in terms of post-PCI TIMI flow and no-reflow phenomenon (OR: 0.58; 95% CI: 0.35-0.96). Similarly, unfractionated heparin was associated with a reduction in the likelihood of no-reflow (OR: 0.62; 95% CI: 0.41-0.94). Aspirin, enoxaparin, 300 mg loading dose of clopidogrel, did not significantly impact the occurrence of the no-reflow.

Conclusion: A strong independent predictor of in-hospital mortality. Pre-procedural administration of 600 mg loading dose of clopidogrel and unfractionated heparin is associated with reduced incidence of no-reflow.

4289 | BEDSIDE
Diabetes mellitus and coronary microvascular function in asymptomatic patients with severe aortic stenosis and nonobstructed coronary arteries


Background and aim: It has been shown that coronary flow reserve (CFR) is impaired in patients with aortic stenosis (AS) and that impaired CFR has a prognostic value in patients with asymptomatic AS. We investigated whether the diabetes mellitus type II (DM) additionally impairs microvascular circulation assessed with CFR in patients with AS, normal left ventricular ejection fraction (LVEF) and nonobstructed coronary arteries.

Methods: A total of 127 patients, mean age 66±11.102 (59.52% males), with severe AS [aortic valve area (AVA) ≤ 1 cm²], maximal aortic valve velocity (Vmax) >4 m/s, and normal LVEF (LVEF=55%) were enrolled in this prospective study. Patients with DM were considered those who were treated for DM or had documentation confirming the diagnosis of DM type II. All patients underwent coronary angiography and had no obstructive coronary disease (defined as having no stenosis >75%) and a standard transthoracic Doppler-echo study and adenosine stress transthoracic-echo for CFR measurement. CFR was measured in LAD artery and was recorded by pulsed-wave Doppler. The LAD was searched as a laminar flow toward transducer with color Doppler in foreshortened apical two-chamber view or in three-chamber view, to reach optimal alignment with the interventricular sulcus.

Results: A total of 26 patients (20.47%) had DM. The groups were similar in age (66.39±10.65 vs 66.38±10.92, p=ns). There was no significant difference in AVA between diabetic and non-diabetic patients [AVA (0.81±0.18cm² vs 0.85±0.13cm²) and Vmax (4.20±0.56 vs 4.21±0.48m/s); p=ns]. There was also no significant difference in E/E’ between two groups of patients (12.59±4.63 vs 12.76±5.31, p=ns). Mean CFR in diabetic patients was 1.98±0.48, while mean CFR in non-diabetic patients was 2.64±0.54 (P<0.01). The mean LAD basal flow velocity (μAPV/R) was higher in diabetic patients, but not significantly [0.34±0.08 vs. 0.30±0.05; p=0.063]. DM was the best independent predictor of CFR [B=−0.41, CI 95% (−0.0781 to −0.0142), p=0.005].

Conclusion: Diabetes mellitus additionally impairs coronary microvascular function assessed by CFR in patients with asymptomatic severe aortic stenosis and nonobstructed coronary arteries. The markedly reduced coronary flow reserve in asymptomatic diabetic AS patients suggest these patients should receive special attention as they might have a high risk for subsequent myocardial ischemia and sudden cardiac death.

4288 | BEDSIDE
The association between coronary artery calcium & coronary flow reserve assessed by integrated rubidium positron emission tomography/CT in women with angiia and no obstructive coronary artery disease


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Background: Women with angiia pectoris but no obstructive coronary artery disease (NO-CAD) have an increased risk of cardiovascular events. Coronary microvascular disease (CMD) is a possible explanation, and can be assessed by Positron Emission Tomography (PET) measured coronary flow reserve (CFR). Increased CFR was associated with increased cardiovascular risk and may be an early marker of atherosclerosis. Computer Tomography (CT) assessed Coronary Artery Calcium (CAC) correlates to cardiac atherosclerosis and CAD severity.

Purpose: The aim was to evaluate the association between CAC and CFR in patients with angiia pectoris and NO-CAD suspected for CMD.

Methods: Patients were randomly selected from a cohort of women with angiia pectoris and NO-CAD assessed by a clinically indicated coronary angiogram (defined as ≥50% stenosis). CT and Rubidium-82-PET was performed simultaneously. CFR was measured during adenosine infusion (0.84 mg/kg) and CAC was obtained by the method described by Agatston.

Results: CFR and CAC were measured in 110 women, mean age (SD) 62.4 years (8.8), 51% (n=56) had a CAC of zero. Median (IQR) CFR was 2.67 (2.29-3.10). No significant correlation between CFR and CAC was found (R=0.2-0.0012; p=0.911 for all patients, and R2=0.015; p=0.379 for patients with CAC above 0. CAF and CAC were correlated to the presence of hypertension and CFR was correlated to diabetes. Furthermore, increasing age and atheromatosis on CAG were associated with a higher CAC (Table 1).

Table 1

Conclusions: In patients with angiia pectoris and NO-CAD suspected for CMD, there is no association between CAC and CFR, suggesting that CFR and CAC provide different information regarding cardiovascular risk and the atherosclerotic process. Therefore CAC score cannot be used to identify CMD.
**Introduction:**

To assess whether IMR measured at the end of primary percutaneous coronary intervention (PPCI) has potential to stratify patients at risk of subsequent IMH.

**Methods:**

We performed a single centre cohort study in 245 restudied STEMI patients. IMR was measured at the end of PPCI using guidewire based-thermodilution. Cardiac magnetic resonance (CMR) was assessed 2 days and 6 months (n=228 (93%)) later. Cine-CMR was used to measure LV ejection fraction (LVEF). IMH was defined as a hypointense infarct core with a T2* value >20ms. Microvascular obstruction (MVO) was defined as a hypointense infarct core as revealed by late gadolinium contrast-enhanced CMR (Dotarem, 0.15 mmol/kg).

**Results:**

The median IMR [IQR] was 25 [15–48]. 101 patients (49%) had IMH and 133 patients (54%) had MVO. All of the patients with IMH had MVO, but 32 patients had MVO (13%) without IMH. IMR was higher in patients with IMH (37 ±15) than in patients without IMH (17 ±12), including those that had MVO in the absence of IMH (17 [13–39]; p=0.001). In multivariable regression IMR was inversely associated with LVEF at 6 months including after adjustment for baseline LVEF (regression coefficient −0.05 (95% CI −0.08, −0.01); p=0.02).

**Conclusion:**

The RRR predicts acute infarct characteristics and was more closely associated with myocardial injury in acute STEMI than CFR.
CPR-2.0. In a survival analysis adjusting for cardiovascular risk factors CPR above 2.0 independently predicted cardiovascular event free survival (HR: 2.8, p<0.028). In a multivariate linear regression analysis adjusting for cardiovascular risk factors, high Homeostatic model assessment for insulin resistance (HOMA-IR) was independently associated with low CPR (β=−0.018, p=0.026). In gender specific analysis, the relation was statistically significant in women (β=−0.034, p=0.016) but not in men (β=−0.004, p=0.685). Also, women with CPR below 2.0 displayed increased HOMA-IR as compared to women with CPR equal or above 2.0 (p<0.05).

Conclusions: In non-diabetic patients with angina symptoms but no MPS-verified ischemia, abnormal CPR is of prognostic value. Insulin resistance determined by HOMA-IR is associated with impaired CPR, especially in women and could potentially add value in risk stratification in this relevant patient group.

Acknowledgement/Funding: Agreement concerning research and education of doctors

BEST POSTERS SESSION 5

BEST POSTERS IN IMPLANTABLE AND SUBCUTANEOUS DEFIBRILLATOR THERAPY

P4297 | BEDSIDE

The evolution of ICD programming practice: What is the relative impact of clinical evidence on current practice?

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Introduction: Numerous clinical trials have evaluated ICD detection programming primarily as a means to reduce shocks. However, the factors that influence compliance with evidence-based programming in clinical practice are largely unknown. This retrospective evaluation was designed to understand the impact of single manufacturer’s “out-of-box” ICD settings on initial device programming.

Methods: Data from 105,462 single and dual chamber ICDs and CRT-Ds in the de-identified CareLink Data Warehouse were queried from 2008–2014. Initial programming was based on the earliest transmission post-implant. Initial programming over time was investigated in reference to programming evidence publications and changes in out-of-box settings. Programming variables of interest included ventricular fibrillation number of detections to trigger VF (VFNI) and supraventricular tachycardia discrimination limit (SVT/Limit).

Results: Mean age 66±12 years. 73% male. The figure shows an example of progression in programming of VFNI. The “up arrows” reflect clinical evidence publications supporting VFNI = 30/40: PREPARE (2008), ADVANCE III (2013). The “down arrows” reflect change in out-of-box VFNI settings: 24/32 (2013) and 20/32 (2014). The largest changes in initial VFNI programming occurred following changes in out-of-box settings. Similar findings were also found for initial SVT/Limit programming. Compliance with current evidence for VFNI and SVT/Limit is greater than 50% now that these have become nominal values.

Conclusion: Clinical trials have demonstrated that shocks can be significantly reduced and patient quality of life improved by careful programming of detection and therapy parameters. Yet, utilization of evidence-based programming appears to be principally driven by manufacturer changes to nominal settings.

P4298 | BEDSIDE

Efficacy and safety of the implantable cardioverter defibrillator in pediatric patients with channelopathies

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Purpose: Cardiac channelopathies induce risk of Sudden Cardiac Death (SCD), that may require an Implantable Cardioverter Defibrillator (ICD) in pediatric patients. Limited information exists for the long-term outcome of young patients affected by channelopathies and carriers of an ICD.

Methods: We studied patients diagnosed with inherited arrhythmias in structurally normal hearts who received an ICD by age 18.

Results: N=83 pediatric patients (36 males,43%) received an ICD for the following diagnoses: 49 (59%) Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT), 26 (31%) Long QT Syndrome (LQTS), 3 (4%) Brugada Syndrome (BrS), 2 (2%) Short QT Syndrome (SQTS). N=3 (4%) patients had an aborted SCD (aSCD) without diagnosis (Idiopathic Ventricular Fibrillation, I VF). N=67 (81%) patients carried a pathogenic mutation and 27 (33%) had a family history of SCD within 40 years. N=76 (92%) patients had symptoms before ICD implant. N=37 (45%) patients were implanted for “secondary prevention”, post aSCD (n=34) or documented polymorphic ventricular tachycardia (n=3); n=46 (55%) patients were implanted for “primary prevention”. Age at implant was 12±4 years. Follow-up: 3 months was available for 76 patients (median 78, IQR 38–131 months); 39 (51%) patients received 131 appropriate shocks (median 2, IQR 1–4, per patient) in separate arrhythmic episodes; the first shock was delivered 29 (IQR 3–48) months post-implant. Appropriate shocks occurred in 29/46 CPVT patients, 8/23 LQTS, 0 BrS, 1/2 SQTS and 1/3 I VF. No statistically significant difference was observed in the occurrence of appropriate shocks between “primary” or “secondary” prevention patients (p=0.498). A boy with QT3 died at 18 months during an arrhythmic storm, despite several appropriate shocks.

A patient had a pneumothorax during ICD placement and 26 (34%) patients had major complications, 14 (ICD 4–76) months post-implant. Of these, 21 subjects had device dysfunction or lead fracture and 5 had significant infections. Inappropriate shocks occurred in 14 (18%) patients due to T-wave over-sensing and supraventricular arrhythmias or sinus tachycardia, in one third of cases respectively. Overall 35 (46%) patients had documented complications.

Conclusions: Half of our pediatric patients affected by inherited arrhythmias with an ICD experienced appropriate shocks, regardless of whether the ICD was placed for “primary” or “secondary prevention” of SCD. The high incidence of major complications (36%) requires solid justifications for use of the ICD in children. Accurate programming of the ICD is essential to reduce inappropriate shocks.

P4299 | BEDSIDE

Learning curve associated with inappropriate shocks of the subcutaneous implantable defibrillator: results from a pooled analysis of 882 patients from the IDE study and EFFORTLESS Registry

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Introduction: The subcutaneous ICD (S-ICD) uses a morphology based discrimination algorithm that requires a unique programming strategy. We evaluated the inappropriate shock (IAS) rate of the S-ICD versus increasing center experience, to determine whether a learning curve is present.

Methods: In a pooled cohort from two clinical S-ICD databases, the IDE Trial and the EFFORTLESS Registry, the IAS rate was assessed at one-year follow-up. Kaplan-Meier (KM) estimates for freedom of IAS, percentage dual zone programming and zone cut-off rate grouped by implanting center experience as initial (1–4 implants), early (5–20 implants) and late (>20 implants) were calculated.

Results: A total of 882 implants in 61 implanting centers with a median of 4 implants (IQR 1–8) and a total of 235 IAS in 94 patients were analyzed between 2009 and 2013. There was a non-significant trend towards higher freedom of IAS from 86.3% (CI 79.5–92.3) to 91.6% (CI 88.4–93.9) with increasing experience (p=0.12), and a significant trend in dual zone programming (p<0.001). Multivariable analysis was performed for confounders (atrial fibrillation and NYHA class III/IV).
for IAS showed that dual zone programming was associated with a hazard ratio of 0.45 for IAS (P = 0.001), whereas experience and zone cut-off rate were not significant. Figure 1 shows the KM estimates for freedom of IAS at 1 year with increasing center experience, the percentage dual zone programming and the lower zone cut-off rate in beats per minute.

Conclusions: A non-significant trend from 12.7% to 8.4% towards higher freedom of IAS with increasing center experience. However dual zone programming did increase significantly with increasing experience. Dual zone programming was associated with less IAS adjusted for known confounders.

BEST POSTERS IN CORONARY ARTERY DISEASE AND COMORBIDITIES

P4301 | BEDSIDE Depression is the strongest predictor of angina and is independent of underlying coronary artery disease severity in patients with cardiovascular disease

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Introduction: Angina pectoris (AP) is a hallmark of obstructive coronary artery disease (CAD). Depression is three times more common in patients with CAD and is associated with worse morbidity and mortality. While patients with CAD and depression tend to experience chest pain more frequently than those without depression, it is unclear whether this is due to differences in underlying CAD severity.

Purpose: To determine whether depression is associated with AP independently of underlying CAD severity.

Methods: 5825 patients underwent left heart catheterization (LHC) between 2004 and 2013 at Emory Healthcare sites and were recruited into the Emory Cardiovascular Biobank. Patients completed the Seattle Angina Questionnaire (SAQ) to screen for depression. A lower SAQ score is indicative of more frequent chest pain.

Results: Mean SAQ score was 75 ± 21, p = 0.0001. The highest SAQ score was 100, indicating no angina. Angina was more frequent with severe depression (score of 10–14), moderatesevere depression (score of 15–19), and severely depressed (score of 20–27). PHQ-9 scores categorized patients as not depressed (score of 1–4), mildly depressed (score of 5–9), moderately depressed (score of 10–14), moderate severe depression (score of 15–19), and severely depressed (score of 20 to 27). An angiographic CAD severity was estimated using the Gensini score. Multivariable analysis using linear regression was performed with the SAQ as dependent variable and the Gensini score and Gensini scores in addition to demographics and clinical characteristics as independent variables.

Results: Mean age was 63 ± 12 years, 64% male, 76% white, 65% with CAD severity >50% in at least one coronary artery. There was a significant negative correlation between PHQ-9 and AF (r = 0.284, p = 0.0001) indicating that angina was more frequent with more severe depression. Patients with even mild depression (22%) had significantly lower AF score (73 vs. 84, p = 0.0001) compared to those without depression (63%). In a multivariable linear model, both the Gensini, (relative importance 16%, p < 0.001) and PHQ-9 (relative importance 69%, p < 0.0001) were independent predictors of AF. PHQ-9 remained an independent predictor of AF even in the subset of patients without significant CAD.

Conclusions: Depression is an independent and important contributor to AP in patients with and without CAD. Whether treatment of underlying depression improves AP needs to be further studied.

P4302 | BEDSIDE Role of CHA2DS2-VASc score in evaluating patients with atrial fibrillation (AF): undergoing percutaneous coronary intervention (PCI)

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Purpose: AF is an independent predictor of mortality in those with coronary artery disease. This represent a particularly challenging group with optimal antithrombotic therapy remaining controversial. The CHA2DS2-VASc score has been validated in predicting stroke risk in AF and is used to guide management with oral anticoagulation. We aimed to evaluate the CHA2DS2-VASc score in predicting adverse outcomes in patients with AF undergoing PCI.

Methods: CHA2DS2-VASc score was calculated in 584 consecutive patients with AF undergoing PCI in a large Australian multicentre registry between May 2007 and November 2013. Patients were divided into categories of low (score 1–2), intermediate (3–4) and high (5–6) risk. Clinical and procedural data, 30-day, 12-months and long-term outcomes were compared between the 3 groups. Patients with out-of-hospital arrest, cardiogenic shock and incomplete data to calculate scores were excluded.

Results: Mean CHA2DS2-VASc score was 4.4±1.6. By definition, the high-risk group were significantly more likely to be older and female, have more diabetes, hypertension, vascular disease, cerebrovascular disease and congestive cardiac failure. Renal impairment and multivessel disease were also significantly higher within the high-risk groups. The high-risk group were less likely to receive Gp2b3a inhibitors; surprisingly the use of drug eluting stents was not different between the groups (30%, 30% and 25% respectively). Anticoagulation use in intermediate and high-risk patients was 43% and 44% at 30 days, and 48% and 47% at 1 year.

When compared with the low-risk group, intermediate CHA2DS2-VASc scores (HR 3.57, 95% CI 1.28–9.92, p = 0.015) and high CHA2DS2-VASc scores (HR 7.82, 95% CI 2.88–21.24, p < 0.001) were strong predictors of long-term mortality.

Conclusions: Higher CHA2DS2-VASc scores, in patients with AF undergoing PCI, are associated with significantly worse outcomes. Despite being high risk, these patients are undertreated with anticoagulation. CHA2DS2-VASc score may be a useful tool in identifying those patients at high risk who need aggressive therapy.

P4303 | BEDSIDE Non-ST-elevation acute coronary syndromes with renal impairment - which formula serves better?


Introduction: Chronic Kidney Disease (CKD) and acute kidney lesion are frequent co-morbidities in patients admitted for non-ST-elevation acute coronary syndromes (NSTE-ACS) and are associated with a worse outcome. There are several equations to correctly identify patients with CKD through glomerular filtration rate (GFR), but it is still not consensus which one is the most appropriate in the setting of NSTE-ACS.

Purpose: We aimed to compare which of the 3 most commonly used formulas - Cockcroft-Gault (CG), Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] - is more effective in predicting worse outcomes at 1-year follow-up in NSTE-ACS.

Methods: Prospective study of 613 patients [age 67.18±12.79; 67.2% men; 32.1% diabetics; 73.1% hypertensive; 10.4% known CKD] admitted for NSTE-ACS between October 2009 and September 2013. GFR estimated from CG, MDRD and CKD-EPI were compared in terms of mortality risk prediction and primary composite endpoint (cardiovascular death, non-fatal myocardial infarction or stroke) were independent predictors of AF. PHQ-9 remained an independent predictor of AF even in the subset of patients without significant CAD.

Results: The prevalence of GFR > 60 ml/min/1.73m2 was 48.1% using the GFR, 48.8% with MDRD and 45.8% with CKD-EPI. All formulas had a good discrimination power in predicting 1-year primary composite endpoint with CG proving to be the best formula by the ROC curve analysis [AUC (CG): 0.733 vs AUC (MDRD): 0.684 vs AUC (CKD-EPI): 0.699]. All formulas were also good in predicting total mortality at 1-year follow-up with CG to evidencing the best results [AUC (CG): 0.736 vs AUC (MDRD): 0.678 vs AUC (CKD-EPI): 0.696].
P4304 | BEDSIDE
Persistence to secondary prevention drugs in ACS patients with reduced renal function and long-term outcome
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Purpose: The high risk of recurrent events in patients with reduced renal function following an acute coronary syndrome (ACS) may in part be due to suboptimal secondary prevention. We aimed to i) describe the association between renal dysfunction and persistent use of established secondary prevention drugs after an ACS, and ii) to determine whether persistence was associated with improved outcome also in patients with reduced renal function.

Methods: We used the SWEDHEART registry to identify all patients admitted to any Swedish coronary care unit for ACS between 2005–10, and whom survived for at least 1 year (N=80,886). Excluded were 86,834 patients, creatinine levels were available to estimate glomerular filtration rate (eGFR by CKD-EPI). Data on drug use was extracted from the Prescription registry recording all dispensed drugs in Sweden. Persistence was measured for 1 year and patients with a gap < 30 days between end of dispensed supply and next dispensed prescription were considered to have discontinued treatment.

Results: Loss to follow up 0%. Compared with patients with eGFR ≥ 60 ml/min, after adjustment for age, patients with eGFR 30–59 ml/min that initiated treatment within 30 days, were more likely to discontinue ASA (HR 1.22, CI 95% 1.16–1.28), ACE/ARB (HR 1.35, CI 95% 1.26–1.41), statins (HR 1.14, CI 95% 1.08–1.20) and beta-blockers (HR 1.07, CI 95% 1.01–1.13). After adjustment for age, sex, diabetes, hypertension, heart failure, stroke and drugs on admission, performed PCI or CABG during hospitalization, being persistent on each of the four drugs at 1 year was associated with an improved 3-year outcome (combined death and reinfection) also in patients with eGFR 30–59 ml/min. The associations in the smaller group of patients with eGFR < 30 did not reach significance.

Conclusion: Patients with moderately reduced kidney function are less likely to be persistent on secondary prevention drugs. However, persistent use is associated with improved prognosis.

BEST POSTERS IN EARLY DETECTION OF CARDIAC DISEASE

P4305 | BEDSIDE
Subclinical left ventricular systolic dysfunction by strain imaging in chronic kidney disease subjects with preserved ejection fraction: The prospective CASCADE study
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Purpose: Abnormal cardiac structure and function is frequent in chronic kidney disease (CKD). However, conventional echocardiography is not sensitive enough in detecting early decline in cardiac function. Speckle tracking echocardiography with strain analysis enables a more accurate assessment of systolic function. This study aims to determine whether CKD subjects with preserved left ventricular ejection fraction (LVEF) may exhibit subtle systolic dysfunction, and whether abnormalities in global strain parameters may be associated with the severity of kidney dysfunction in CKD.

Methods: We conducted a prospective observational study in 273 stages 3–5 CKD subjects with preserved LVEF (defined as EF >50%) and 65 controls. All participants underwent conventional echocardiography with strain imaging together with assessment of clinical and biochemical parameters.

Results: CKD subjects showed lower systolic global longitudinal strain (GLS) [−20.1±2.3 vs. −21.6±2.4, P < 0.001] and circumferential strain (CS) [−18.1±2.8 vs. −19.4±2.5, P < 0.001] compared with controls. When stratifying into CKD stages 3a, 3b, 4 and 5 GLS [3a vs 3b vs 4 & vs control; P < 0.001] and radial strain [P=0.012] showed significant decrease with increasing severity of CKD stages. However, only GLS remained independently associated with kidney function in multivariate regression after adjustment of relevant clinical and biochemical parameters (Coefficient, −0.03; 95% CI, −0.05 to −0.01; P < 0.001).

Conclusions: Strain imaging detects subclinical LV systolic dysfunction in CKD subjects with preserved LVEF and shows an independent relationship with the severity of CKD. It is a more accurate imaging technique to detect subclinical cardiac functional abnormalities in CKD.

P4307 | BEDSIDE
Normal range of LV global longitudinal strain in asymptomatic lymphoma survivors
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Background: LV global longitudinal strain (GLS) has emerged as a sensitive marker of LV systolic function and is included in the latest guidelines for detecting cardiotoxicity during administration of chemotherapy. However, little is known about the normal range of LV GLS in asymptomatic cancer survivors years after carditoxic therapy.

Purpose: To determine the normal range of LV GLS after cardiac treatment including anthracyclines (AC) and radiotherapy involving the heart (RT), assessed in asymptomatic lymphoma survivors (LS).

Methods: All LS treated with autologous hematopoietic stem cell transplantation (auto-HCT) in Norway from 1987–2008 and aged >18 years at auto-HCT were eligible, but only asymptomatic LS are included in this report. LV GLS was estimated by two-dimensional speckle tracking echocardiography (Vivid 7 or E9, GE Vingmed Norway) in a 16-segment model, and stratified according to age and lymphoma type (AC alone vs AC+RT). Results in the LS were compared with those found in a healthy control group, matched in a 1:1 fashion based on age, gender, systolic blood pressure and body mass index.

Results: In total, 274 LS (69% of all eligible) participated, of whom 245 were asymptomatic. The feasibility of LV GLS was 85%. Median observation time since lymphoma diagnosis was 12 years (range 4–34) and 61% were males. Mean cumulative exposure in LS treated with AC and AC+RT was 298±104 vs 325±147mg/m2 (p=0.10), respectively. LV GLS was reduced in LS after AC+RT compared with AC alone (−17.8±1.8 vs −19.0±2.4, p=0.001). Furthermore, both treatment groups had reduced LV GLS compared with controls (LV GLS=−20.1±1.9, p<0.001 for both). LV GLS according to age in the two treatment groups and controls are presented in the table.

P-value by one-way ANOVA.

Conclusions: We present normal values for LV GLS in asymptomatic LS, stratified according to age and cardiotoxic treatment.

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P4308 | BEDSIDE
Usefulness of 2D strain parameters to rule out acute rejection after heart transplantation
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Background: AR is a limiting factor of survival after HT. The only validated method to detect AR is endomyocardial biopsy (EB). Recent advances in 2D-strain imaging may allow early detection of AR.

Correlation between eGFR and GLS
Objective: To analyze the usefulness of conventional and new echocardiographic parameters to exclude acute rejection (AR) after heart transplantation (HT).

Methods: We prospectively included 55 consecutive adult recipients admitted at our center for an OHT. A total of 383 pairs of EMB and echocardiograms were performed. A median of 7 (IQR 6–8) studies per patient were performed along the first year of follow-up. We analyzed classic echocardiographic parameters, speckle-tracking derived left ventricular global longitudinal strain (LV GLS), and global and free wall right ventricular longitudinal strain (Free wall RVLS).

Results: AAR was detected in 33% of EMBs (n=128), 8% (n=31) required specific treatment (AAR>2R). Lower absolute values of LV GLS and Free Wall RVLS were observed in patients with AAR>2R (14.9±3.4% vs 18.2±3.1% and 17.0±4.8% vs. 20.8±5.2%). An average long LV longitudinal strain <15.5% presented 67.7% sensitivity (Se), 74.1% specificity (Sp), 96.1% negative predictive value (NPV), 19.8% positive predictive value (PPV), and 73.6% accuracy (Acc) for the presence of AAR>2R. Free wall RV longitudinal strain <17% presented 60.0% Se, 80.0% Sp, 95.1% NPV, 23.4% PPV and 78.1% Acc for AAR>2R. Both variables were normal in 193 echocardiograms (50.4%), only 2.6% of them presented with AAR >2R.

Conclusions: We propose the combination of two new parameters, namely global LV and free wall RV Long-strain to detect AAR after OHT. In case of exclusions of these findings, this novel measure could be a reliable tool to diagnose AAR and to alleviate the burden of repeated EMB.

P426 | BEDSIDE
Early detection of abnormal left atrial and left ventricular coupling using two-dimensional speckle tracking echocardiography in patients with preserved left ventricular ejection fraction

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Background: Left atrial (LA) structural remodeling is reflecting the duration and severity of diastolic left ventricular (LV) dysfunction. An accurate examination of alternations in not only LA structure but also function is an important and necessary step forward to early diagnosis of abnormal LA-LV coupling.

Purpose: The aim of this study was to detect the abnormalities of LA-LV coupling using two-dimensional speckle tracking echocardiography in patient with preserved LV ejection fraction.

Methods: A total of 177 asymptomatic patients with preserved LV ejection fraction were studied. Global LV longitudinal peak strain (GLS) and global LA longitudinal strain during systole (S-LAS) were measured. The ratio of E/Ea to S-LAS was used as an index of LA stiffness.

Results: The patients were classified into 2 groups: impaired group (n=81; GLS<-18%) and normal group (n=96; GLS>-18%). Both GPS and S-LASs were reduced in the impaired group (p<0.001). Moreover, LA stiffness was increased in the impaired group. In the normal group, there was no significant correlation between GLS and LA volume index. Moreover, there was no significant correlation between GLS and LA stiffness (Figure). On the other hand, in the impaired group, GLS significantly correlated with correlated with the LA stiffness (Figure). Similarly, GLS significantly correlated with LA volume index (r=-0.36, p=0.001).

Conclusions: Patients with preserved longitudinal LV systolic function, LA structure and function are preserved. However, LV structure and function are rapidly impaired in patients with reduced longitudinal LV systolic function. LV longitudinal systolic dysfunction may cause the LA wall to become stiffer rapidly, deteriorating LA relaxation and then causing increase of LA volume.
Rho-associated kinase 1 (ROCK1) is involved in endothelial dys- function. A key variable in the pathogenesis of atherosclerosis. Calcium channel blocker (amlodipine) has been used for atherosclerotic cardiovascular diseases treatment. However, whether amlodipine could inhibit ROCK1 activity is unclear. Purpose: The aims of present research are to explore: (1) whether amlodipine could reduce from insulin-sensitive angiotensin-II (Ang-II); (2) whether the mechanism is associated with ROCK1 inhibition; (3) whether different enantiomers of amlodipine (in terms of levotrorotatory, dextrorotatory and racemic) have the same effects on endothelium and ROCK1 activity. Methods: Human umbilical vein endothelial cells (HUVECs) were used and were divided into 5 groups: blank control; Ang-II (10–6 mol/L); levorotatory (5×10–6 mol/L) + Ang-II (10–6 mol/L); dextrorotatory (5×10–6 mol/L) + Ang-II (10–6 mol/L) and racemic (5×10–6 mol/L) + Ang-II (10–6 mol/L). Twenty-four hours later, HUVECs were collected for the following evaluations. Expressions of endothelial nitric oxide synthase (eNOS) and phosphorylated-eNOS (p-eNOS), Bel-2 and Bax, and phosphorylated-ROCK1 were detected by western blot. Nicotin oxide (NO) concentration within HUVECs was quantitatively assessed by 4-amino-5-methylamino-2,7'-difluorescein (DAF-FM) diacetate was stained by green colour. Flow cytometry with Annexin V-fluorescein isothiocyanate (FITC)/propidium iodide (PI) staining was performed to quantitatively evaluate the apoptotic index of HUVECs. Results: As compared to blank control group, expressions of eNOS and p-eNOS in Ang-I group were profoundly reduced in Ang-II group. None theless, endothelial dysfunction was reversed by each enantiomer of amlodipine therapy. ROCK1 activity (as indicated by phosphorylated-ROCK1 expression) was significantly enhanced in Ang-II group, while was offset by each enantiomer of amlodipine. Moreover, amlodipine could normalize Ang-II-induced apoptosis as well as ROCK1 activity (as indicated by phosphorylated-ROCK1 expression) was significantly enhanced in Ang-II group, while was offset by each enantiomer of amlodipine. Conclusion: Our study suggests that amlodipine could suppress Ang-II-induced endothelial dysfunction and apoptosis, and dextrorotatory and racemic amlodipine seem to be more potent than levotiorotatory amlodipine. The benefits may be associated with ROCK1 activity diminishment.

Endothelial p53 is crucially involved in regulating vascular function under hyperglycemic and hypoxic conditions. Inhibition of endothelial dysfunction as well as reducing blood flow recovery in ischemic tissue induced upon cellular stresses. Recently, accumulating evidence has shown that p53 has undesirable effects on aging and age-associated diseases. Here we show that endothelial dysfunction under hyperglycemic conditions is associated with up-regulation of endothelial p53 expression. Moreover, amlodipine could normalize Ang-II-induced apoptosis as well as p53 expression.

Methods: To investigate whether lipids management affects mid-term outcomes in patients following bioprosthetic aortic valve replacement. A total of 1346 patients who underwent heart valve replacement with bioprosthesis from 2004 to 2010 were reviewed, and only those patients for whom 5-year clinical follow-up (FU) was available were included in the analysis. The events considered were all-cause mortality, cardiovascular death, myocardial infarction, coronary revascularization, stroke, and other cardiovascular events, cerebrovascular events, and noncardiovascular death. We used proportional hazards regression to investigate the independent effects of potential predictors on both cardiovascular and cerebrovascular outcomes.

Results: A total of 874 patients (mean age 68.7±9.2 years, 62.3±male), of whom 552/874 (63.2%) underwent aortic valve replacement, 116/874 (13.3%) mitral valve replacement, and 206/874 (23.6%) double valve replacement. Mean FU time was 58±11 months. LDL cholesterol was considered <100 mg/dL, and four subgroups were identified: 1) patients receiving statins with achievement of LDL goal; 2) patients receiving statins not attaining LDL goal; 3) patients administered without statins and attaining LDL goal; and 4) patients administered without statins not attaining LDL goal. Cox-Meier method has been used to compare survival rates and to investigate major adverse cardiac and cerebrovascular events (MACCE) during FU.

Conclusions: Lipid management appears to be a key issue also in the postoperative course of patients receiving a bioprosthetic heart valve. In particular, those not attaining the LDL goal of <100 mg/dL showed higher incidence of MACCE at 5-year follow-up.

Background: Patients undergoing aortic valve replacement are at risk of developing valve thrombosis and systemic thromboembolism. Current guidelines recommend antithrombotic therapy with aspirin or vitamin K antagonists (VKA) during the first three months after the procedure. As a consequence, the most appropriate antithrombotic therapy is still a matter of debate. This retrospective study was aimed to analyse thromboembolic and bleeding complications in patients with either anticoagulation or antiplatelet therapy one year after bioprosthetic aortic valve replacement.

Methods: A total of 402 patients undergoing bioprosthetic aortic valve implantation at the University Medical Centre and subsequently treated at three regional hospitals were included. The individual duration of either vitamin K antagonists (acenocoumarol) or aspirin was determined and related to thrombotic and bleeding events. Patients were followed and censored at 1 year postoperatively for survival, cerebral ischemia, myocardial infarction, peripheral arterial embolism and minor and major haemorrhages.

Results: A total of 24 thromboembolic complications and 3 bleeding episodes occurred. Multivariate analyses revealed that acenocoumarol caused more bleeding events (relative risk (RR): 8.4; 95% CI: 0.26–19.79) and a similar amount of thromboembolic events (RR: 1.2; 95% CI: 0.47–3.02) compared to aspirin after one year of follow up. Prior use of acenocoumarol was found to be a predictive risk factor for thromboembolic events (RR: 3.1; 95% CI: 1.31 to 7.19). For bleeding events, gender, diabetes, prior percutaneous coronary intervention, prior use of acenocoumarol and concomitant coronary artery bypass grafting were found to be predictors.

Conclusion: In patients one year following bioprosthetic aortic valve replacement, acenocoumarol therapy was associated with a significant increase in bleeding events and no reduction of thromboembolic events compared to antiplatelet therapy. These findings support the recommendations of aspirin over VKA as post-operative thromboprophylaxis during three months.
valve replacement has been the treatment of choice in left side prosthetic valve thrombosis (PVT) in critically ill NYHA Class III-IV patients. Thrombolytic therapy is normally recommended for NYHA III patients with small thrombus burden. 

Purpose: We have analyzed the results of thrombolytic therapy in left sided prosthetic valve thrombosis in critically ill NYHA III/IV patients where surgery was either refused due to financial constraints or by the surgical team.

Methods: 11 patients with left sided prosthetic valve thrombosis (8 mitral and 3 aortic) in NYHA III/IV were studied. Patients belonged to small villages/towns and had poor financial background without any insurance support. They were administered intravenous streptokinase (STK) in dose of 500,000 units bolus over 15–20 minutes and followed by infusion of 100,000 units/hour for 3 days. Results were assessed clinically, 2DECHO and by fluoroscopy.

Results: 11 patients, 35–60yrs, female 4 and male 7 had mechanical bileaflet prosthetic valves implanted: mitral (8) and aortic (3). One patient had both mitral and aortic prosthetic valves. One patient had diabetes and had undergone prior PCI with DES implantation to ostial left main. The interval between prosthetic valve implantation and thrombosis varied between 2–11 years. Three had associated atrial fibrillation and one had multiple VPCs. All had significant cardiomegaly and LVH. EF varied between 30–50%. Mean gradient across valves was increased on 2DECHO in all patients. All had only one mobile leaflet of prosthetic valve on fluoroscopy. INR varied between 1.0–1.8 at the time of diagnosis of PVT. 4 patients were in severe hypotensive shock and 6 presented with pulmonary oedema. 3 patients with aortic prosthesis expired within 6–12hours of hospitalization. 8 patients with mitral valve thrombosis responded to thrombolytic therapy and survived with complete resolution of thrombus and return of full mobility of leaflets on echocardiography and resolution of valve gradients as assessed on 2D/3D echo. All responders have survived (4–10 years) till date. There has been no episode of recurrence of PVT or CVA.

Conclusions: IV streptokinase may be life saving in critically ill NYHA III/IV patients with non-obstructive PVT. Thrombolytic therapy is much cheaper and easier to administer than surgical replacement of thrombosed prosthetic valve.

P4319 | BEDSIDE

Thrombolysis versus unfractionated heparin as first line strategy for non-obstructive prosthetic valve thrombosis

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Background: Thrombolytic therapy (TT) is efficient and relatively safe in patients with prosthetic valve thrombosis (PVT). However, current guidelines recommend optimized anticoagulation as an initial approach and thrombolysis is restricted to very high risk surgical candidates in patients with non-obstructive PVT with a thrombus diameter ≥10 mm.

Purpose: To compare the short term efficacy and safety of optimized anticoagulation with unfractionated heparin (UFH) versus TT with recombinant tissue plasminogen activator (t-PA) in patients with PVT.

Methods: Overall 58 patients (38 female, age 49±10 years) with non-obstructive PVT and a thrombus diameter ≥10 mm assessed by transthoracic echocardiography (TEE) and without a contraindication to TT were prospectively included between 2011 and 2014 in a single center. Patients were assigned to either TT (29 patients) or anticoagulation (29 patients) strategies. The TT regimen was ultra-slow (25-hour) infusion of low dose (25 mg) t-PA with repetition (maximum total dose 200 mg). The anticoagulation regimen was continuous infusion of UFH with optimized partial thromboplastin time until treatment success or for maximum 28 days. The treatment efficacy was assessed by serial TEE. The end-points were in-hospital treatment success, mortality and complication rates.

Results: There were no difference between the two groups in terms of baseline clinical and TEE characteristics including age (p=0.89), gender (p<1), heart rhythm (p=0.43), functional capacity (p=0.63), elapsed time since valve surgery (p=0.3), thrombosed valve position (p=0.7), thrombus area (p=0.96), baseline valve area (p=0.63), history of stroke or transient ischemic attack (p=0.54). The overall success rate was 81%. For successful cases, the mean t-PA dose and UFH treatment duration were 46±19 mg and 14±8 days, respectively. Success rate was significantly higher in t-PA group compared to UFH group (96.6% vs 65.5%, respectively, p=0.003). The only univariate predictor of an unsuccessful result was being in the UFH treatment group (RR: 9.0, 95% CI: 2–65, p=0.003). Overall 6 (10.3%) patients suffered from complications. There were one intrabdominal bleeding requiring transfusion and 2 minor bleedings in t-PA group. There were one death requiring transfusion and 2 minor bleedings in UFH group. No embolism was observed. In the t-PA group compared with UFH group.

Conclusion: Ultra-slow (25 hours) infusion of low dose (25 mg) t-PA is superior to UFH as first line treatment strategy in patients with non-obstructive PVT.

P4321 | BEDSIDE

Diabetes and cause-specific mortality: evidence from 55 000 deaths in 700 000 adults in 44 prospective studies


Background: We aimed to assess reliably the effect of self-reported diabetes (DM) on vascular and non-vascular mortality, using individual data from 44 prospective observational studies.

Methods: Information was obtained on 690,700 adults with no previous vascular disease recorded at baseline. We assessed the age and sex-specific associations of DM with cause-specific mortality using Cox proportional-hazard regressions on a large data cohort, age at risk: 35–89, 30% female, body mass index (BMI), systolic blood pressure (SBP), the shape and strength of the associations between conventional vascular risk factors (BMI, TC and SBP) and ischaemic heart disease (IHD) were compared between people with and without diabetes after correction for regression dilution. Survival curves were estimated based on these hazard ratios and standardised age and sex-specific WM mortality rates in the UK in 2010.

Results: During 13 million person-years of follow-up there were about 27,000 vascular deaths and 28,000 non-vascular deaths between ages 35–89. Overall, diabetes was associated with a doubling in risk of IHD mortality in old age (HR 2.1; 95% CI 1.9–2.3) and among men (2.2; 2.0–2.3) and a tripling in risk in early middle age (2.9; 2.5–3.3) and among women (3.2; 2.9–3.6). Consequently, the association was most extreme in women in early middle age (6.0; 4.3–8.3). Diabetes was very strongly associated with death from other (non-vascular) causes (HR 2.2; 1.8–2.7). A heart disease, stroke, cirrhosis, renal disease, and cancer of the mouth, liver and pancreas (all p<0.05). The relative risks of IHD associated with a given change in BMI and TC were similar among people with and without diabetes (both p>0.5), whereas the associations with SBP was smallest among those without diabetes (p=0.01). However, because people with diabetes are at higher risk of IHD, the absolute risks associated with all these conventional risk factors were considerably greater among those with diabetes. Diabetes was associated with reduced median survival of about 7 years in men and 10 years in women. Control of blood pressure, cholesterol and obesity are particularly important to reduce this premature mortality among people with diabetes.

P4322 | SPOTLIGHT

Dietary intake of alpha-linolenic acid and risk of myocardial infarction: a Danish cohort study

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Introduction: The plant-derived omega-3 fatty acid alpha-linolenic acid (ALA) has been associated with cardioprotective mechanisms but there is limited evidence for a protective effect on risk of coronary heart disease and myocardial infarction (MI).

Purpose: The objective was to investigate the association between dietary intake of ALA and development of incident MI and to assess possible effect modification by linoleic acid and long-chain marine omega-3 fatty acids (LC-ω3) intake.

Methods: A total of 57,053 participants 50–64 years of age were between 1993–1997 enrolled into the Danish Diet, Cancer and Health Cohort. Dietary intake of ALA was assessed by a validated semi-quantitative food frequency questionnaire. Potential cases of incident MI were identified by record linkage with nationwide registers. Statistical analyses were performed stratified by gender in Cox proportional hazard regression models with age as underlying time axis adjusted for a priori defined established coronary risk factors. Intake of ALA was included as both a continuous and a categorical variable.

Results: During a median of 17 years of follow-up, we identified 3089 incident cases of MI. Multivariate Cox regression using restricted cubic splines showed a weak non-significant negative association with intake of ALA in men (2124 cases) and a weak non-significant U-shaped association in women (854 cases). When Dietary intake of ALA and incident MI

Quintiles of intake

Men

Women

Incident MI Hazard ratio (95% CI)

Quintiles of ALA intake (g/d)

Incident MI Hazard ratio (95% CI)

Q1 ≤1.67 390 1 Q1 ≤1.24 1

Q2 1.67–1.94 409 0.96 (0.83–1.11) Q2 1.24–1.43 170 1.08 (0.86–1.37)

Q3 1.94–2.19 448 1.00 (0.86–1.17) Q3 1.43–1.62 183 0.85 (0.66–1.10)

Q4 2.19–2.54 447 0.99 (0.84–1.14) Q4 1.62–1.88 163 0.99 (0.78–1.29)

Q5 ≥2.54 440 0.89 (0.74–1.06) Q5 ≥2.54 158 0.83 (0.67–1.02)

p-value: 0.57 p-value: 0.21

ALA, alpha-linolenic acid; MI, myocardial infarction; Q, quintile.
expressed in quintiles ALA intake was not associated with incident MI neither among men nor women (Table). No effect modification was observed when a cross-product term was added in between analyses including tertiles of energy-adjusted dietary intake of ALA and LC-ω3 acid or linoleic acid.

**Conclusion:** Dietary intake of ALA was not significantly associated with incident MI neither among men nor women.

**P4324 | BEDSIDE**

Association between persistent psychological distress and 12 year cardiovascular and total mortality in patients with stable coronary artery disease


**Purpose:** To determine whether persistent or intermittent psychological distress is associated with cardiovascular and total mortality in patients with stable coronary artery disease.

**Methods:** 940 participants enrolled in the Long Term Intervention with Pravastatin in Ischaemic Disease (LIPID) trial completed a General Health Questionnaires (GHQ-30) at baseline and after 6 months, 1, 2, and 4 years. The hazard ratio (HR) for cardiovascular (CV) and total mortality were determined after follow-up for the next 12.1, (IQR 8.6,12.5) years for subjects who reported mild (GHQ score > 5) and more severe (GHQ score > 10) psychological distress which was either intermittent (on one or two occasions), or persistent (on 3 or more occasions) compared with those reporting no distress. HR’s were adjusted for baseline variables.

**Results:** Moderate to severe psychological stress was reported >60% of the time by 35 (4%) subjects. These patients had higher CV (adjusted HR 2.50, 95% CI 1.44 to 4.36, p=0.0012), and all-cause mortality (adjusted HR 2.02, 95% CI 1.32 to 3.14, p=0.0013). In contrast, 188 (18%) patients who reported moderate-severe distress once or twice did not have higher CV (adjusted HR 0.93, 95% CI 0.64 to 1.34, p=0.69) or all-cause mortality (adjusted HR 0.94, 95% CI 0.73 to 1.22, p=0.65). The associations between less severe psychological distress (GHQ-5) present >60% of the time and CV (adjusted HR 1.17, 95% CI 0.76 to 1.82, p=0.47) and total mortality (HR 1.30, 95% CI 0.96 to 1.76, p=0.08) were not statistically significant, and there was no association with mortality if present <50% of the time.

**Conclusion:** In patients with stable coronary artery disease, persistent moderate-severe psychological distress was associated with a substantially higher risk of long-term CV and total mortality, but distress that was not persistent was not associated with mortality. Further research is needed to determine whether reducing persistent psychological distress improves outcomes in this high risk group.

**P4324 | BEDSIDE**

European HeartQoL reference values in patients with coronary heart disease

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**Background and Introduction:** In comparison with the general population, Heart Related Quality of Life (HRQoL) outcomes are significantly impaired in coronary heart disease (CHD) patients. Recently, the HeartQoL instrument was developed, from which a global HeartQoL score and two subscale scores (physical and emotional subscale), each ranging between 0 (worst) and 3 (best), can be calculated.

**Purpose:** The aim of this study was to set HeartQoL reference values in a population of stable coronary patients stratified by age, gender, diabetes and educational level. Additionally, we aimed to investigate the association between HeartQoL and the patients coronary risk profile.

**Methods:** Analyses are based on the EUROASPIRE IV (EUropean Action on Secondary and Primary prevention through Intervention to Reduce Events) survey. Patients eligible for inclusion were males and females, who had been hospitalised for a first or recurrent coronary event. HeartQoL scores were available for 7261 patients.

**Results:** Significantly worse outcomes were observed in higher risk patient groups, with lower scores in females, older patients and lower educated patients.

**Conclusion:** Metabolic risk factors such as diabetes, obesity and central obesity as well as behavioural risk factors such as smoking and insufficient physical activity were also associated with worse HeartQoL outcomes. A closer look at the number of risk factors indicated worse HeartQoL scores as the number of risk factors increases. Mean reference values for global HeartQoL amounted to 2.27 (0.65), 2.30 (0.61) and 2.18 (0.64) for males ≤60 years; between 60 and 69 years and >70 years respectively. Likewise in females the global HeartQoL reference values amounted to 2.02 (0.66), 2.01 (0.66) and 1.83 (0.70) respectively. The ceiling effect in males amounted to 11.4%, 10.4% and 7.4% for the age classes respectively, whereas in females the ceiling effect was 5.2%; 3.5%; and 1.9% in those <60 years, between 60 and 69 years and >70 years respectively. Clinically relevant differences between males and females were found in the complete sample, as well as in the diabetes patients and the lower educated patients. Relevant differences mainly occurred on the global and physical scale and in the 60–69 years age class.

**Conclusion(s):** This study is the first to provide reference values for the HeartQoL instrument. Similar to previous studies a worse risk factor profile was associated with poor HeartQoL values, with an increase in number of risk factors being associated with worse HeartQoL outcomes. In general behavioral changes were associated with favourable HeartQoL outcomes.

**BEST POSTERS IN RISK FACTORS AND OUTCOMES AFTER PCI**

**P4325 | BEDSIDE**

Differential impact of diabetes on platelet reactivity and stent thrombosis in women and men: insights from the ADAPT-DES study

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**Introduction:** Diabetes mellitus (DM) has been reported to be a strong risk factor for stent thrombosis (ST) after DES implantation. Previous data have shown that the clinical impact of DM is greater for women than for men.

**Objectives:** To examine differences in the prevalence of high platelet reactivity (HPR) on clopidogrel between sexes according to DM status and to assess the sex-specific impact of DM on cumulative definite/probable ST at 2 years, adjusting for baseline clinical confounders and HPR.

**Methods:** Patients from the prospective, multicenter ADAPT-DES study were stratified by sex and the DM status. HPR was defined as a P2Y12 reactivity units >208.

**Results:** Of 8,582 patients included in ADAPT-DES, 9.6% were women with DM and 16.2% were women with no DM, while 22.8% were men with DM and 51.3% were men with no DM. Women with DM had higher BMI and prevalence of insulin resistance compared to men with DM. Conversely, men with DM had more comorbidities and more severe CAD. Presence of DM was associated with a higher prevalence of HPR irrespective of sex (Figure), with the highest values observed in women with DM (p<0.01). The unadjusted risk for ST associated with DM was higher in both men (0.8% vs. 1.6%, p=0.01) and women (0.8% vs. 1.7%, p=0.03); however, after multivariable adjustment for baseline clinical confounders, including HPR, these associations were no longer significant in women (adjHR: 0.84; 95% CI: 0.22–3.29) or men (adjHR: 1.57; 95% CI: 0.89–2.77), with no interaction between DM status and sex (p=0.05).
Mortality trends after unprotected left main PCI in England and Wales, 2005-2014: Analysis of 10,825 cases from the British Cardiovascular Intervention Society (BCIS) national registry

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Purpose: To report temporal trends in the treatment and outcomes after UPLMS PCI according to presentation by ST-elevation myocardial infarction (STEMI), non-ST-elevation acute coronary syndrome (NSTEACS) and chronic stable angina (CSA).

Methods: Prospective population-based linked cohort study of 10,825 patients from the BCIS database, 1st Jan 2005 through 31st March 2014.

Results: Compared with 2005, in 2013 the annual numbers of cases increased from 348 to 2,122. Between 2005 and 2014 the proportion of cases treated as STEMI increased (10.4% vs. 19.4%). Overall, baseline risk increased; cardiogenic shock: 7.9% to 13.1%, P<0.001; severe left ventricular systolic dysfunction, 9.0% to 12.5%, P=0.002; age >80 years, 20.7% to 24.2%, P=0.046. Radial PCI increased from 18.4% in 2005–6 to 61.2% in 2013–14. Compared with 2005–6, 30-day mortality in 2013–14 was stable (STEMI: adjusted odds ratio (aOR), 95% confidence interval (CI) 0.93, 0.53 to 1.6; NSTEACS 0.9, 0.6 to 1.4; CSA 1.2, 0.2 to 6.4). Likewise, 1-year mortality remained stable (STEMI aOR 1.2, 95% CI 0.7 to 2.3; NSTEACS 1.6, 1.1 to 2.2; CSA 1.8, 0.9 to 3.8). By 2013–14, for STEMI with cardiogenic shock, 30-day mortality rates decreased by 13.4% (95% CI, 10.9% to 16.0%) and 1-year mortality rate increased by 2.5% (1.5% to 4.0%).

Conclusions: Between 2005 and 2014, the number of cases of UPLMS PCI in England and Wales increased by over 6-fold. Although baseline risk increased, mortality was stable across all clinical presentations. Early mortality rate for STEMI with cardiogenic shock declined, however late mortality rate remained high.

Impact of platelet reactivity in anemic and non-anemic patients with coronary artery disease undergoing percutaneous coronary intervention: insights from the adapt-des study

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Background: High platelet reactivity (HPR) on clopidogrel predicts major adverse cardiovascular events (MACE) post PCI. Anemia is also known to be strongly associated with adverse prognosis and bleeding risk.

Purpose: To investigate the impact of HPR, according to anemia status, on MACE on clopidogrel during 2 years in patients undergoing PCI.

Methods: Patients from ADAPT-DES were stratified according to the presence of anemia and HPR. Anemia was defined according the WHO definition. HPR was defined as VerifyNow P2Y12 reactivity units ≥208 on clopidogrel after DES implantation.

Results: Of 8,413 patients included in the study cohort, 1,816 (21.6%) were anemic. Compared to those without anemia, anemic patients were older with a greater prevalence of comorbidities and HPR (58.3% vs. 38.4%; P<0.01). MACE rates were highest among those with both anemia and HPR and lowest in the absence of both conditions (Figure). The adjusted impact of HPR on MACE was similar in magnitude and direction in both anemic (adjHR: 1.31; 95% CI: 0.93–1.81) and non-anemic patients (adjHR: 1.37; 95% CI: 1.06–1.72; for interaction p >0.05). The rates of bleeding were highest in anemic patients without HPR and lowest in non-anemic patients with HPR (Figure). HPR was associated with a lower risk for bleeding in both non-anemic (adjHR: 0.82; 95% CI: 0.68–0.99) and anemic patients (adjHR: 0.84; 95% CI: 0.64–1.11) without significant interaction (p for interaction >0.05).

Conclusions: Combined HPR and anemia has a synergistic effect on thrombotic risk after PCI, whereas anemia in the absence of HPR is associated with a higher risk for bleeding. The independent impact of HPR on both ischemic risk and freedom from bleeding appears uniform irrespective of baseline anemia status.
BEST POSTERS IN VENTRICULAR FUNCTION / HAEMODYNAMICS

P4321 | BEDSIDE
Effect of high-intensity interval training combined with strength exercise on aortic-ventricular coupling in patients with chronic heart failure. A randomized phase III clinical trial
C. Chrysohou1, A. Angelis, G. Tatsintakis, E. Herouvim, D. Tsichris, P. Papakoulias, I. Pitsavos, I. Vogiatzis, N. Koulouris, D. Tousoulis. University of Athens, Athens, Greece

Background: It is known that heart failure causes changes in cardiac mechanics, like an unfavorable alteration of ventricular/vascular coupling is associated with increased arterial stiffness and has been linked directly to the subsequent development of adverse cardiovascular outcomes. Aim of this work was to evaluate the effect of high-intensity interval exercise (i.e., 30 sec at 100% of max workload, followed by 30 sec at rest, on 3 days/week 45 minutes working-out schedule for 12 weeks), on left ventricular function and aortic elastic properties among chronic heart failure (CHF) patients.

Methods: A phase III clinical trial. Of the 100 consecutive CHF patients (NYHA class II-IV, ejection fraction <50%) that were randomly allocated, 72 completed the study (exercise training group, n=33, 63±9 years, 88% men, and control group, n=39, 56±11 years, 82% men). All patients underwent cardiopulmonary stress test, non-invasive high-fidelity tonometry of the radial artery, pulse wave velocity measurement using a SphygmoCor device and echocardiography before and after completion of the training program.

Results: Both groups reported similar medical characteristics and physical activity status. General mixed effects models revealed that the intervention group reduced pulse wave velocity by 9% (p=0.05); Emv/Vp by 14% (p=0.06); E to A ratio by 24% (p=0.004), E to Emv by ratio by 8% (p=0.05), MLHFG score by 66% (p=0.001), MIT score by 19% (p=0.03); increased augmentation in delay by 29%; VTI by 4% (p=0.05), 6-minutes-walk distance up to 13% (p=0.05), peak oxygen uptake by 28% (p=0.001) and peak power by 25% (p=0.005). There were no significant changes in the control group.

Conclusion: Interval high-intensity aerobic training, combined with strength exercise, seems to benefit aortic dilatation capacity and augmented systolic pressure in parallel with improvement in left ventricular diastolic function and quality of life. Those findings reflect a beneficial impact of exercise on arterial-ventricular coupling that creates boost of systolic pressure and the wave reflection of the aorta regains a positive influence on pressure.

P4322 | BEDSIDE
Lung function in relation to cardiac dysfunction and heart failure in the general population
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Background: Lung and heart diseases share common risk factors and dyspnea as main clinical symptom. Impairment of lung function may cause symptoms of heart failure, although no overt cardiovascular or structural heart disease is found in many cases. The relation between respiratory impairment and left ventricular impairment in the general population remains to be investigated.

Methods: In 5000 individuals from the general population (mean age 55±11 years, age range 46–65 years, 50.8% men) in the Gutenberg Health Study we performed spirometry with the microdial sio USB and multimodal echocardiography with an iE33 echocardiography system with an 55–1 sector array transducer, a phased array with 80 elements and a 5- to 1-MHz operating frequency range. Lung function parameters (FEV1, FVC, FEV1/FVC) were associated with echocardiographic measures of cardiac structure and systolic and diastolic function.

Results: The mean left ventricular ejection fraction (EF) was 64±7% (current smoking 19.2%, COPD 4.8%). The common cardiovascular risk factors age, male gender, smoking, current smoking and hypertension were associated with FEV1 and FVC. Diabetes and hypertension showed a stronger association with FEV1/FVC. The linear regression analysis showed significant associations (p<0.001) both for FEV1 and FVC with IVST, LVEDD, E/E’, EDV, SV and EF, whereas FEV1/FVC was significantly related to LVEDD (p=0.0017), ESV (p=0.003); LVEDD and LVESD with EF and VTI; EFV1 and FVC with FEV1/FVC with E/A and Ti-e index were found. In the COPD subgroup, the Tiffeneau-index (FEV1/FVC) was significantly related to E/A (p=0.0028), LVESD (p=0.044) and EF (p=0.046). In addition, study participants with COPD showed associations of FEV1 and FVC with EF (p=0.0052 resp. p=0.023) and FEV1 with EF (p=0.038).

Conclusions: In the general population, central lung function tests, FEV1, FVC and FVC/FVC were significantly related to systolic and diastolic left ventricular function. The associations may indicate early stages of hypertension, reduction of left ventricular filling and cardiac output, whereas the relation with diastolic function may be explained by subclinical changes with a shortened diastolic filling, hypoxemia and reduced preload. Such associations have been suggested in COPD patients and were confirmed in our sample.

P4323 | BEDSIDE
A single-centre experience in the hemodynamic improvement and prognosis of heart failure patients with pulmonary hypertension treated with sildenafil
M. Oliveira-Santos1, R. Ramalho1, R. Baptista1, S. Leao2, S. Costa1, A. Marinho-Da-Silva1, R. Martins1, F. Franco1, M. Pego1. University Hospital of Coimbra, Cardiology, Coimbra, Portugal; 1Hospital Center of Tras-os-Montes and Alto Douro, Cardiology, Vila Real, Portugal

Background: The post-capillary reactive form of pulmonary hypertension (PH) due to left heart disease (group 2 PH) is characterized by increased transpulmonary pressure gradient (TGP) and pulmonary vascular resistance (PVR). Pulmonary arterial vasodilator treatment with phosphodiesterase 5 inhibitors is sometimes used in order to meet eligibility criteria for heart transplantation (HTx). We aimed to study the hemodynamic and clinical effects of sildenafil in a reactive group 2 PH cohort and the prognostic implications of the hemodynamic response.

Methods: Retrospective analysis of 107 patients with reactive group 2 PH (TPG > 12 mmHg) referred for HTx, on optimal medical therapy, treated with sildenafil 20 mg tid, at a single centre (2004–2014). We studied clinical and hemodynamic data before and after treatment. Clinical endpoints: time to all-cause death, HTx and first hospitalization after sildenafil initiation. Hemodynamic positive response was defined as lowering of PVR to 3.5 Wood units, provided that the cardiac index (CI) was not reduced. Statistical analysis: Wilcoxon/McNemar tests, Kaplan Maier and Cox regression methods.

Results: Mean age was 55±11 years, 73% were male. Half of the patients were in NYHA IV class, with median BNP 605 (IQR 665) pg/dL and peak VO2 15.6 (IQR 15) mL/kg/min. The Tiffeneau index (FEV1/FVC) was significantly related to E/A (p=0.0028), SV (p=0.030), LVESD and EF (p=0.046). In addition, study participants with COPD <0.001) both for FEV1 and FVC with IVST, LVEDD, E/E’, EDV, SV and EF, whereas FEV1/FVC was significantly related to LVEDD (p=0.0017), ESV (p=0.003); LVEDD and LVESD with EF and VTI; EFV1 and FVC with FEV1/FVC with E/A and Tei-index were found. In the COPD subgroup, the Tiffeneau-index (FEV1/FVC) was significantly related to E/A (p=0.0028), LVESD (p=0.044) and EF (p=0.046). In addition, study participants with COPD showed associations of FEV1 and FVC with EF (p=0.0052 resp. p=0.023) and FEV1 with EF (p=0.038).

Conclusions: In the general population, central lung function tests, FEV1, FVC and FVC/FVC were significantly related to systolic and diastolic left ventricular function. The associations may indicate early stages of hypertension, reduction of left ventricular filling and cardiac output, whereas the relation with diastolic function may be explained by subclinical changes with a shortened diastolic filling, hypoxemia and reduced preload. Such associations have been suggested in COPD patients and were confirmed in our sample.
Intense stimulation significantly increased CBF in ACC as compared to sham stimulation using SPM8, a common analysis tool for neuroimages. Blood samples from the aortic arch were obtained during sham stimulation (1.5V) and intense stimulation (7.5–8V) using [15O]H2O PET. The CBF images of intense stimulation were compared with those of sham stimulation. Before the measurement, mode of cardiac pacemaker was changed to ventricular mode (VVI) to avoid cardiac stimulation. We thus examined brain activity and plasma catecholamine levels in response to cardiac electrical stimulation in humans.

Methods: We studied 10 patients (74±13 yr, M/F 9/1) with cardiac pacemaker implantation. Before the measurement, mode of cardiac pacemaker was changed to VVI 80–90 bpm with 1.5V intensity. Cerebral blood flow (CBF) was measured during sham stimulation (1.5V) and intense stimulation (7.5–8V) using [15O]H2O PET. The CBF images of intense stimulation were compared with those of sham stimulation using SPM8, a common analysis tool for neuroimages. Blood samples were obtained from the cubital vein before and after CBF measurements for plasma catecholamine levels (one patient was excluded for the analysis due to urination before the last blood sampling).

Results: Intense stimulation significantly increased CBF in ACC as compared to sham stimulation (intense, 64.6±0.7 vs. sham, 61.0±1.3 ml/100g/min, P=0.008, n=10 each) (Figure, yellow arrowhead). Plasma adrenaline level was significantly increased in response to intense stimulation as compared with sham stimulation (intense, 6.1±1.8 vs. sham, 0.1±3.0 pg/ml, P=0.031, n=9 each).

Conclusion: This study demonstrates for the first time that electrical stimulation of cardiac pacemaker activates ACC with increased plasma adrenaline level.

Increased cardiovascular sympathetic modulation as a predictor of death in patients with amyotrophic lateral sclerosis

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Background: Amyotrophic Lateral Sclerosis (ALS) is one of the most devastating of adult-onset neurodegenerative disorders, characterized by a marked heterogeneity in both presentation and rate of progression, and by motor and extramotor neural loss. There is increasing evidence that the autonomic nervous system (ANS) is also affected as part of the complex degenerative process. ALS has a progressive course with death occurring as a mean in 3 y, but with some variability among patients. The predominant cause of death is respiratory failure, but sudden death has also been reported.

Purpose: Aim of this study was to investigate the cardiovascular neural regulation in ALS.

Methods: We enrolled 31 ALS patients (14 F, 17 M, age 61±13 y), ECG, arterial pressure and respiration activity signals were continuously recorded at rest and during a 75° head-up tilt. Autoregressive spectral analysis provided the indices of the total cardiovascular sympathetic modulation (LF_RR and HF_RR, respectively) and the sympathetic vasomotor control (LF_SAP). Data are expressed as mean±SD. Discriminant analysis was applied to spectral indices and all clinical characteristics.

Results: All the patients were characterized by low RR variance both at rest and during tilt (731±746 and 490±467 ms²) and by an altered response to orthostasis, as reflected by the absence of increase of LF_RR, LF_SAP and LF/HF ratio during tilt. Disease duration (DD) significantly separated our population in Group 1 (15 pts, DD 36 mo) and Group 2 (16 pts, DD 36 mo). At rest, sympathetic cardiac indices were higher in Group 1 than Group 2 (LF_RR 64±19 vs. 44±30 nm). At follow-up, 8 patients died, 7 of Group 1 (31±14 mo from disease onset) and 1 of Group 2 (56 mo from disease onset).

Conclusion: Our study outlined that ANS is invariably impaired in ALS, and patients can present with different patterns that can be relevant in terms of prognosis. At rest, patients with high or low sympathetic activity directed to the heart differed for disease duration. The cut-off corresponded to the mean survival time in ALS, and might have clinical relevance in separating slow versus fast progresses. Accordingly, different patients were significantly higher in the group with high sympathetic modulation. These findings support the new concept of ALS as a multisystem disorder with phenotypic heterogeneity, and that the patient’s sympathovagal profile could provide prognostic indices. A comprehensive ANS evaluation is needed for a better understanding of the physiopathology of this complex neurodegenerative and multisystem disorder and to confirm our hypothesis.
Regensburg, Germany; 2 Hospital Bayreuth, Cardiology, Bayreuth, Germany

"First in man" evaluation of the new ablation catheter Thermocool procedures.

Background: M. Christoph, C. Wunderlich, Y. Huo, M. Forkmann, J. Mayer, J. Salmas, M. Pohl, smarttouch sf in atrial fibrillation ablation

P4341 | BEDSIDE

system with a real time monitoring of tissue contact force. Three important properties were subdivided into two groups (PVAC and PVAC GOLD). The first 20 patients were treated with the PVAC. The subsequent 20 patients were treated with the PVAC GOLD.

Results: All 164 targeted PVs could be isolated successfully. There were 23 patients with paroxysmal AF and 17 patients who had persistent AF. CAD was present in 15 patients (37.5%), a history of hypertension in 32 patients (80%) and diabetes in 11 patients (27.5%). The baseline characteristics did not significantly differ in between these two groups of consecutive patients. Comparing the clinical performance of PVAC vs. PVAC GOLD showed a significant reduction in total number of ablations needed for PVAC (34.7±7.0 vs. 27.0±6.5), fluoroscopy time (29.5±9.5 vs. 23.4±7.0) and procedure time (93.8±18.9 vs. 83.1±10.6). Improvements in procedural efficacy may have been a result of reduction of low power ablations from (6% to 2%) and an almost 10% increase in mean effective energy delivery (134.4 to 147.4 J) using PVAC GOLD. There were no adverse events in either group.

Conclusions: The PVAC GOLD system allows a reduction in radiofrequency ablation time, higher effective energy delivery, fewer low power ablations and improved biophysical efficiency when compared to the first generation PVAC system. Further studies are needed to rule out if the improved acute parameters result in increased efficacy for PVAC and freedom from AF.

P4340 | BEDSIDE

Initial results of a second-generation multielectrode mapping and ablation catheter for pulmonary vein isolation (PVAC GOLD)

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Background: Antral pulmonary vein isolation (PVI) with radiofrequency energy is widely used as a strategy for catheter ablation of atrial fibrillation (AF). With the increasing demand for ablation procedures, new circular mapping and ablation catheters have been especially developed for AF ablation.

Purpose: The purpose of this study was to investigate the acute efficacy of the 2nd generation PVAC catheter (PVAC GOLD) in patients with AF. Performance data were compared with the results in the 1st generation PVAC catheter (PF, mean±SEM: normotensive: 27.5±2.1 versus hypertensive 37±2.2 p=0.02).

Conclusion: We have shown for the first time that regional cerebral blood flow to the brain stem is reduced in hypertensive patients. We have also shown that in normotensive patients with reduced brainstem blood flow, MSNA is increased. These data support our hypothesis that a reduction in brain blood flow and increased sympathetic nervous activity may contribute to hypertension via the Cushing’s mechanism.

P4342 | BEDSIDE

Superior efficacy of pulmonary vein isolation with online contact force measurement persists after the learning period: a prospective case control study

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Background and purpose: Use of online contact force (CF)-measurement during circumferential pulmonary vein (PV) isolation (CPVI) for atrial fibrillation (AF) has demonstrated improvements in procedural parameters and mid-term clinical outcome. However it is unknown if experience gained with CF-measuring catheters improves the efficacy of subsequent CPVI procedures performed without CF-measurement.

Methods and results: This prospective trial compared procedural results of CPVI performed without a CF-measuring catheter to a control group performed with CF-measuring catheter, by an operator with prior experience with CF-technology. Thirty-six eligible paroxysmal (n=27) or persistent (n=9) AF patients were consecutively enrolled. Twelve patients underwent CPVI with the non-CF-clinical control group – in recall period and 24 with the CF-catheter (CF+ group). After the first circumferential lesion set the number of PV pairs requiring additional touch-up lesions to achieve adenosine-proof electrical isolation was significantly less in the CF+ group (2 of 4 (4.2%) vs. 7 of 24 (29.2%) of the CF− group respectively, p=0.005). The procedure time was significantly lower in the CF+ group (117.9±23.3 min vs. 134.1±25.3 min, p=0.033), RF and fluoroscopy time did not differ between groups (31.5±7.1 min vs. 31.8±7.0 min and 11.8±5.6 min vs. 11.0±5.8 min in the CF+ and the CF- group, respectively).

Procedural results

<table>
<thead>
<tr>
<th>CF− group</th>
<th>CF+ group</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>N (n=12)</td>
<td>N (n=24)</td>
<td></td>
</tr>
<tr>
<td>Number of PV pairs requiring touch-up (n, %)</td>
<td>7/24 (29.2)</td>
<td>2/24 (8.3)</td>
</tr>
<tr>
<td>Number of patients requiring touch-up (n, %)</td>
<td>7/12 (58.3)</td>
<td>2/24 (8.3)</td>
</tr>
<tr>
<td>Number of ablation- induced reocclusion PV pairs (n, %)</td>
<td>1/12 (8.3)</td>
<td>0/12 (0)</td>
</tr>
<tr>
<td>Total procedure time (min)</td>
<td>134.1±25.3</td>
<td>117.8±23.3</td>
</tr>
<tr>
<td>RF time (min)</td>
<td>31.8±7.0</td>
<td>31.5±7.1</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>11.0±5.8</td>
<td>11.8±5.6</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation or absolute number (n) + percentage (%). CF−: group in which CPVI is performed without the Navistar® Thermocool® ablation catheter; CF+: control group in which CPVI is performed with the Thermocool® SmartTouchTM catheter.

Conclusion: With the use of online CF-measurement PV isolation is more frequently complete following the first circumferential lesion set. A previous learning period with direct CF-feedback is not a substitute for real-time direct CF-measurement to maintain this advantage.

P4343 | BEDSIDE

Pulmonary vein isolation for paroxysmal atrial fibrillation using a novel gold multi-electrode duty cycled radiofrequency ablation catheter. First results

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Purpose: Pulmonary vein isolation (PVI) is the cornerstone of ablation in paroxysmal atrial fibrillation (PAF). With the multi-electrode duty cycle PVI isolation can be performed with less RF-energy applications and without additional 3D-mapping. The aim of this study was to investigate procedural characteristics and efficacy of the novel gold multi-electrode duty cycled radiofrequency ablation catheter (PVAC Gold).

Methods: A total of 91 consecutive patients (65±9 years old, 49 male) with PAF undergoing PVAC with PVAC Gold were studied. All procedures were performed with use of a non-stereotactic transseptal sheath. The primary endpoint was defined as
P4344 | BEDSIDE
Do patient and doctors differ in their perception of the patients symptom relief after ablation of atrial fibrillation?

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Introduction: Success of atrial fibrillation (AF) ablation is usually defined as freedom of AF, although symptomatic relief often is what patients’ desire. The symptom relief after an intervention may be perceived differently by the patient and the physician.

Purpose: To assess symptom relief after AF ablation as perceived by the patient using the AF-specific symptom questionnaire AF6 and as classified by the physician using the EHRA score.

Methods: 57 patients, who underwent AF ablation, filled out the validated AF-specific symptom questionnaire AF6 and were classified by their physician using the EHRA classification at baseline, 6, 12 and 24 months. The AF6 items were “breathing difficulties at rest”, “breathing difficulties upon exertion”, “limitations in day-to-day life due to atrial fibrillation”, “feeling of discomfort due to atrial fibrillation”, “tiredness due to atrial fibrillation” and “worry/anxiety due to atrial fibrillation.” Each item could score 0 to 10. Symptom recurrence was documented by continuous ECG monitoring (implantable loop recorder). The generic health-related quality of life was measured by SF-36.

Results: In total 55 patients completed the forms at baseline and 52 at 24 months. The AF6 symptom score decreased in 77% of the patients, and the EHRA class improved in 56%. The mean AF6 score improved from baseline to 6 months (27±14 to 19±16) and further at 12 months (12±13), but stayed at this level at 24 months (13±14). All six items in AF6 improved. The physician-assessed EHRA class also improved over time, also from 12 to 24 months. The number of patients in EHRA class improved from 20 (42–28–44 at baseline, 6, 12 and 24 months) and decreased in EHRA II (23–10–15–7), III (13–4–2–0) and IV (1–0–0–0). EHRA classes most often improved by one class (II to I, n=20), (II to II, n=1), less often two or three classes (III to I, n=10), (IV to I, n=1).

Conclusions: Assessed symptom relief after AF ablation as perceived by the patient and the physician. Patient-perceived symptoms (AF6) significantly improved. The physician-estimated symptom improvement than the patient.

P4345 | BEDSIDE
Comparison in Long-Term Efficacy between First and Second Generation Cryoballoon Ablation Catheter


Introduction: Cryoballoon (CB) ablation has emerged as a novel treatment option for drug-refractory atrial fibrillation (AF). The second generation, CB Advance (ADV) catheter was redesigned with technical modifications resulting in a larger balloon’s surface aiming at procedural outcome improvement in the setting of AF ablation. Aim of the study is to compare the efficacy of the two different technologies on a long-term follow-up.

Methods: In total 120 patients were enrolled in this study. Sixty patients underwent CB using the first generation catheter and 60 patients with the ADV catheter. All patients enrolled completed 3 years of follow-up. All patients underwent regular blinded ECG recording and outpatient clinic evaluation every 3 months during the first year after ablation and annually thereafter.

Results: There was no significant difference between the two groups regarding patients’ characteristics including the age (59.1±12.2 vs 57.2±10.9 years re-
spectively; p=0.35), the left atrial area (22.0±6 vs 22.5±4.7 cm² respectively; p=0.61) and the left ventricular ejection fraction (62.5±5.6 vs 60.9±7.4% respectively; p=0.23). Procedures performed with the old balloon showed longer fluo-
roscopy time (56.3±26.8 vs 32.2±13.5 min respectively; p=0.0001) and longer procedure times as well (193.1±52 vs 162±44.8 min respectively; p=0.019). The overall long-term success was significantly different between the two groups (68.3 vs 86.7% respectively; p=0.017). Interestingly, no difference were found in the le-
sion area of left and right pulmonary vein between the two groups (respectively; p=0.61 and 0.57). There was one case of cerebral embolization among patients treated with the old balloon and one case of reversible phrenic nerve palsy for each group.

Conclusion: The ADV catheter compared to the first generation balloon allows to obtain a significantly higher success rate after a single procedure during the long-term follow-up. Fluoroscopy and procedural times were significantly longer in the first generation CB catheter group than in the ADV catheter group.

P4347 | BEDSIDE
Acute recovery of pulmonary vein conduction in contact force-optimized circumferential pulmonary vein isolation is associated with minor catheter tissue contact angles

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Background: Sufficient contact force (CF) during antral pulmonary vein isolation (PVI) with radiofrequency (RF) energy is associated with acutely durable PVI. All such reports concentrated on analysing total CF, however, the importance of lateral and axial contact force at the catheter tip has not been analysed. Axial CF enable the catheter tip to swing with the beating heart, whereas lateral CF is associated with more shifting on the tissue.

Objective: We assessed the impact of ablation catheter-tissue angle on acute pulmonary vein reconnection (PVR) after PVI with CF-guided RF ablation catheter.

Methods: Contact force-controlled RF ablation (SmartTouch, CARTO 3, Biosense Webster) for circumferential PVI was performed in 14 consecutive patients (pts; 8 male) with paroxysmal atrial fibrillation. Acute PVR was defined as recovery of pulmonary vein (PV) conduction after a 20 min waiting period and unmasking of dormant PV conduction by intravenous adenosine injection (at least 10 mg). Bipolar atrial potentials were detected in six segments. Point by point relationships between total CF values, ablation catheter-tissue angle and reconnected PV segments were evaluated.

Results: Acute PVR occurred in 26 PV segments. The mean CFs during RF ablation in no-reconnection and reconnection points were 12.4±4.4 and 10.1±4.6 g (p=0.09), however, reconnection occurred in 11% and 89% of segments with catheter-tissue angle above and below 45°, respectively. Reconnection was significantly associated with a predominant catheter-tissue angle of less than 45°.

Table 1

<table>
<thead>
<tr>
<th>Contact force angle</th>
<th>Acute PVR</th>
<th>45°</th>
<th>Acute PVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent (0°)</td>
<td>136 (96%)</td>
<td>6 (4%)</td>
<td>Present</td>
</tr>
<tr>
<td>Present</td>
<td>3 (11%)</td>
<td>23 (89%)</td>
<td></td>
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</table>
P4348 | SPOTLIGHT
Risk factors of recurrence of paroxysmal atrial fibrillation after radiofrequency catheter ablation
X.L. Zhang, H. Fu, X. Wei, Y.J. Liang, H. Tang. West China Hospital Sichuan University, Cardiology Department, chengdu, China, People's Republic of

Background: Looking for risk factors of recurrence after radiofrequency catheter ablation (RFCA) of paroxysmal atrial fibrillation (AF) is still the important goal

Purpose: To investigate the value of echocardiographic parameters of LA size and function in predicting the recurrence of AF after RFCA.

Methods: A cohort of 125 consecutive patients underwent PAF catheter ablation were included in our study. Real-time tri-plane echocardiography (RT-3PE) and quantitative tissue velocity imaging (QTVI) were used to evaluate the LA structure and function preoperatively (off-line EchoPac workstation). Patients were followed up 1, 3 and 6 months after RFCA. The symptoms, 12-lead ECG, 24hrs-Holter and echocardiography were followed up. The recurrence of PAF was defined as that AF recurred 3 months after RFCA. According to the recurrence of PAF, the patients were divided into two groups: the AF-NR group with 81 patients and the AF-R group with 34 patients.

Results: Univariate analysis showed that LADiap, mitral peak A, E/A ratio, LAVmax, LAVpI, LAVminI, LAAEF, LATEF, LAexpl, Va were related to the recurrence of PAF. In ROC curve analysis, the cutoff value of 32ml²/m² for baseline LAVmax was associated with a sensitivity of 67.2%, specificity of 62.4%, positive predictive value of 47.5%, and a negative predictive value of 75.8% (area under ROC curve, 0.674; 95% CI, 0.573–0.769) for AF recurrence. The cutoff value of 25% for LAAEF was associated with a sensitivity of 78.4%, specificity of 67.5%, positive predictive value of 56.8%, and a negative predictive value of 78.6%. Using of these echocardiographic parameters, the prediction rate was calculated.

Conclusion: LA size and function are related to the recurrence of PAF after RFCA. In patients undergoing PAF ablation, the LAA peak flow velocity is a marker of risk of recurrence. These findings suggest that this echocardiographic parameter can be used in addition to clinical variables for better selection of these patients.

P4349 | BEDSIDE
Low flow velocities in the left atrial appendage can predict atrial fibrillation recurrence in patients undergoing ablation
S. Guerreiro, R. Ribeiras, J. Abecasis, P. Adragao, F.B. Morgado, D. Cavaco, M.J. Andrade, M. Mendes. Hospital de Santa Cruz, Lisbon, Portugal

Background: Atrial fibrillation (AF) is the most common arrhythmia and the catheter ablation is one of the strategies used in the treatment of these patients. The aim of this study is to test if left atrial appendage (LAA) peak flow velocity, assessed by transesophageal echocardiography (TEE), can predict AF recurrence after catheter ablation.

Methods: Retrospective study of single centre including 91 patients (mean age 57±12 years; 71.4% male) who underwent AF catheter ablation between July 2011 and December 2012 and who underwent TEE pre-procedure. We excluded patients with severe valvular heart disease or prosthetic heart valve. The primary endpoint was the recurrence of AF.

Results: During a follow up of 2.1 years, the AF recurrence was seen in 25 patients (27%). The LAA flow velocity was lower in patients who had relapsed compared to those who did not (48 cm/s versus 63 cm/s respectively, p=0.007). Using a ROC curve, the best cut-off to predict the recurrence of AF was ≤ 70.1 cm/s. There was a statistically significant difference in the primary endpoint between the 2 groups of patients divided by this cut-off (see chart 1).

In patients with paroxysmal AF (73 patients) the LAA flow velocity was also lower in patients with AF recurrence compared to the others (49 cm/s vs 65cm/s, p=0.03). On the contrary in permanent AF (18 patients) there was no significant difference between the 2 groups.

Conclusion: In patients undergoing ablation of AF, the LAA peak flow velocity is a marker of risk of recurrence. These findings suggest that this echocardiographic parameter can be used in addition to clinical variables for better selection of these patients.

P4350 | BEDSIDE
Pulmonary vein reconnection: is contact force more important than stability?
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Background: Pulmonary vein reconnection has been described as a frequent cause for atrial fibrillation recurrence after ablation. Contact force catheters have been recently developed and radiofrequency delivery with over 10g of force related to improved outcomes. All new technology value pressure and radiofrequency power to determine a better lesion. The aim of our study was to compare the pulmonary vein reconnection rate after pulmonary vein isolation with magnetic navigation (contact force under 5 gr and high catheter stability) with manual navigation (higher pressure, lower stability).

Methods: and results: Thirty-three patients were compared. 124 consecutive patients submitted to atrial fibrillation re-ablation with magnetic navigation (14.0% of 885 patients) and 125 consecutive patients submitted to re-ablation with manual navigation (14.4% of a series of 868 patients). Pulmonary vein reconnection rates were analyzed and the more common veins to recur were described. At least one pulmonary vein was reconnected in 116 procedures (93.6%) of the magnetic group versus 114 (91.2%) in manual navigation group. The number of reconnected veins on the different groups were (magnetic vs manual respectively) four veins in 40 procedures (32.3%) vs 52 (41.6%); three veins in 26 procedures (23.4%) vs 11 (8.9%); two in 30 procedures (24.2%) vs 37 (26.9%) and one in 17 procedures (13.7%) vs 14 (11.2%) (p=NS). In the manual group, the first procedure was performed with contact force catheter in 21 procedures (16.8%). During re-ablation, in the manual group, the number of reconnected veins was not different whether the first procedure was performed with contact force catheter or not (at least one reconnected vein in 90.5% of the procedures and four reconnected veins in 52.6%). In both groups (magnetic and manual) the commonest reconnected vein was the right superior (75.8% vs 72.8%) followed by the right inferior (65.3% vs 71.2%). The left superior vein was reconnected in 61.3% vs 58.3% of the procedures and the left inferior in 59.7% vs 60.6% (p=NS).

Conclusion: The majority of patients submitted to atrial fibrillation re-ablation have more than one reconnected vein. We didn’t observe a significant difference whether first ablation was performed with magnetic navigation (lower pressure and high stability) or manual navigation catheters and thus a higher pressure during radiofrequency delivery didn’t correlate with lower prevalence of reconnected veins.

Long term efficacy of the radiofrequency ablation depends on an adequate ablation with magnetic navigation or manual navigation catheters. This study suggests no significant difference whether first ablation was performed with magnetic navigation (lower pressure and high stability) or manual navigation catheters and thus a higher pressure during radiofrequency delivery didn’t correlate with lower prevalence of reconnected veins.

References: Our study was performed using new Ticar technology (contact force under 5 gr and high catheter stability) with manual navigation (higher pressure, lower stability). Ablation of atrial fibrillation I / Ablation of atrial fibrillation II 731
Ablation of atrial fibrillation II

Acknowledgement/Funding: Study performed by the support of National Telemedicine Center, Olomouc, Czech Republic.

P4352 | BEDSIDE

Left atrial surface area that remains not isolated after ablation of persistent atrial fibrillation predicts long term outcomes

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Introduction: Arrhythmia recurrence following catheter ablation of persistent atrial fibrillation (AF) is high compared with paroxysmal AF. Patients often have larger atria that require more extensive ablation in addition to pulmonary vein isolation (PVI). However, the quantification and impact of isolated and non-isolated left atrial surface area (LASA) remains unevaluated.

Aims: To utilize cardiac computed tomography and electro-anatomical navigation system to evaluate the impact of isolated and non-isolated LASA on long-term arrhythmia recurrence after PVI.

Methods: We recruited 164 patients (female 31, age 60±10 years) presenting for catheter ablation with highly symptomatic AF (paroxysmal 95, persistent 69). Pre-procedural cardiac CT’s were acquired and merged with a three dimensional non-fluoroscopic mapping system (CARTO-XP, Biosense Webster). Existing software was used to calculate total LASA. Post procedurally, the surface area enclosed by ablation lesions (marked manually during the procedure) was calculated to determine the LASA not isolated and proportion of LASA isolated. Parameters were correlated with arrhythmia recurrence in patients with persistent and paroxysmal AF after 62±9 months follow up.

Results: One hundred and four (63%) patients had recurrent arrhythmia after AF ablation (paroxysmal 54, persistent 50). Persistent AF patients with arrhythmia recurrence had significantly higher total LASA (202.3±34.6 cm² vs 185.7±30.0 cm², p=0.05), higher LASA not isolated (150.5±28.2 cm² vs. 127.9±21.0 cm², p<0.002) and lower proportions of LASA isolated (25.6±6.3% vs 30.7±8.3%, p=0.008), compared with patients without recurrence. However, in the paroxysmal AF group there were no differences between patients with and without recurrence. Multivariate survival analysis utilizing a Cox regression model demonstrated LASA not isolated >145 cm² independently predicted AF recurrence in persistent AF patients (HR 2.66 95% CI (1.47, 4.80), p=0.001).

Conclusion: LASA not isolated is an important predictor of AF recurrence after ablation of persistent but not paroxysmal AF. Importantly, LASA not isolated is an important predictor of AF recurrence after initial PVI in patients with both PAF and PEF (PAF: HR 1.04, 95% CI 1.01 –1.06, p=0.008; PEF: HR 1.04, 95% CI 1.01 –1.07, p=0.002). However, AF was an independent predictor of AF recurrence after initial PVI in patients with PAF (HR 1.03, 95% CI 1.00 –1.06, p=0.034) but not in those with PEF. In patients with AF, the sensitivity and specificity of an LASA >145 cm² to predict AF recurrence were 67% and 68%, respectively (HR 3.12, 95% CI 1.38 –7.67, p=0.005). In Kaplan-Meier analysis, the incidence of AF recurrence was significantly higher in patients with AHI >14.1 (n=37) than in those with AHI <14.1 (n=46) in patients with PAF (P<0.004) (Figure).

Acknowledgement/Funding: National Health and Medical Research Council of Australia grant (ID Nos: 512223).

P4353 | BEDSIDE

Low amplitude of fibrillatory waves on surface ecg predicts non-responder for ablation in patients with long-standing persistent AF

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Background: Catheter ablation of long-standing persistent atrial fibrillation (AF) was a challenging task.

Purpose: To evaluate the characteristics of non-responder for ablation in patients with long-standing persistent AF.

Methods: Eighty-eight consecutive patients (78% men, age 66±9, LAD 49±6mm, duration of continuous AF 69±67 months) who underwent long-standing persistent AF ablation and were followed at least 12 months were enrolled in this study. Mean amplitude of fibrillatory-waves (f-waves) were measured in V1. Pulmonary vein (PV) isolation, superior vena cava isolation, non-PV foci ablation, and linear ablation including roof line, bottom line, and mitral isthmus line were performed. The recurrent AF was evaluated through auto-triggered external loop recorder for 7 days (3, 6, 12, 24 months after ablation). Non-responder was defined as patients who responded as persistent form even if using antiarrhythmic drugs after the last session. The duration of continuous AF, echocardiographic parameters, the presence of structural heart disease, AF cycle length and mean amplitude of f-waves were analyzed with respect to clinical success and non-responder after ablation. To analyze independent predictive factors of clinical success and non-responder after ablation, univariate factors presenting p<0.01 were analyzed using logistic regression (multivariate analysis).

Results: After the last procedure (mean 1.2±0.4 procedures), the clinical success rate with or without any antiarrhythmic drugs was 71%, while the rate of non-responder was 19%. Follow-up period was 16±9 months. In the univariate analysis, the duration of continuous AF (p=0.018) and mean amplitude of f-waves (p=0.005) were associated with non-responder and the duration of continuous AF (p=0.019) and mean amplitude of f-waves (p=0.018) were associated with clinical success. The mean amplitude of f-waves (p=0.004) was the only independent predictor of non-responder. There was no independent predictor of clinical success. At a cut-off point <0.85mV identified ROC curve, the positive and negative predictive values of the mean amplitude of f-waves to predict non-responder were 75% and 89%, respectively.

Conclusion: Low amplitude of f-waves in V1 predicted non-responder for ablation in patients with long-standing persistent AF.

P4354 | BEDSIDE

Apnea-hypopnea index evaluated by type-3 portable monitoring predicts outcome following initial pulmonary vein isolation in patients with paroxysmal atrial fibrillation

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Background: Sleep-disordered breathing (SDB) is a predictor of atrial fibrillation (AF) recurrence following pulmonary vein isolation (PVI). However, the relationship between PVI outcome and SDB evaluated using type-3 portable monitoring (PM) is still unknown.

Purpose: The purpose of this study was to investigate high risk patients with AF recurrence after initial PVI using the apnea-hypopnea index (AHI) measured by type-3 PM.

Methods: One hundred twenty-four consecutive AF patients who underwent initial PVI were enrolled. There were 85 males; the average age was 62±10 years, 83 had paroxysmal AF (PAF) and 41 had persistent AF (PEF). AHI was measured by type-3 PM in all patients.

Results: AHI measured by type-3 PM in all patients.

Conclusion: AH measured by type-3 PM is a useful predictor of outcome follow ing initial PVI in patients with PAF.

P4355 | BEDSIDE

Different right atrial conduction pattern between paroxysmal and persistent atrial fibrillation

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Background: The fastest interatrial pathways (FIP), which impulses travel from the earliest atrial activation site (EAS) via the FIPs to the AV node (AVN), have been contested.

Purpose: To determine the earliest atrial activation time using the FIPs from the earliest atrial activation site (EAS) via the FIPs to the AVN between the sinus to the AV node (AVN), have been contested. To analyze independent predictive factors of clinical success and non-responder after ablation, univariate factors presenting p<0.01 were analyzed using logistic regression (multivariate analysis).

Methods: One hundred twenty-four consecutive AF patients who underwent initial PVI in patients with paroxysmal AF were enrolled. There were 85 males; the average age was 62±10 years, 83 had paroxysmal AF (PAF) and 41 had persistent AF (PEF). AHI was measured by type-3 PM in all patients.

Results: AHI measured by type-3 PM is a useful predictor of outcome follow ing initial PVI in patients with PAF.
Conclusion: The patients with paroxysmal AF had more cranially located EAS and more anteriorly descending FIP at baseline. In persistent AF, after sympathetic stimulation, the EAS and the FIP showed upward shift. The location of the EAS and the FIP was well correlated in most patients, suggesting that the FIP was selected by the EAS rather than the preexisting inferopartrial interatrial pathway.

P4356 | BEDSIDE
Acute changes during atrial fibrillation ablation targeting rotor sources
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Background: Catheter ablation of atrial fibrillation (AF) is an established method for patients with paroxysmal AF and for selected patients with persistent AF. Substrate ablation targeting rotor activities has emerged as an interesting new method that aims to modify the sustaining mechanism of atrial fibrillation (AF).

Purpose: To evaluate the frequency of AF modifications during ablation of focal sources in the right and left atria. The primary endpoint was acute AF termination or organization (change to atrial tachycardia (AT) or ≥10 cycle length prolongation).

Methods: Fourteen patients (70±8 years, 7 males) undergoing catheter ablation of paroxysmal AF and persistent AF (respectively 4 and 10 patients) were investigated using the FIRM (focal impulse and rotator mapping) 64 poles basket catheter during biaxial three-dimensional mapping. The FIRM map was obtained in different placement firstly in the right atrium and after right-sided ablation it was delivered transeptally into the left atrium. The rotator activities (spiral waves) were targeted with an irrigated catheter. No focal source was identified. All the patients underwent to pulmonary vein isolation after ablation at rotor sources.

Results: Rotor activities were documented in both atria (right atrial rotors ≥1.1 [range 1–3], left atrial rotors ≥0.8 [range 0–3]). The primary endpoint was achieved in 9 patients. AF organization to AT was documented in 5/14 (36%) pts of which 4/5 in the right atrium. A prolongation of AF cycle length was documented in 3/14 (21%) pts: in one patient the modification was documented during rotors ablation in both atria and in each atrium in the other 2 pts. Acute termination of AF was documented in one patient during ablation at rotor source area in the posterior antrum of left inferior pulmonary vein. Ablation in the right atrium led to primary endpoint in 6/9 patients (66%).

Conclusions: These initial results suggest that also the right atrium plays an important role in sustaining atrial fibrillation. Ablation at sites of rotational activities in both atria has led to acute AF termination or AF organization in 65% of patient population.

P4357 | BEDSIDE
Baroreflex, heart rate and blood pressure variability after circumferential pulmonary vein ablation: a 2-year follow-up pilot study
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Background: Impact of circumferential pulmonary vein ablation (CPVA) on heart rate variability (HRV) has been reported but there is no data evaluating baroreflex sensitivity (BRS) and blood pressure (BP) variability after such a procedure.

Purpose: To examine the long-term effects of CPVA on cardiac autonomic function.

Methods: CPVA was performed in 9 patients with paroxysmal atrial fibrillation. Beat-to-beat HR and systolic BP time series were calculated respectively from analog ECGs and non-invasive BP waveforms using a software (RECAN) during 10-min recordings in supine and standing positions. We also recorded mean HR, HRV using time domain (RMSSD, SDNN) and spectral (HF power) analysis as well as BP variability (standard deviation -SD- of systolic BP) on selected 5 min periods with stationary HR and systolic BP. BRS was assessed using the sequence method on 10 min periods. We defined 5 time points: the day before CPVA (preablation), 24 h, 3 months, 1 year and 2 years after CPVA. As the study is not finished yet, statistical analysis was not performed. Data are presented in the table as mean±SD.

Results: Mean age was 61±8 years. At 1 year, AF recurrence occurred in 3 patients (24 h after CPVA, in all patients, mean HR increased and HRV and BRS decreased as compared to preablation in both supine and standing positions. At 2 years, 3 of 5 recorded patients had persistent HRV and BRS attenuation while BP variability and mean HR remained high.

Conclusion(s): CPVA may be associated with persistent parasympathetic withdrawal. A prospective study is ongoing to exclude confounding factors (e.g., age, medication) and examine clinical consequences of CPVA-induced cardiac autonomic modulation.

P4358 | BEDSIDE
Long-term outcome and predictors of atrial tachycardia recurrence following catheter ablation of left atrial flutter

Introduction: Recurrent left atrial flutter (LAF) is a challenging ablation procedure. Left atrial linear ablation for atrial fibrillation (AF) may be proarrhythmic, leading to left atrial macro-reentrant tachycardia. There are still missing data regarding LAF outcome and recurrence predictors.

Objectives: The aim of this study was to evaluate the clinical characteristics, the outcome and the recurrence predictors after left atrial flutter ablation.

Methods: Between January 2011 and September 2014, LAF ablation was performed in 92 patients (85% after AF ablation). Follow-up was done on all patients after the procedure.

Results: Mean number of procedures per patient was 2.0±0.75. Mean recovery time was 20±22.7 months. During the last procedure, the critical isthmus was the same as the index procedure in 50.7% patients. Mital isthmus (MI) or roof conduction block at the last procedure was achieved in 48.1% patients despite acute conduction block during the index procedure. MI and the roof block were achieved in 89.7% patients during the last procedure. A recurrence of left atrial flutter was documented in 21 patients (22.8%). In univariate analysis, predictive of recurrence were female gender with OR=4.3, CI95% 1.3–14.2, P=0.012, and cardioversion at the end of the last procedure with OR=8.7, CI95% 1.9–39.2, P<0.001. In multivariate analysis, both of them were independent predictors (OR=8.7, CI95% 1.9–39.2, P=0.007 and OR=11.9, 95% CI 2.5–58.0, P=0.002 respectively). In patients with non bidirectional conduction block at the last procedure, there was non-significant trend for recurrence (44.4% vs. 22.4%, P=0.15).

Conclusion: This study allowed to assess the follow up of patients who underwent left atrial flutter ablation. The absence of restoration of sinus rhythm during ablation and female gender are predictors of recurrence.

P4359 | BEDSIDE
LA fibrosis predicts LVEF improvement in HF patients undergoing AF ablation

Background: In pts. with heart failure (HF) and atrial fibrillation (AF) improvement of left ventricular ejection fraction (LVEF) has been described following AF catheter ablation. Not all HF pts. benefit the same way. Furthermore, presence and amount of left atrial (LA) fibrosis is increasingly recognized as a marker of advanced AF disease status and predictor of ablation success. We thought to investigate the relationship between LA fibrosis and the extent of LVEF improvement in HF patients after successful AF ablation.

Methods: Forty-six pts. (36 male, median 64 years, median LVEF 30%, 31 DCM) underwent catheter ablation of symptomatic AF (37 persistent AF). Pulmonary vein (PV) isolation was performed in all pts. LA voltage mapping was used to identify low voltage zones (LVZ; threshold <0.5mV) outside PVs as surrogate of LA fibrosis. Individualized linear ablation lines were added to dissect/isolate/connect LVZs as substrate modification. Follow-up (FU) was performed with device-based

Abstract P4357 – Table 1. HR and BP variability indices at baseline (preablation), 24 h, 3 months, 1 year and 2 years after CPVA

Preablation (n=9) 24 h (n=9) 3 months (n=8) 1 year (n=5) 2 years (n=5)
supine standing supine standing supine standing supine standing supine standing

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<tr>
<th>Index</th>
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<th>3 months</th>
<th>1 year</th>
<th>2 years</th>
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<td>rMMSD</td>
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<td>SDNN</td>
<td>36.9±18.2</td>
<td>33±18</td>
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<td>In HF RR</td>
<td>3.9±1.4</td>
<td>3±1.2</td>
<td>1±4.2</td>
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<tr>
<td>SD SBP</td>
<td>6.5±1.7</td>
<td>8.5±2.8</td>
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<tr>
<td>BRS</td>
<td>8.2±5.9</td>
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<td>1.2±0.4</td>
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Ablation of atrial fibrillation II / Ablation of atrial fibrillation III

P4360 | SPOTLIGHT
An increased sympathetic tone after ablation predicts recurrence of atrial fibrillation: Investigation using cardiac iodine-123-metaiodobenzylguanidine (123I-MIBG) scintigraphy.


Kansai Rosai Hospital, Cardiovascular Center, Amagasaki, Japan; 2Osaka University Graduate School of Medicine, Cardiology, Suita, Japan;

Purpose: To investigate the factors associated with the AF recurrence after catheter ablation, including the pre- and post-procedural sympathetic nervous activity assessed by cardiac iodine-123-metaiodobenzylguanidine (123I-MIBG) scintigraphy.

Methods: Forty consecutive patients scheduled for AF ablation were enrolled. Extensive encircling pulmonary vein isolation was performed in all patients. At baseline and 3 months after ablation, 123I-MIBG scintigraphy was performed. The heart to mediastinum ratio of the 123I-MIBG uptake, a marker of the sympathetic nervous distribution, was measured at 15 min (H/M15min) and 240 min (H/M240min). Washout rate (WR) was also evaluated as a marker of the sympathetic nervous tone.

Results: During a mean follow-up period of 11±4 months after ablation, excluding the blanking period of the initial 3 months, 8 (20%) patients developed AF recurrence. There were no differences in the age, sex, type of AF between the patients with and without LVZs. However, the washout rate (WR) at 3 months after ablation 41.3±4.8 was significantly lower in patients with LVZs compared to patients without LVZs 30.9±10.1 (p=0.003). In multivariate analysis washout rate and presence of LVZs were significantly associated with AF recurrence. In particular, LVZs were an even more significant predictor than washout rate in the multivariate model (p=0.02). The area under the ROC curve was 0.87.

Conclusions: An increased sympathetic nervous tone 3 months after ablation is a reliable predictor of AF recurrence.

P4361 | BEDSIDE
Pulmonary vein isolation suffices for the first session but not for the second in ablation of persistent atrial fibrillation

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Japan; 1National Hospital Organization Tokyo Medical Center, Department of Cardiology, Tokyo, Japan; 2Keio University Hospital, Department of Cardiology, Tokyo, Japan;

Purpose: Pulmonary vein isolation (PVI) is an effective and safe therapy for the paroxysmal form of atrial fibrillation (PAF). Nevertheless, radiation exposure still remains a major concern to most electrophysiologists. The CARTOUnivu™ Module is a novel, advanced image integration module for the CARTO® 3 System. It combines fluoruo images with 3D-electro-anatomical maps into a single accurate 3D-view on the CARTO® 3 System. We report our results working with this novel system in terms of procedural radiation exposure reductions.

Methods: This study is designed as a randomized controlled trial. Between June 2014 and November 2014, a total of 60 patients with PAF (74% male, 64±9 years), who underwent PVI with the endpoint of unexcitibility of the ablation line, were randomized to either image integration module (IIM, CARTOUnivu™ Module) additional to a conventional 3D mapping system or to only conventional 3D mapping system (CARTO® 3 System).

Results: There was no significant difference in mean age, gender distribution and body mass index between the two groups. The median ablation procedure time was 143 min in both groups. A significant decrease of median fluoroscopy time from 12.09 min to 09.00 min (p<0.0006) and median fluoroscopy dose from 883 cGy cm² to 476 cGy cm² (p<0.001) was achieved (Table I). No major complications occurred during the procedures in either group.

Table 1. Results

<table>
<thead>
<tr>
<th>Procedure duration (min)</th>
<th>CARTOUnivu™</th>
<th>CARTO® 3</th>
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<td>143±36</td>
<td>143±40</td>
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<th>Fluoroscopy time (min)</th>
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<th>Area dose product (cGy² cm)</th>
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</table>

Conclusions: CARTOUnivu™ Module easily integrates into the workflow of pulmonary vein isolation with the endpoint of unexcitibility of the ablation line without prolonging the procedure time. It is associated with a more than 50% reduction in fluoroscopy dose when compared to a conventional 3D-mapping system.

P4363 | BEDSIDE
Clinical characteristics and outcomes of adenosine induced atrial fibrillation after pulmonary vein isolation

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Introduction: Adenosine (ADE) has been used to identify dormant pulmonary

<table>
<thead>
<tr>
<th>HR</th>
<th>95% CI</th>
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<th>HR</th>
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<td>0.97</td>
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<tr>
<td>0.39</td>
<td>0.47–1.18</td>
<td>0.41</td>
<td>0.26</td>
<td>0.12–0.52</td>
<td>0.27</td>
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<tr>
<td>0.29</td>
<td>0.37–1.11</td>
<td>0.04</td>
<td>0.98</td>
<td>1.10–0.76</td>
<td>0.21</td>
</tr>
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Abstract P4360 – Clinical parameters associated with the recurrence of atrial fibrillation after ablation

<table>
<thead>
<tr>
<th>With</th>
<th>Without</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years old</td>
<td>65±7</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>7 (88)</td>
</tr>
<tr>
<td>Persistent atrial fibrillation, n (%)</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Left atrial volume index, cm³/m²</td>
<td>49±29</td>
</tr>
<tr>
<td>HM/MV of baseline</td>
<td>1.98±0.18</td>
</tr>
<tr>
<td>HM/MV of baseline</td>
<td>1.98±0.21</td>
</tr>
<tr>
<td>WR at baseline</td>
<td>36.3±9.3</td>
</tr>
<tr>
<td>WR at baseline</td>
<td>2.08±0.13</td>
</tr>
<tr>
<td>WR at 3 months after ablation</td>
<td>1.94±0.15</td>
</tr>
</tbody>
</table>

Conclusion: There was no significant difference in mean age, gender distribution and body mass index between the two groups. The median ablation procedure time was 143 min in both groups. A significant decrease of median fluoroscopy time from 12.09 min to 09.00 min (p<0.0006) and median fluoroscopy dose from 883 cGy cm² to 476 cGy cm² (p<0.001) was achieved (Table I). No major complications occurred during the procedures in either group.

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Ablation of atrial fibrillation III 735

vein (PV) conduction after PV isolation (PVI) in patients with atrial fibrillation (AF). ADE is also known to have a potential to induce AF, even if it was rarely reported. The mechanism responsible for ADE induced AF is not clearly known. Previous reports suggested that ADE induced proarrhythmic effects through shortening atrial action potential duration and refractoriness. Recently ADE is known to result in atrial fibrillation as in vagally mediated AF, in which acetylcholine like signal transduction cascade via specific G protein-coupled receptor mediated. This study presents 12 cases with ADE induced AF and clinical outcomes of these patients after PVI.

Methods: Total 141 consecutive patients (87% male, 55±10 years) with AF who underwent PVI. AF duration conduction test with 12mg ADE were included. Among them, AF was induced in 12 patients (8.5%) within 2 minutes after ADE.

Results: The patients diagnosed as paroxysmal AF were 78.7% and the others as non-paroxysmal AF were 21.3%. The dormant PVI AF duration test was performed in 20.6% of patients. The ADE induced AF was documented in 12 (8.5%) patients. The sites harboring trigger of ADE induced AF were variable, including PV inside (n=6), vein of Marshall (n=3), coronary sinus (n=1), right atrial septum (n=2), right atrial crista terminals (n=2), superior vena cava (n=1) and right atrial appendage (n=1). All 12 patients (male 75.0%, age 52.5±2.8) with ADE induced AF had a paroxysmal AF and underwent additional ablation until AF was no longer induced. The recurrence rate of these patients was 25% and that of patients (male 88.4%, age 55.4±0.9) without ADE induced AF was 12.9% (p=0.449).

Conclusion: ADE induced AF occurred in 8.5% of patients while testing dormant conduction after PVI and only in patients diagnosed as paroxysmal AF. The recurrence rate of these patients was 25%, which is higher trend than that of patients without ADE induced AF was 12.9% (p=0.449). Further study including larger number of the patients with longer follow up is warranted to see clinical significance of ADE induced AF post-PVI.

Acknowledgement/Funding: None

P4364 | BEDSIDE
Long-term results of a surgical treatment of stand-alone atrial fibrillation with the use of right thoracoscopic approach and a microwave or monopolar radiofrequency energy source

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Background: Minimally invasive surgery for atrial fibrillation (AF) is going through a rapid development lately. The long-term efficacy of most of these procedures is poorly known.

Methods: Patients with drug-resistant, symptomatic, stand-alone AF were enrolled. They underwent fully thoracoscopic, unilateral, off-pump surgical ablation. Microwave or monopolar radiofrequency energy system was used to create a box lesion (isolation of all pulmonary veins and left posterior atrial wall). Patients were prospectively followed at 1, 3, 6, 9, 12 months and every six months further using ECG and Holter monitoring. Additional catheter ablation was offered to patients with recurrence of arrhythmia.

Results: Between 2006 and 2010, 38 patients underwent the procedure (age 60±11 years, body mass index 24±3 kg/m2, left ventricular ejection fraction 51±7%, New York Heart Association class 3±1). Sixteen patients (42%) had paroxysmal, 9 (24%) persistent and 13 (34%) long-standing persistent AF. We had no hospital deaths, one conversion to sternotomy because of bleeding. Mean follow-up duration was 70±19 (range 20–90) months. Arrhythmia-free survival rates after the procedure were 50%, 44.4%, 24.1% and 10.8% at 6, 12, 36 and 60 months, respectively, with most recurrences over the first 6 months. Twelve patients underwent one or more additional catheter ablations and since the last intervention, 75% of them were in stable sinus rhythm (SR) with a mean follow up of 31±23 months. Overall, at the end of follow-up, only 3 patients maintained in SR without any arrhythmia recurrence. Major complications (cerebral or peripheral embolism or bleeding) occurred in 5 patients.

Conclusions: Unilateral, thoracoscopic AF ablation is safe and technically feasible procedure. However, clinical results of microwave and monopolar radiofrequency devices are less than satisfactory, with gradual decline in arrhythmia-free survival over long term follow-up.

Acknowledgement/Funding: Charles University Cardiovascular Research Programe PRVOUK P35

P4365 | BENCH
A phantom study to assess the accuracy of a new electromagnetic catheter guidance technology (MediGuide).

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Introduction: This study is the first to quantify the accuracy of catheter localization for the new MediGuide technology based on phantom experiments.

Materials and methods: A realistic heart phantom was generated in a 3D-Photo software. When a heart was generated, the phantom containing holes as location markers. The phantom itself served as ground-truth reference to ensure exact and reproducible catheter placement during the experiments. A MediGuide ablation catheter was repeatedly tagged at selected phantom holes to assess accuracy of point localization (n=40) by means of localization reproducibility. The catheter was additionally used to acquire a MediGuide-scaled geometry in NavX. The acquired geometry (MediGuide-scaled and not-MediGuide-scaled) was fused with a CT segmentation of the heart phantom in order to quantify their concordance. Distances between landmarks were measured in the (not-) MediGuide-scaled geometry and the CT dataset for Bland-Altman-comparison.

Results: Point localization performance was 0.5±1.3 mm. The 3D-accuracy of the geometries were 1.1±1.4mm (MediGuide-scaled) and 3.2±1.6mm (not MediGuide-scaled). The Bland-Altman plots comparing distance measurements are shown in the figure.

Figure 1. Bland-Altman plots comparing distance measurements between MediGuide, EnSite and the CT dataset.

Conclusions: The MediGuide system showed a high level of accuracy, which can be ascribed to the magnetic field localization technology; the observed offsets between the geometry visualization and the real phantom were below a clinically relevant threshold.

P4366 | BEDSIDE
Differences in X-ray dose in patient and physician during pulmonary vein isolation

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Background: The circumferential HF ablation in combination with a 3D mapping system (HF) is accepted as the gold standard for this procedure. Competing in addition stand the Cryoballoon (CB) as well as the robotic navigated PVI (RN) side by side. But the resultant x-ray exposure for the patient and physician could be different by compete methods and was examined in this study.

Methods: From January to November 2014 all PVI n=108 were investigated with a GE Innova by two investigators. The x-ray exposition at the patient’s entrance side by side. But the resultant x-ray exposition for the patient and physician could be different by compete methods and was examined in this study.

Results: The procedure and fluoroscopy time of CB was significant shorter than
HF and robotic navigated RN (114 versus 162 versus 202 min; 17 versus 25 versus 24 min). The dose area product (DAP) was significant lower for CB than for HF and RN (2.037 versus 3075 and 2510 cGy/cm²).

Conclusion: Potential advantages in fluoroscopy and procedure time of CB are not reflected in the x-ray dose of the patient. The x-ray dose for patient in group CB are significant higher than in HF and RN.

P4360 | BEDSIDE
Treatment of atrial fibrillation using second-generation cryo balloon: characteristics of recurrences and periprocedural findings during re-do procedures
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Background: Two years ago a second-generation CB was introduced, aiming more uniform and durable lesions. First mid-term results have been reported, showing significantly higher efficacy as compared to first generation CB. Our aim was to evaluate characteristics of recurrences after PVI with second-generation CB and intraprocedural findings in pts., who underwent repeated ablation for AF.

Methods: Consecutive pts with symptomatic paroxysmal or persistent AF were included. After a single transseptal access PVI was performed utilizing a 28 mm second-generation cryoballoon (Arctic Front Advance™, Medtronic Inc.) and an Achieve™ catheter. In pts with persistent AF, who didn’t convert into SR during additional cryo applications between LSPV and RSPV were performed, creating roof line. Conduction block across the LA roof was assessed using developed differential pacing maneuvers. After ablation all pts were prospectively followed with 7 days Holter ECG recordings every three months. The first three months were considered as the blanking period. Primary end point was defined as occurrence of any atrial arrhythmia > 30 sec without antaryrhythmic drugs. Pts. with symptomatic recurrences of atrial arrhythmias after blanking period underwent repeated ablations or were treated with AADs according to their preference.

Results: We included 348 pts (214 female, 88 persistent AF, age 59±0.6 years, EF 61±0.3%, LA area 20±0.2 cm², CHA2DS2-VASc 1.6±0.1). The mean procedure duration was 213±03 h with a fluoroscopy time of 21±0.5 min. Roof line was created in all pts. After a mean follow up of 14±0.4 months 47 pts (14%) have reached primary endpoint. 35 pts (75%) have developed AF, 5 (11%) both AF+ ATs, 6 (13%) AF’s only and 1 (2%) typical atrial flutter. The rate of ATs didn’t differ between pts treated with and without roof line (4.4% and 3% respectively, p=ns). 22 pts (48%) underwent repeated ablation. During re-do procedure we found reconnection of all PVs only in 2 pts (9%), of ≥ 2 PVs in 6 (27%), 1 PV in 7 (32%) and persistent isolation of all 4 PVs in 7 pts (32%). Reconnection of LSPV occurred in 6 pts (27%), LIPV in 9 (41%), RSPV in 8 (36%) and RIPV in 8 pts (36%) respectively.

Conclusion: The majority of AF/AT recurrences after initial PVI with second-generation CB seem to be still caused by recovery of PV conduction. Nonetheless almost one third of pts with recurrences have revealed non PV dependent arrhythmias during repeated ablation. Creation of additional linear lesion at LA roof with a second-generation CB didn’t increase rate of LA tachycardias.

P4369 | BEDSIDE
Long-term outcome and the mechanisms of pulmonary antrum radial-linear ablation in patients with paroxysmal atrial fibrillation
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Background: The aim of this study was to determine the mechanisms and effectiveness of pulmonary antrum radial-linear (PAR) ablation in comparison with pulmonary vein isolation (PVI) in patients with paroxysmal atrial fibrillation (AF) after a long-term follow-up.

Methods: A total of 135 patients with documented paroxysmal AF were enrolled from 5 centers and randomized to PVI or PAR group. CARTO was used for left atrial mapping. Event ECG recorder and Holter monitoring were conducted during the follow-up for all patients.

Results: The procedure time was 151±23 min in PAR group and 178±43 min in PVI group (P=0.001). The fluoroscopy time was 21±7 min in PAR group and 27±11 min in PVI group (P=0.002). AF triggering foci were eliminated in 59 patients (89.4%) in PAR group compared to 4 patients (6.0%) in PVI group (P=0.001). Vagal reflex occurred during ablation in 48 patients (72.7%) in PAR group compared to 26 patients (38.8%) in PVI group (P=0.001). At median 36 months of follow-up after single ablation procedure, 43 of 66 patients in PAR group (65%) and 28 of 67 patients in PVI group (42%) had no recurrence of AF off antiarrhythmic drug (AAD) (P=0.007); and 47 of 66 patients in PAR group (71%) and 32 of 67 patients in PVI group (46%) had no recurrence of AF with AAD (P=0.006). At the last follow-up, the burden of AF was significantly lower in PAR group than in PVI group (0.3% ± 2.3% vs 4.9% ± 9.9%; P=0.008). No major adverse event was observed except one pericardial tamponade.

Conclusion: The data suggest that PAR ablation is a simple, safe, and effective strategy for the treatment of paroxysmal AF with better long-term outcome than PVI. PAR ablation may work with multiple effective mechanisms against multiple AF mechanisms.

Acknowledgement/Funding: National natural science foundation of China/Registration Number:CHCTR-TRC-11001191
Objective: To investigate the impact of left atrial epicardial adiposity on recurrence of AF after catheter ablation.

Methods: From 2009 to 2010, consecutive patients with AF who underwent circumferential pulmonary vein ablation guided by 3-D mapping system were enrolled in the retrospective study. Left atrial (LA) epicardial fat thickness was measured in consecutive cardiac CT angiograms performed for AF. Patients were grouped by AF burden: paroxysmal (n=100), or persistent (n=49) AF. The short-axis view was reconstructed as a plane perpendicular to the long axis of these 2 views at the level of the mid LA. In this short-axis view, the pericardial epicardial fat thickness was measured at the esophagus (LA-ESO), main pulmonary artery (LA-PA), and descending thoracic aorta (LA-TA). A short-axis view at the mid LA, perilateral epicardial fat thickness was measured at the esophagus (LA-ESO), main pulmonary artery, and thoracic aorta.

Results: 100 had paroxysmal AF, and 49 had persistent AF. The association between AF burden by grade (paroxysmal 1, persistent 2), Perilatinal LA-ESO fat thickness was assessed by ordinal logistic regression. Univariate, LA-ESO, LA-TA, LA-PA, and LAD were significant predictor of AF burden. After adjusting for age, BMI, LA-LA-PA-LAD and LAD, the association remained significant. Of 149 patients, 98 (65.8%) remained free of recurrence after a single ablation procedure after 12 month follow-up. The recurrence patients had a significantly thicker LA-ESO fat pad than the normal patients after ablation. LA-ESO fat depots were individually predictive of the recurrence of AF.

Conclusions: Left atrial epicardial adiposity is associated with the burden of AF, and poorer outcomes after AF ablation. LA-ESO fat depots were individually predictive of the recurrence of AF.

P4371 | BEDSIDE
Impact of right atrial lines on eight-line rhythm outcome following bipolar radiofrequencymaze

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Background: Eight-year clinical results of surgical bipolar radiofrequency (BRF) atrial fibrillation (AF) ablation were analyzed.

Methods: One hundred and twenty-two patients undergoing BRF without (n=57) or with (n=65) concomitant right atrial (RA) RA ablation were assessed for sinus rhythm recovery at a median follow up of 38.8 months (27.0–86.5). A competing risk model was used to appropriately estimate the incidence of AF and surgical techniques were analyzed for their association with AF recurrence employing a competing risk regression corrected for atrial dimensions using sub-hazard ratios (SHRs) as measure of association.

Results: The percentage of patients in normal sinus rhythm and off- antiarrhythmia drugs were 75.4% (n=43) in the RA ablation and 56.9% (n=37) in the no-RA ablation Groups (p<0.001). Eight-year cumulative incidence of AF recurrence was significantly lower in the Group receiving RA lines (Figure 1). The absence of RA ablation (SHR 3.84 [95% CI 1.27–4.68], p=0.001) was the only surgical factor independently associated with AF recurrence at follow up. Roof (SHR 1.54 [95% CI 1.03–2.29], p=0.03) and mid atrial line (SHR 1.56 [95%–4.06], p=0.012) were significant for pulmonary veins (SHR 1.56 [95%–4.06], p=0.012) and mitral isthmus (SHR 1.67 [0.94–4.23], p=0.151) lines were not significant.

Conclusions: Our experience suggests that a right-sided ablation should be routinely added to BRF left atrial ablation for atrial fibrillation. Further studies are necessary to confirm our results.

P4372 | BEDSIDE
Internet-based evaluation with the arrhythmia-specific questionnaire ASTA before and after treatment with catheter ablation for atrial fibrillation

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Background: Approximately 2000 ablation procedures for atrial fibrillation (AF) are performed per year in Sweden. The indication for treatment is according to current guidelines. i.e. primarily to reduce symptoms. Evaluation of treatment outcomes and the patients’ daily life situation needs to be assessed with patient reported outcomes measures (PROMs). There was a lack of a questionnaire suitable for arrhythmia-patients assessing both symptom burden and health-related quality of life (HRQoL). We developed and validated the disease-specific questionnaire ASTA (Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia). The questionnaire is now used in our clinical routine and available for use through our website: www.astaweb.com

Conclusion: The ASTA questionnaire gives similar results to the Lasso; it shows evidence of improved results with operators of sufficient experience. The 2nd generation cryoballoon has improved procedure efficiency without increasing complications.

Acknowledgement/Funding: Research Funding from the Medtronic

P4374 | BEDSIDE
Body mass index and recurrent atrial fibrillation following catheter ablation: a meta-analysis


Introduction: A significant percentage of patients undergoing atrial fibrillation ablation are overweight or obese. We sought to systematically characterize the
impact of incremental increases in body mass index (BMI) on recurrence of AF post-ablation.

Methods: Comprehensive searches of electronic databases and reference lists were undertaken. Estimates of relative risk (RR) were abstracted or calculated from studies reporting on associations between BMI and post-ablation AF. Where risk estimates were reported as a series of dose-specific risk estimates compared to a reference BMI category, these were transformed into risk estimates per unit of BMI as previously described given linearity between BMI and AF. Authors were contacted for additional data allowing transformation where it was not reported in the publication. Risk estimates per unit of BMI were subsequently pooled using random effects meta-analysis.

Results: A total of sixteen studies involving 5,864 individuals were included (mean age 56, mean percent female 30%, mean follow-up 20 months). The overall summary estimate indicated that there was a 3.1% greater excess risk of recurrent AF post-ablation for every one unit increase in BMI (RR 1.03, 95% CI 1.00–1.07). This translates into a 16% increased risk for every five unit increase in BMI (RR 1.16, 95% CI 1.00–1.34). There was significant heterogeneity due to differences between studies (I² statistic 68.7%) but no evidence of significant publication bias.

Conclusion: Incremental increases in BMI are associated with significant excess risk of recurrent, post-ablation AF. These data support weight reduction as a strategy to improve AF ablation outcomes.

P4375 | BEDSIDE
Comparison of substrate ablation with or without anatomical ablation for atrial fibrillation: does pulmonary vein isolation prior to substrate ablation improve the outcome?
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Background: The effect of atrial ablation (AF ablation) guided by complex fractionated atrial electrograms (CFAE) solely or combined with pulmonary vein isolation (PVI) is still controversy. This study was designed to analyze the additional effect of PVI prior to CFAE ablation on outcome.

Methods: We analyzed 160 consecutive AF patients who underwent catheter ablation with PVI prior to CFAE ablation (PVI+CFAE group, n=80) or without PVI (CFAE group, n=80) in their first session and followed for mean of 30 months. There were 50 paroxysmal and 30 persistent AF in both groups. In PVI+CFAE group, PVI was performed prior to CFAE ablation during either the spontaneous AF or by the induced AF in order to confirm AF termination by PVI. PVI was confirmed with a circular catheter and completed electrically in the end of the session in PVI+CFAE group.

Results: In patient characteristics including age, left atrial (LA) diameter, LA volume, left ventricular ejection fraction, and AF duration in persistent AF, there was no significant difference between two groups. In PVI+CFAE group, AF was terminated during PVI prior to CFAE ablation in 30% of paroxysmal and in 13% of persistent AF patients. AF was not inducible only in four (8%) of paroxysmal AF patients after PVI. There was no significant difference in the total termination rate of paroxysmal and persistent AF between two groups (PVI+CFAE vs CFAE: paroxysmal 94% vs 98%; p=0.62, persistent 73% vs 93%; p=0.08). Radiofrequency (RF) duration (PVI+CFAE vs CFAE: 92.5±25.2 min vs 84.9±24.7 min, P=0.05), fluoroscopic time (22.8±12.9 min vs 12.8±8.9 min, p=0.001), and procedural time (242±45 min vs 196±41 min, p=0.001) were significantly longer in PVI+CFAE group compared to CFAE group. Although acute AF recurrence in three days after the procedure in PVI+CFAE group was less than that in CFAE group (PVI+CFAE vs CFAE: 33% vs 68%, P=0.001), there were no significant difference in AF free rate during follow up period in both groups (PVI+CFAE vs CFAE: 59% vs 60% in paroxysmal; p=0.55, 60% vs 50% in persistent; p=0.60).

Conclusions: Our results suggest that the additional PVI prior to CFAE ablation did not help to improve the outcome, although it required significant longer RF duration, fluoroscopic time and procedural time.

P4376 | BEDSIDE
The impact of time delay after atrial fibrillation diagnosis and ablation on age-based 5-year outcomes after atrial fibrillation catheter ablation
T. Bunch, T.L. Bair, H.T. May, V. Jacobs, B.G. Cran dall, M. Cutler, J.P. Weiss, C. Mallender, J.L. Anderson, J.D. Day, Intermountain Medical Center, Murray, United States of America

Background: Catheter ablation of atrial fibrillation (AF) is an established therapeutic rhythm approach in symptomatic patients. Delays from AF diagnosis to catheter ablation have been shown to negatively influence long-term outcomes. We hypothesize that the age at AF diagnosis will enhance the impact of these delays over long-term follow-up.

Methods: 923 patients that underwent their index AF ablation and had 5 years of follow-up were studied. Patients were followed for AF recurrence, heart failure, stroke, death, and cardiac function. Patients were separated and compared in 5 age-based groups (<50, 51–60, 61–70, 71–80, >80 years) and then from time of initial AF diagnosis to ablation (30–180, 181–545, 546–1825, >1825 days).

Results: The average age of the population was 66±11 years and 59% male. The AF was paroxysmal in 55%, persistent in 27%, and longstanding persistent in 18%. Hypertension, heart failure, stroke, and coronary artery disease increased significantly with age strata. Time from AF diagnosis to ablation increased significantly with age (median: 229, 245, 311, 617, 405, p=0.001). 5-year AF recurrence rates were associated with delays in time to ablation, with the most notable benefit seen in patients ≥60 years of age.

Conclusion: Delays in ablation from AF diagnosis negatively influence 5-year rates of AF/Flutter recurrence. Older patients experienced greater delays and had more comorbidities. Patients ≥60 years of age received the relative largest benefit in early ablation; a finding that likely highlights the impact of the acquisition of coexistent diseases that drive arrhythmia recurrences.

P4377 | BEDSIDE
Plasma von Willebrand factor activity: a novel predictor of recurrence after catheter ablation for atrial fibrillation

Background: Plasma von Willebrand factor (vWF) level has been supposed to reflect not only endothelial dysfunction but also atrial structural remodeling. The aim of the present study was to evaluate the impact of plasma vWF activity on recurrence after catheter ablation for AF.

Methods: We enrolled consecutive 76 patients who underwent catheter ablation for AF. Plasma vWF activity measured before the first procedure. We defined recurrence as a current 12-lead ECG recording or 24-hour Holter recording of atrial tachyarrhythmia lasting more than 1 minute after a 3-month blanking period. We conducted ROC analysis to examine the predictive value of plasma vWF activity for recurrence and to determine an optimal cut-off point.

Results: The mean age was 65 (±9) years, male was 78%, persistent or long-standing persistent AF was 26%, and the mean left atrial diameter was 41 (±5) mm. The mean plasma vWF activity was 167 (±57)%. Circumferential pulmonary vein isolation was completed in all 76 patients. Recurrence of atrial tachyarrhythmia was seen in 18 (24%) patients during a median 181 (range 90–351) days follow-up. ROC analysis revealed the optimal cut-off point of 184% for plasma vWF activity (area under the curve 0.81, sensitivity 72% and specificity 81%). The Cox proportional hazards regression model showed that high plasma vWF activity (184% and above) was a significant predictor of recurrence (HR 8.55, 95% CI 3.02–24.2, p<0.001).
D.G. Katritsis1, S.M. Narayan 2.

We studied 76 patients with AF (61.1±9.1 years, 74% persistent) sub-
in AF but the relation of rotors to ganglionated plexi (GP) has not been studied.

Introduction: PVI group after one (log-rank test, p freedom from AF was significantly higher in the GP+FIRM group compared to the after a mean number of 1.3±0.5 procedures. According to Kaplan-Meier analysis, protocol followed by conventional ablation (FIRM group) or conventional ablation injected to direct or coincidental source ablation according to the CONFIRM trial subjected to direct or coincidental source ablation according to the CONFIRM trial protocol followed by conventional ablation (FIRM group) or conventional ablation alone (PVI group). Electroanatomic shells were analyzed for lesion overlap with superior/inferior left GP (SLGP, ILGP) or anterior/inferior right GP (ARGP, IRGP) and patients with such overlap were categorized in a GP+FIRM group. Results: Out of 47 patients with AF sources ablated (FIRM group), 40 patients (85%) had lesions overlapping with GPs (GP+FIRM group). At the end of a median follow-up of 875 days (interquartile range: 363–1533), 23 (56.1%) patients in the GP+FIRM group and 9 (32.1%) patients in the PVI group were free from AF after a mean number of 1.3±0.5 procedures. According to Kaplan-Meier analysis, freedom from AF was significantly higher in the GP+FIRM group compared to the PVI group after one (log-rank test, p < 0.001) or multiple procedures (log-rank test, p=0.029).

Conclusions: Plasma vWF activity was associated with recurrence of atrial tach-
yrhythmia. It may be a useful marker for recurrence and the risk of ischemic stroke after catheter ablation in AF patients.

P4378 | BEDSIDE
Ablation of fibrillatory rotors and autonomic denervation in atrial fibrillation
T. Zografos1, T. Baykaner2, J.A. Zaman3, I. Pantos4, D.E. Krummen5, D.G. Katritsis1, S.M. Narayan2, 1Euroclinic of Athens, Athens, Greece; 2University of California San Diego, San Diego, United States of America; 3Imperial College London, London, United Kingdom

Introduction: Localized electrical rotors and focal impulse sources are prevalent sustaining mechanisms for human atrial fibrillation (AF), and can be treated by fo-
cal ablation. The cardiac autonomic nervous system also plays an important role in AF but the relation of rotors to ganglionic plexus (GP) has not been studied.

Methods: We studied 76 patients with AF (61±1±9.1 years, 74% persistent) sub-
ject to direct or coincidental source ablation according to the CONFIRM trial protocol followed by conventional ablation (FIRM group) or conventional ablation alone (PVI group). Electroanatomic shells were analyzed for lesion overlap with superior/inferior left GP (SLGP, ILGP) or anterior/inferior right GP (ARGP, IRGP) and patients with such overlap were categorized in a GP+FIRM group. Results: Out of 47 patients with AF sources ablated (FIRM group), 40 patients (85%) had lesions overlapping with GPs (GP+FIRM group). At the end of a median follow-up of 875 days (interquartile range: 363–1533), 23 (56.1%) patients in the GP+FIRM group and 9 (32.1%) patients in the PVI group were free from AF after a mean number of 1.3±0.5 procedures. According to Kaplan-Meier analysis, freedom from AF was significantly higher in the GP+FIRM group compared to the PVI group after one (log-rank test, p < 0.001) or multiple procedures (log-rank test, p=0.029).

Conclusions: Successful ablation of fibrillatory rotors may inadvertently affect GP and suggests a role of the autonomic nervous system for AF source formation. The potential of improved ablation outcomes through this approach merits further investigation

Cumulative freedom from AF

P4379 | BEDSIDE
Leptin levels are associated with atrial fibrillation recurrence after pulmonary vein isolation
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Objective: The aim of this study was to investigate the relationship between leptin levels and atrial fibrillation (AF).

Background: There is accumulating evidence indicative of a link between obe-
oby, inflammation and AF. Leptin is known for its pro-inflammatory properties, and elevated leptin levels and leptin resistance are associated with obesity, raising the possibility of arrhythmogenic effects of leptin on cardiac tissue.

Methods: A population of AF male patients undergoing pulmonary vein isolation (PVI) was followed for 3 months for AF recurrence. Leptin levels were measured prior PVI. Patients were divided into two groups according to AF recurrence: 57 patients (age 55±10.3 years) maintained in sinus rhythm and 15 patients (age 58±8.6 years) experienced AF recurrence.

Results: Patients relapsing into AF had significantly more elevated levels of leptin (11.9 [8–29.2] vs 8.6 [4.5–11.3] ng/mL, p=0.013). NT proBNP (511 [119–774] vs 196 [44–402] ng/mL, p=0.09), CRP (2.4 [1.4–3.7] vs 1.4 [0.6–3.3] mg/L, p=0.05), TGF-β1 [271–1263] vs 100 [71–130] mg/dL, p<0.001 and greater left atrial diameter (32.6±6.5 vs 52.5±9.9 mm, p=0.013) and BMI (36.2 [29.9–35.6] vs 27.7 [25.2–30.9] kg/m², p=0.001) than SR maintainers. Importantly, univariate analysis revealed that baseline leptin levels (RR=1.04, 95% CI: 1.006–1.061, p=0.02) BMI (RR=1.13, 95% CI: 1.045–1.239, p=0.004) and left atrial BMI (RR=3.89, 95% CI: 1.201–10.129, p=0.03) predicted AF recurrence after PVI.

Conclusion: A high leptin levels predict short-term AF recurrence. Therefore, interventions reducing leptin levels may be beneficial, potentially offering a new strategy for treating atrial fibrillation.
P4382 | BEDSIDE
Radiofrequency ablation of atrial fibrillation: comparison of success rate of circular ablation vs point-by-point ablation with contact force in paroxysmal and persistent atrial fibrillation
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Introduction: Circumferential Pulmonary Vein Isolation (CPVI) with radiofrequency (RF) ablation is now standard care for atrial fibrillation (AF). New improvements include use of contact-force that measure contact-force to improve tissue-contact or irrigated circular ablation catheters that allow simultaneous mapping and ablation from ten electrodes. These novel techniques have not been compared.
Methods: We compared the success rate of CPVI with: 1) “point by point” RF using an irrigated tip ablation catheter with contact force assessment vs. 2) irrigated circular ablation catheter (that is, Navistar Thermocool Smart Touch vs. nMARQ, Biosense Webster) in 86 pts. with AF. The endpoint if the procedure was the elimination of all PV potentials recorded by a second circular catheter inside the PV. Success was freedom from AF during follow-up.
The two groups had similar characteristics: Navistar-group with 50 patients, age 59±10 years, 64% male; nMARQ group with 36 patients, 75% male, age 62±9 years. Echocardiographic parameters and comorbidities were also similar. Importantly, the duration of AF was 6.4±2 years in the Navistar group vs. 7.3±3 years in the nMARQ group. Finally, follow-up periods were similar (11±7 months).
Results: Freedom from atrial fibrillation at follow up was achieved in 41 of 50 patients in the Navistar group and in 30 of 36 patients with the nMARQ (success rate 82% vs. 83%, p=0.64). In paroxysmal AF the success rate was 85% with Navistar vs 82% for nMARQ (p=0.5). For persistent AF, the success rate was 75% with Navistar and 84% with nMARQ (p=0.52). Pulmonary vein isolation could not be achieved with the nMARQ in 4 (11%) patients and was completed with a Navistar. Crossover from Navistar to nMARQ was never necessary. No complications occurred.
Conclusions: High and comparable success rate in curing atrial fibrillation by CPVI are now achievable with either point-catheters measuring contact force or with irrigated circular catheters.

P4383 | BEDSIDE
Impact of reduced freezing times on midterm outcome: a single center study evaluating an improved version of the cryoballon in ablation of paroxysmal atrial fibrillation
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Background: Cryoballon (CB) ablation (CBA) has been adopted by many centers as a new tool in atrial fibrillation (AF). An improved version of the CB providing homogenous cooling at its total front side has been introduced. We aimed to evaluate, whether reduction of cooling times in application of this advanced CB is possible without affecting the outcome.
Methods: 44 patients (68±13 years) suffering from paroxysmal AF were prospectively assigned to CB pulmonary vein isolation choosing either 2 x 4 minutes (group 1) or 2 x 3 minutes (group 2) of freezing per vein. In case of pull-down maneuvers 120 s application time at the superior edge was followed by an additional freezing of 3 or 4 minutes respectively after pull-down. Follow-up scheduled at 3, 6, 12 months included a clinical visit and a 7 day Holter or a readout of an implanted device for evaluation of AF burden.
Results: Groups were well balanced in terms of left atrial size, left ventricular function, concomitant diseases and duration of AF. Total procedure time was reduced from 116±28 to 109±23 minutes (p=0.004). Freezing time per pt decreased from 38.7±8.2 to 31.2±6.9 minutes (p<0.00001). Fluoroscopy time was similar between the groups (10.3±5.8 vs. 12±5.5 min; p=ns.). During a follow-up of 11±3.0 months recurrence of AF was observed in 12% of pts in group 1 versus 40% of pts in group 2 (p<0.001). No major complications occurred in either group.
Conclusion: Reduction of freezing time in CB ablation applying the improved version of the CB catheter seems to increase recurrence of AF. Therefore, it is advisable to stay at longer freezing times. A prolonged follow-up will be available and presented at the Meeting.

P4384 | BEDSIDE
Impact of complex-fractrional atrial electrograms and low voltage areas on identification of atrial fibrillation sources
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Introduction: The mapping of electrical propagation to identify underlying mechanisms of atrial fibrillation (AF) is difficult. However, if the measurement of pace capture is used to stop the RF ablation, it is possible to create lesions that are effective for AF.
Methods: To evaluate the impact of the complex-Fractrional Atrial Electrograms (CFAEs) and low voltage areas (LVAs) on the identification of rotors or focal sources (AF sources) after pulmonary vein isolation (PVI).
Results: Contact mapping using a 64-pole basket catheter and 20-pole circular mapping catheter was performed in 30 patients with persistent AF. Left atrial voltage maps were created during sinus rhythm. LVAs were defined as areas with bipolar peak-to-peak voltage amplitudes of <0.5 mV. CFAEs were mapped after the PVI. If AF was sustained or induced after the PVI, activation maps to identify AF sources (Rotor maps) were created using the Velocity system. In this study, CFAEs were mapped with the Contact Force catheter (TactiCath, St. Jude Medical) and a 20-pole circular mapping catheter was placed on the left atrial septum, and then a 64-pole basket catheter was advanced into the left atrium through a steerable sheath. The absolute peak of the atrial electrogram was used to automatically detect the local activation. The points of continuous CFAEs were excluded with manual verification. If the AFCL was shorter in the right atrium than left atrium, the basket catheter was advanced into the right atrium. After the basket catheter and circular mapping catheter were set, the activation sequence of AF was observed by 30 minutes. A rotor was defined as reproducible reentrant atrial activity, which was repeatedly present for more than 40% of the 3.8 second observation time. Focal sources were identified as sites with a centrifugal activation pattern. The accuracy of the Rotor map was confirmed by the termination of AF.
Conclusion: Thirteen AF sources were identified in 13 patients (42%). The sources were left atrial in 12, right atrial in 1, and 10 were rotors. The percentage of CFAEs points was higher in the unsuccessful Rotor maps than in the successful Rotor maps (42% vs. 16%, p<0.01), while the percentage of LVAs was similar (7.4% vs. 5.6%, p=0.6).

P4385 | BEDSIDE
Circumferential pulmonary vein isolation in patients with atrial fibrillation: comparison of contact force versus pace ad ablate approach during ablation
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Background: Catheter ablation has become a corner stone for the treatment of atrial fibrillation (AF). Creation of transmural and continuous lesions is challenging. Catheter-tissue contact is essential for creation of effective ablation lesions. Real-time contact force (CF) catheters optimize electrode-tissue contact and generate more effective lesions.
Objective: Aim of this study was to compare simultaneous pacing and ablation through the tip of the ablation catheter with CF information.
Methods: For this study, 20 AF patients in sinus rhythm receiving circumferential PV ablation were included. In all cases, a CF catheter (TactiCath, St. Jude Medical) was used, and the operator was blinded to the CF information. At each designated ablation point, CF information, as well as minimal pacing threshold to capture the tissue was determined before energy application was delivered. Pacing was continued during ablation with the minimal pacing output. When loss of pace capture occurred during ablation, CF parameters were recorded. If no loss of pace capture occurred during the delivered energy application, the procedure was terminated after 60 s. Force-time integral (FTI) > 500gs and/or lesion size index (LSI) > 4 were determined as values indicating effective lesion creation.
Results: Altogether 600 energy applications were assessed and evaluated. Bidirectional block was achieved in 26% of PVs (106/404 energy applications). CF information was achieved in all patients. There was no correlation between CF before ablation and pacing threshold (Figure 1). In 90.5% of ablation pulses, loss of pace capture occurred during ablation. In none of them, loss of pace capture was due to loss of contact (mean CF before ablation 16.6±11.1±12.2 vs. 17.5±12±11.9 kg at loss of capture, p=0.26). In 55% of RF pulses with loss of pace capture, FTI and/or LSI were below the values indicating effective lesion creation (FTI > 500gs; LSI > 4). On the other hand, in 9.5% of ablation pulses, no loss of pace capture occurred during 60 s of energy application. Despite no loss of pace capture, in 55% of pulses an FTI > 500gs could be achieved (indicating effective ablation)
Conclusion: Neither pacing threshold before ablation, nor loss of pace capture during ablation are adequate surrogate parameters for CF or effective lesion creation during RF ablation of atrial fibrillation.

P4386 | BEDSIDE
Percutaneous left appendage closure: a very low rate of perioperative complications during initial experience in a dedicated electrophysiology team
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Purpose: Percutaneous left atrial appendage closure (LAAC) is now accepted as a valuable alternative to oral anticoagulation (OAC) for patients (pts) in atrial fibrillation (AF) with high risk of thromboembolism, especially in case of contra-indication for OAC or hemostatic events. Percuticular complications seem related to operator experience but little is known concerning complication rates in electrophysiology (EP) teams.
Methods: We analyzed periprocedural data and complications in a dedicated
EP team since the beginning of our LAAC experience (2013). The team consists in 2 experienced electrophysiologists (AF ablation >200 per year), 1 dedicated echocardiog, 1 anesthesiologist.

All pts had an ambulatory visit with the electrophysiologist and a CT scan to check the left appendage anatomy and rule out thrombi before the procedure. Procedures are done under general anaesthesia with a peroperative transoesophageal echography (TEE).

All procedures were done in a dedicated EP room with in-hospital cardiac surgery facilities in case of complications. All LAAC procedures were performed with Watchman devices.

Results: 43 pts were enrolled (male 74%, age 76±6 years, paroxysmal AF 44%, permanent 56%). The CHADS2 VASC average score was 4.6±1.3; 4.47%. The HASBLED average score was 3.8±1; 4.37%. All indications were according to contraindications for OAC due to haemorrhagic events: neurologic 71%, gastrointestinal 14%, urologic indications 6%, epilepsy 3%. The CT scan ruled out any thrombus before the procedure for all pts with a perioperative TEE confirmation.

Success rate of implantation was 100% with an average time of procedure of 71±8 min under general anaesthesia (technical procedure time 51±11 min, time after transapical puncture 35±8 mn, time for device deployment 10±4 mn). Average scopy time was 8±3mn (204±1125 µly M2). The implanted device sizes were: 21 mm/4 pt (9%), 24 mm/19 pts (44%), 27 mm/16pts (37%), 30 mm/pt (4.7%), 35 mm/2 pt (4.7%). Device repositioning was necessary after the first deployment in 7% of pts, switch to larger device in 5% of pts.

There were no peri-procedural complications, especially no pericardial effusion, no systemic embolization, no stroke and no major bleedings for the first 43 pts. Only one patient had early sepsis (<24h post procedure) with a favorable outcome under antibiotics.

Conclusion: In a single center with a large experience in EP, initial experience in LAAC was performed with a very low rate of complication. Tailored approach with EP experienced team leads to safe procedures and high accurate success rate.

P4387 | BEDSIDE
Visually guided laser ablation: a single centre long term experience
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Introduction: Durable isolation of the pulmonary veins (PV) remains the cornerstone of treatment for paroxysmal atrial fibrillation (PAF) and is also used in the treatment of some patients with persistent atrial fibrillation. Visually Guided Laser Ablation (VGLA) has been proven to be safe and effective as a treatment for atrial fibrillation (AF). It has shown high levels of durable PVI, even in the hands of less experienced users. This paper presents the long term clinical outcomes of all patients treated with VGLA over the course of 4 years in the world’s most experienced centre: from early product feasibility work treating only PAF patients to our work using the commercially available product, when we also treated persistent AF patients.

Methods and results: 194 patients (63 females, mean age 61 years) with either a history of drug refractory PAF (time since initial diagnosis: 60.73 months) or persistent AF (time since initial diagnosis: 62.75 months) were treated in our lab with the VGLA system between January 2009 and 17th May 2013. Follow-up of all patients was consistent with our standard clinical practice with a 7 day Holter being performed at the first visit clearance between 4 and 6 months and, for most patients, again at 12 months post-procedure. 12 lead ECGs were performed at all clinic visits. The presence of AF is defined as any documented AF episode >30 seconds. Acute procedural results show that 692 veins were acutely isolated with a mean fluoroscopy time of 226 minutes and 20.4 minutes respectively.

Conclusion: Assessment of LA remodeling by TTE with STE correlates well with the extent of LA fibrosis assessed by EAM. Thus, TTE may be useful in non-invasive assessment of LA fibrosis and proper selection of candidates for CA. These preliminary findings warrant further examinations.

P4389 | BEDSIDE
Comparison of mid-term success rate between single-shot technologies for paroxysmal atrial fibrillation ablation

Introduction: In the last years, efforts have focused on developing ablation techniques, so-called single-shot ablation, with the possibility of a shortened learning curve, a single transseptal access and the simultaneous application of energy in order to perform easier, faster and safer procedures with less complications and increased success. Aim of this study was to compare the acute and chronic success between three different single-shot technologies available in our Centre for pulmonary vein isolation (PVI): cryoenergy using the Arctic Front Advance™, radiofrequency using the mQuaTM catheter and laser energy using the HeartLight™ Laser Catheter. The study was done in 3 groups: 1. Complete PVI, 2. Procedure failure, and 3. Procedure success. AF ablation was performed in 108 pts with paroxysmal atrial fibrillation (AF) who underwent AF ablation with the second-generation cryoballoon (CB) to matched patients with irrigated circular multipolar catheter (ICMC) and 40 patients with the laser balloon (LB). All patients underwent regular follow up with 7-day-Holter-ECG recording and outpatient clinic evaluation every 3 months for 1 year after AF ablation.

Results: There was no significant difference between the three groups regarding patients’ characteristics and procedure parameters, except for the longer procedure times in the LB group (148±45, 152.7±45.5, 190±47.3 min, respectivly, p<0.01), which was statistically different compared to the other groups. Complete PVI was achieved in 94% of the CB and LB ablation, and in 92% of ICMC ablation. The 1-year freedom-from-AF in the CB group and in the LB group was 92.6%, whilst in the ICMC was 84% with no statistically significant difference (p=0.33). The study showed more incidence of pericardial effusion in the LB group, one case of cerebral embolization in ICMC group and one case of reversible phrenic nerve palsy in the CB group.

Conclusion: Single-shot technologies for paroxysmal AF ablation are feasible and safe techniques and seem to have a similar mid-term success rate. Fluoroscopy times were similar in all groups, whilst procedural times using the LB were significantly longer than the other groups.

P4390 | BEDSIDE
Optimal ablation strategies in long standing persistent atrial fibrillation

Introduction: Catheter ablation (CA) is widely used as a treatment option for symptomatic atrial fibrillation (PFAF) in paroxysmal AF where single-procedure success rates are still suboptimal with patients often requiring multiple procedures. We report preliminary results from a prospective study...
Ablation of atrial fibrillation V

P4391 | BESIDE
Spatial relationship of focal impulses, rotors and low voltage zones in patients with persistent atrial fibrillation

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Introduction: Focal impulses and rotational activity have been related to occurrence and maintenance of AF and ablation of these sources leads to AF termination and prevention of recurrences. Ablation of low voltage zones (LVZ) represents an ablation strategy that may be associated to a lower incidence and lower recurrence rates of AF. The aim of the study was to characterize the relation between focal and rotational sources of AF and atrial LVZ.

Methods: In patients (pt) with persistent (pers) AF, focal impulses and rotors were mapped during AF. Voltage map of both atria was done during AF (<0.5 mV regarding as LVZ) using EnSite™ NavX™ Endocardial source mapping using RhythmViewTM followed. Basket catheter was placed in complementary positions in case of insufficient LA or RA covering. Endocardial surface area of RA and LA, size and percentage of LVZ areas in RA and LA and the number and localization of sources were determined.

Results: In the study, 24 pt undergoing their first ablation for pers AF (6/24 (25%) long pers, mean age 61±11 years, 17/24 (71%) male) were included. LVZ covered 13±12% of RA endocardial surface and 33±25% of LA endocardial surface. LA showed large LVZ (>30%) in 12 of 21 pt (57%). Median number of sources per patient in RA was 1 [1–3], and 3 [1–4] in LA. Rate of RA rotors correlated with RA size (r=0.513; p=0.018).

In the RA only 1/37 (3%) of sources were located within a LVZ, whereas 5/37 (14%) were adjacent to a LVZ. Of the 37 RA sources 31 (83%) were found remote of LVZ. Of the 59 sources mapped in LA 23 (39%) were localized within LVZ, 12 (20%) adjacent to LVZ, and 24 (41%) remote of LVZ, 10 (17%) were detected within a typical circumferential PV line.

Altogether 16 (27%) of LA sources are not associated to LVZ or pulmonary veins. During ablation of rotors significant AF CL prolongation (at least 10%) was observed in 10/22 (45%) of patients. In two of the patients (9%) AF converted to a regular AT, and in one pt (5%) to sinus rhythm. Of the 11 cases of CL prolongation or AF termination 6 occurred during ablation in RA (55%) and 5 (45%) in LA. In most pt these sites (87%) were observed during ablation of sources remote of LVZ.

Conclusions: LVZ are rare and small in RA, but common in LA of pers AF cases. RA sources have no relation to LVZs. In LA 2/3 of sources are located in or adjacent to LVZs or within PV. CL prolongation or regularization occurred mostly remote of PVs and LVZ in the RA and LA. This finding suggests, that targeting focal impulses and rotors may focus on LA and RA areas different from PV1 and LVZ.

P4393 | BESIDE
Peri-operative atrial fibrillation (POAF) complicating non-cardiac surgery: a case-control pilot study

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Introduction: Retrospective analyses suggest that peri-operative atrial fibrillation (POAF) complicates non-cardiac surgery in 3% of patients. It is not known whether POAF is associated with adverse outcomes.

Purpose: We intended to determine the frequency of POAF at our Hospital Civic Campus (OCH) and establish whether POAF had implications for patient outcomes and hospital costs.

Methods: Retrospective case-control study. All ECGs performed at OCH in July 2013 were overread for the presence of atrial fibrillation (AF) and/or atrial flutter (AFL), and then screened for patient surgical status. POAF was defined as ECG documentation of AF/AFL within 30 days of non-cardiac surgery occurring at OCH. POAF patients were matched to controls according to age, gender, and surgical procedure in a 1:3 ratio (p=1). Electronic health records were then reviewed for patient characteristics and outcomes.

Results: POAF was documented in 42 of 859 (4.9%) patients undergoing non-cardiac surgery; 12 (29%) had de novo AF. Three matched controls were identified for each of 41 POAF patients, with a similar proportion of emergent procedures. POAF patients had greater median ASA class (POAF [IQR] 4 [1] vs control 3 [1]; p=0.004) but similar CHADS2 & CHA2DS2-VASC scores to controls. POAF patients experienced significantly increased rates of ICU admission (POAF 22% vs control 3%, p=0.0006) and in-hospital mortality (POAF 17% vs control 7% p=0.006). While the index admission length of stay was similar, POAF was associated with significantly increased hospital costs (POAF $26724±7308 vs control $15040±2306, p=0.046) and less frequent discharge home (POAF 59% vs control 77%, p=0.04). At median 482 days follow up, readmission rates were almost double in the POAF group; mortality rates remained higher in the POAF group (POAF 22% vs control 5%, p=0.003) but there was no significant difference in rates of ischemic stroke.

Conclusion: POAF occurred in approximately 5% of patients undergoing non-cardiac surgery and was associated with adverse outcomes and increased costs. Prospective research is required to confirm these findings in a larger population and to test the hypothesis that aggressive intervention in POAF improves patient outcomes and/or reduces hospital costs.

P4394 | BESIDE
Less than two minutes, second generation cryoballoon applications achieves acute PV in 76% without pherine nerve palsy: preliminary results of the 1-2-3 study

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Purpose: In patients with paroxysmal atrial fibrillation (PAF), the second generation cryoballoon (Arctic Front Advance) significantly improves procedural outcome of pulmonary vein isolation (PVI) compared to the first-generation. However, this goes hand in hand with an increased risk of complications, especially pherine nerve (PN) palsy (PNP). Considering the increased efficacy and risk of complications, the necessity and safety of the recommended two times 4-minutes cryotherpy per pulmonary vein (PV) might be questioned. The aim of the 1-2-3 study is...
to assess PVI after different freeze time cycles with the second generation cryoballon.

**Methods:** This prospective, single blinded study, includes patients with PAF, 4 PVs as assessed by a prior performed CT scan and a left atrial size <400cm². Patients are randomised to two times 1, 2 or 3 minutes of cryoballon applications per vein. Time is started after the balloon temperature reaches the plateau phase of the freezing cycle. PVI is checked by the Achieve mapping catheter directly after each application and at the end of the procedure, also using edenosine. During applications of the right PVs the PN is constantly stimulated and excusion of the diaphragm is monitored manually. If no PVI can be achieved with the assigned cryoablation therapy of 1, 2 and 3 minutes, more and/or longer applications are applied until PVI is successful. This is classified as primary unsuccessful PVI.

**Results:** Until now 26 patients (age 53±8.7) years have been included. 8/26 patients had been randomized to the 1 minute group, 9 in both the 2- and 3-minute group. In all patients the 28 mm cryoballon was used. In the 1 minute group 25/32 PVs were primary successful, in the 2 minutes group 27/36 and in the 3 minutes group 27/36. The total mean application time per cryoapplication, from the start of cryotherapy, was respectively 113±13, 151±39 and 213±43 seconds in the different groups. With additional and/or longer applications, PVI could be achieved in all primary unsuccessful applications. In one patient the right inferior PV could not be isolated due to PN capture whereas no application had to be repeated prematurely due to loss of PN capture where no application had to be terminated untimely in the one minute group. All PNPs were (eventually) transient.

**Conclusions:** The second generation cryoballon (CB) (Arctic Front Advance, CryoCath) achieves significantly lower temperatures, faster pulmonary vein (PV) isolation times and lower late atrial fibillation recurrence rates compared to its predecessor. However, the higher efficacy goes hand in hand with an increased risk of complications. Besides an increased incidence of right phrenic nerve (PN) palsy, esophageal lesions, atrio-esophageal fistulae and vagal nerve injury, which can result in gastroparesis, have been described. The latter complications have been related to low esophageal temperature (ET). Aims of the study are 1) To assess the incidence of low ET, defined as ET <20°C, during regular PV isolation using the second generation CB. 2) To determine if body mass index (BMI) was inversely related to low ET.

**Methods:** Under general anesthesia, 76 consecutive patients underwent regular CB isolation of the PVs. In all but eight the 28 mm balloon was used. In all patients a temperature probe with 3 thermocouples separated by 10mm (SensiTherm, St Jude Medical) was inserted into the esophagus under fluoroscopic guidance. The position of the probe was adjusted to the fluoroscopic position of the balloon during each application. When reaching temperatures <16°C the application was stopped prematurely. PN palsy was monitored by continuous pacing of the PN. BMI was calculated as mass/length².

**Results:** Complete PV isolation was achieved in 73/76 patients. Ten patients experienced temporary PN palsy, no other complications occurred. In 17 patients, 2 with the 23 mm balloon, the ET reached <20°C. In 6 patients the ET decreased even <15°C despite the cessation of cryotherapy (latency effect). The lowest ET was measured at the left inferior PV in 9/17, while in 7/17 it was reached in the right inferior PV and in 1/17 it was reached in the left superior PV. The mean BMI was 27.2±4kg/m². 9/17 patients with low ET BMI was <25 kg/m². In the 13 patients with ET >24°C, BMI was calculated as mass/length².

**Conclusions:** 1) In our study population second generation CB PV isolation leads to ET <20°C in 21%, and <15°C in 8% of patients. As low ET can result in serious complications, monitoring of the ET during CB therapy is mandatory. 2) High BMI seems to protect against low ET during CB therapy.

**ATRIAL FIBRILLATION AND ANTICOAGULATION**

**P4397 | SPOTLIGHT**

A simulated head to head comparison of stroke and major bleeding with apixaban versus rivaroxaban in high-risk NVAF Patients

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**Background:** No head-to-head trials have been carried out to assess the relative effectiveness and safety of NOACs now approved in EU to treat non-valvular atrial fibrillation (NVAF). Traditional indirect treatment comparisons of NOACs are complicated by differences in the populations studied in trials of these drugs, and administration and outcomes with warfarin in the comparator arms.

**Purpose:** To estimate the relative effectiveness and safety of apixaban and rivaroxaban on stroke or systemic embolism (SSE) and major bleeds (MB), taking into account differences in patient populations using Matching Adjusted Indirect Comparison (MAIC).

**Methods:** The MAIC was based on patient level data from ARISTOTLE and published baseline characteristics and outcomes from ROCKET-AF for rivaroxaban. Balancing weights were derived to match the mean baseline characteristics of the apixaban and rivaroxaban groups. The weights were applied to derive the adjusted rates of SSE and MB, reflecting expected outcomes for apixaban in the ROCKET-AF population. The adjusted apixaban and observed rivaroxaban rates were used to calculate rate ratios (RR) with 95% confidence intervals. Similar analyses were carried out for the warfarin groups to assess comparability of the control arms of the studies. The RR's between matched warfarin arms were used to further adjust the apixaban and rivaroxaban comparisons.
Results: Patients in the ROCKET-AF trial tended to be older and otherwise higher-risk (e.g., CHADS2 score, history of coronary heart disease, and prior stroke or TIA). Reweighting patients in ARISTOTLE to match the ROCKET population yielded an effective sample size of 1,537 for apixaban and 1,574 for warfarin. Comparisons of outcomes based on reweighted results in ARISTOTLE are summarized below.

Conclusions: MAICE suggests that use of apixaban versus rivaroxaban in high-risk patients may be associated with reduction in stroke/systemic embolism and major bleeding.

Acknowledgement/Funding: This study was funded by Pfizer and BMS

P4398 | BEDSIDE
Outcome of rivaroxaban versus warfarin in women and men with nonvalvular atrial fibrillation: results from the ROCKET AF trial
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Background: Rivaroxaban is non-inferior to warfarin for the prevention of stroke and systemic embolism, with less fatal and intracranial bleeding.

Purpose: The relative efficacy and safety in women versus men are unknown.

Methods: ROCKET AF was a multicenter, randomized, double-blind, double dummy, event-driven trial that was conducted at 1178 participating sites in 45 countries. The efficacy and safety of rivaroxaban versus warfarin was compared between women and men.

Results: Women, as compared with men, were older 75 vs. 71 (p < 0.001), had more hypertension 93% vs. 89% (p < 0.001), and had lower creatinine clearance 61 vs. 72 mL/min (p < 0.001). Compared with men, women had a lower risk of myocardial infarction (adjusted hazard ratio [HR] 0.70; 95% confidence interval [CI] 0.60, 0.83), death from vascular causes (adjusted HR 0.70; 95% CI 0.53, 0.93), and major or non-major clinically relevant bleeding (adjusted HR 0.91; 95% CI 0.84, 0.98). However, women had a higher risk of stroke or systemic embolism (adjusted HR 1.21; 95% CI 1.01, 1.44) (Figure). There was no interaction between sex and treatment effect of rivaroxaban compared with warfarin for prevention of stroke or systemic embolism.

Conclusion: Women participating in ROCKET AF had a higher risk of stroke but a lower risk of vascular death and overall bleeding events than their male counterparts. There was modest evidence of heterogeneity for sex and treatment effects with rivaroxaban versus warfarin.

Acknowledgement/Funding: ROCKET AF was funded by Janssen Pharmaceuticaal and Bayer

P4399 | BEDSIDE
Predictive value of CHA2DS2-VASc score for thromboembolic events in non selected outpatients without atrial fibrillation
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Background: Nowadays CHADS2VASc score is a useful tool to stratify thromboembolic risk and to prescribe antithrombotic therapy in non valvular atrial fibrillation (NVAF) patients (pts). Recently, few papers have suggested a predictive value for thromboembolism also in sinus rhythm (SR) in non-selected general population or in pts with coronary heart disease.

Purpose: To evaluate in a large real world non-selected population, the predictive power of CHA2DS2VASc score for thromboembolic events (TE) in SR and NVAF outpatients.

Methods: Between November 1, 2009 and October 31, 2013 we enrolled 19677 consecutive outpatients with SR without history of atrial fibrillation (n=16298) and with NVAF (n=3379). Clinical data were derived from an E-data chart for outpatient clinic. Thromboembolic risk was evaluated by CHA2DS2VASc score in both SR and NVAF pts. During a median follow-up of 29 months (IQR 14–39), events were obtained from Hospital Discharge Database and ICD-9 reports. We compared the predictive value of CHA2DS2VASc score in the two populations by Receiving Operating Characteristic analysis (ROC), adjusting for antithrombotic therapy.

Results: Comparing pts with SR and NVAF, median age was 68 vs 75 years (p < 0.001), male 47 vs 58% (p < 0.001), hypertension 63 vs 78% (p < 0.001), diabetes mellitus 20 vs 26% (p < 0.001), Charlson index >3 in 17 vs 23% (p < 0.001), hypertensive heart disease 42% vs 2% (p < 0.001), heart failure 6% (p < 0.001), previous stroke/TIA 4.6% vs 11.8% (p < 0.001), QFRR < 0.60 mL/min/m² in 17% vs 27% (p < 0.001), anticoagulants 3 vs 53% (p < 0.001). The median CHA2DS2VASc was 3 (1–4) vs 4 (2–5) (p < 0.001) while median HASBLED was 1 (0–2) vs 2 (1–3) (p < 0.001). During follow-up we have recorded 3.1 vs 7.5% (p < 0.001) TE events in SR vs NVAF pts, respectively, with a progressively increasing incidence with increasing score in both of them. To investigate predictive value of CHA2DS2VASc score in these groups we evaluated Area Under Curve (AUC) of ROC: AUC was 0.812 (95% CI, 0.773–0.851) vs AUC 0.696 (95% CI, 0.664–0.728) (p < 0.001), in SR vs NVAF pts.

Conclusions: The incidence of TE events progressively increases with increasing CHA2DS2VASc score in both SR and in NVAF pts. CHA2DS2VASc score is a powerful predictor of TE events in SR pts than in NVAF pts. This suggests that a simple score, largely available in clinical practise of thromboembolic risk stratification in NVAF pts, could be a useful tool to stratify TE in SR population, too. The hypothesis of treating antithrombotic therapy in SR pts with high CHA2DS2VASc score and low hemorrhagic risk should be analysed prospectively.

P4400 | BEDSIDE
Effect of rivaroxaban and warfarin on fibrin clot structure
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Introduction: In atrial fibrillation (AF), oral anticoagulant is vital for stroke prevention. Warfarin, rivaroxaban and aspirin confers different level of protection against thrombosis and bleeding risk, possibly due to different effects on fibrin clot structure.

Methods: Blood samples from 234 subjects were collected: 153 warfarin (Mean INR 2.42, SD 0.69), 44 rivaroxaban and 38 aspirin. Coagulation profile, clot strength and fibrin clot lysis indices are analysed by Thromboelastograph (TEG), fibrinolysis and turbidimetric assay.

Results: Using TEG, the ability of warfarin and rivaroxaban to delay fibrin clot formation was confirmed, with a delay as opposed to aspirin (7.3 min vs 8.4 min vs 5.0 min, p < 0.0001). More gentle α-angle (63.2° vs 63.6° vs 69.1°, p < 0.004) was seen in warfarin and rivaroxaban as compared to antiplatelet user.

No significant differences were seen in Maximum Amplitude (MA) of clot achieved among all three groups. Using fibrinolysis and turbidimetric analysis, warfarin and rivaroxaban caused slower rate of clot formation (17.6 optical density per sec [OD/s] vs 12.3 OD/s vs 25.1 OD/s, p < 0.0001) and shorter time to lyse 50% of fibrin clot (190 s vs 204 s vs 69.1 s, p = 0.026) when compared to aspirin.

When compared directly with warfarin, rivaroxaban results in more prolonged R-time (p < 0.0016), slower rate of clot formation (p = 0.008) and shorter clot lysis time (p = 0.04).

Conclusions: Rivaroxaban and warfarin’s efficacy to impede coagulation is demonstrated by the delay fibrin clot formation (R-time), longer K-time and gentler α-angle, without impact on the tensile strength of clot as shown by similar MA. Both agents also impede the rate of fibrin clot formation and accelerate clot lysis. Rivaroxaban was superior to warfarin, being more efficacious in delaying coagulation, further slowing rate of clot formation and resultting in formation of clots which are more responsive to lysin.
P4401 | BEDSIDE
Determinants of oral anticoagulation control in new warfarin patients: analysis using data from Clinical Practice Research Datalink
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Background: The safety and effectiveness of warfarin therapy depends critically on the quality of anticoagulation control, often assessed using the percentage time in therapeutic International Normalised Ratio (INR) range (TTR). However, few studies have investigated patient-level predictors of anticoagulation control. We aim to identify patient characteristics associated with quality of anticoagulation control on warfarin, as measured by TTR.

Methods: We carried out a population-based retrospective study using data from the Clinical Practice Research Datalink. This study included two cohorts of patients starting warfarin treatment after a first diagnosis of atrial fibrillation (AF) or venous thromboembolism (VTE) between 1 January 2000 and 31 December 2013. We used a multivariate mixed regression model and logistic regression models to predict the fully-adjusted effect of each predictor variable upon TTR, and the directional patterns underlying low TTR (sub- and supra-therapeutic INR range).

Results: The study population comprised 29,717 incident AF patients and 19,113 recent VTE patients who initiated warfarin. For both cohorts, patient characteristics all together explained only 2–4% of the variation in individual’s TTR. Poor anticoagulation control (TTR <70%) driven by subtherapeutic INRs occurred in younger patients (<45 years) and in AF patients with repeated hospitalisations. Poor anticoagulation control driven by supratherapeutic INRs was more common in the VTE patients who were current smokers (AF: OR = 1.21; 95% CI 1.06–1.39 and VTE: OR = 1.36; 95% CI 1.15–1.62), in patients using medications for pain (AF: OR = 1.22, 95% CI 1.07–1.39 and VTE: OR = 1.33, 95% CI 1.09–1.62) and in VTE patients with active cancer (OR = 1.59, 95% CI 1.22–2.08).

Conclusion: In a real world clinical practice setting there is a high amount of radiofrequency pulmonary vein isolation for the prevention of systemic emboliza.

P4403 | BEDSIDE
Importance of fluctuations of kidney function on non-vitamin K oral anticoagulant dosing adjustment in patients with atrial fibrillation and recent acute decompensated heart failure
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Background: Renal impairment and fluctuations in renal function are common in patients with recent acute decompensated heart failure (ADHF) hospitalization, and in those with atrial fibrillation (AF).

Purpose: The aim of the present study was to evaluate the hypothetical need of dosage adjustment (based on fluctuations of kidney function) of dabigatran, rivaroxaban and apixaban during the first 6 months after hospital discharge in patients with concomitant AF and ADHF.

Methods: Observational study of 162 patients (52% male; mean age: 74 years) with non-valvular AF after hospitalization for ADHF who had creatinine determinations along follow-up. Hypothetical recommended dosage of dabigatran, rivaroxaban and apixaban according renal function was determined at discharge. Variations in serum creatinine and creatinine clearance (CrCl) and consequent changes in recommended dosage of these drugs were identified along 6 months of follow-up.

Results: Among overall study population, 44% of patients would have needed dose adjustment of dabigatran during follow-up, 35% would have needed adjustment with rivaroxaban and 29% would have needed adjustment of apixaban dosage. A higher proportion of patients with CrCl <60mL/min or elderly (>75 years) would have needed dosage adjustment during follow-up.

P4402 | BEDSIDE
The patients with atrial fibrillation taking non-vitamin K antagonist oral anticoagulants also need the transesophageal echocardiography for the prevention of systemic embolization
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Background: It is well known that the patients with both paroxysmal and persistent atrial fibrillation (AF) are at an increased risk of systemic embolization. Non-vitamin K antagonist oral anticoagulants (NOAC) have been developed as alternatives to warfarin (WAR) for oral anticoagulation with warfarin (target international normalized ratio [INR] = 2.0–3.0) for 3–4 weeks before electrical or pharmacological cardioversion without exclusion of LA thrombosis by transesophageal echocardiography (TEE). However, there is little information on the safety of cardioversion without TEE on NOAC therapy.

Purpose: The aim of this study was to evaluate the efficacy of screening the presence of the thrombus in left atrium (LA) in AF patients with anticoagulants.

Methods: The 83 AF patients (mean age, 66±9.8 years; 62% men) who underwent transesophageal echocardiography before electrical or pharmacological cardioversion without exclusion of LA thrombus before cardioversion or radiofrequency pulmonary vein isolation for the prevention of systemic embolization.

Results: The aim of this study was to evaluate the evolving pattern of antithrombotic therapy in newly diagnosed atrial fibrillation in GARFIELD-AF.

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Purpose: To study the evolving pattern of antithrombotic therapy in newly diagnosed non-valvular atrial fibrillation (AF) patients with >1 investigator-defined stroke risk factor.

Methods: 27,106 prospective patients were enrolled in three sequential cohorts in 2010–14 in the global GARFIELD-AF registry: C1 (2010–11), n=5516, mean age 73.8 years, median CHADS2 score 2; C2 (2011–13), n=11,652, mean CHADS2 score 3; C3 (2013–14), n=9938, mean CHADS2 score 3.2. Baseline characteristics and antithrombotic therapy initiated at diagnosis were analysed by cohort.

Results: Baseline characteristics were similar in all three cohorts. From C1 to C3, the proportion of patients on anticoagulant (AC) therapy increased (C1 57.5%; C2 60.3%; C3 67.5%). Use of vitamin K antagonist (VKA) ± antiplatelet (AP) decreased (C1 53.3%; C2 48.5%; C3 41.1%), while use of non-VKA oral ACs (NOACs) ±AP increased (C1 4.2%; C2 13.8%; C3 26.4%). The increase in use of non-VKA oral ACs was driven by DOACs, with a 3-fold increase in the proportion of patients on DOACs (±AP) from C1 to C3, from 0% to 13.2% (C3 vs. C1).
Results: Since the introduction of NOACs, newly diagnosed at-risk AF patients are more often receiving guideline recommended therapy driven by increased use of NOACs and less treatment with VKA±AP or AP alone. However, patients with a score of 0 are also using more AC, with a greater proportion receiving NOACs.

Acknowledgement/Funding: The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG.

P4405 | BEDSIDE
Anticoagulation and outcomes of dialysis patients with atrial fibrillation: 3-year cohort study
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Background: Atrial fibrillation (AF) is the commonest cardiac arrhythmia, even more prevalent in end-stage renal failure patients. The role of anticoagulation in this context, taking into account of thomboembolic and bleeding outcomes, remains unproven.

Purpose: We reviewed the characteristics and outcomes of end-stage renal failure patients with AF on dialysis with a focus on warfarin anticoagulation and risk scores.

Methods: All patients starting on dialysis at our hospital during January 2000–December 2008 with AF were studied. Demographics, co-morbidities, renal disease and AF characteristics, as well as embolic, bleeding and/or mortality events were recorded.

Results: There were 141 out of 774 (18.2%) dialysis patients with AF followed-up for 3.4±2.5 years, 75 (53.2%) with pre-existing AF, and warfarin was used for anticoagulation in 41.8% (59). Incidence of ischaemic stroke and intracranial bleed were 3.1/100 person years and 0.82/100 person years respectively, and all embolic complications in patients with non-valvular atrial fibrillation (NVAF).

Conclusions:: Anticoagulation with warfarin did not reduce embolic risk in dialysis patients, but also increased the risk of intracranial or other bleeds. Conventional risk scores remain good discriminators of embolic but not bleeding events in dialysis patients.

P4406 | BEDSIDE
HAS-BLED versus ATRIA at predicting the risk of major bleeding in a real world cohort of patients with non-valvular atrial fibrillation on vitamin K antagonists

Background: Vitamin K antagonists (VKAs) greatly reduce the risk of stroke and still is the most commonly used therapy for this purpose in atrial fibrillation. However, this therapy also conveys a risk of bleeding complications, and the risk-benefit evaluation of oral anticoagulants therapy remains challenging. HAS-BLED and ATRIA are contemporary scoring systems used to predict hemorrhagic complications in patients with non-valvular atrial fibrillation (NVAF).

Purpose: We compared the predictability of both scores in a community based cohort of patients with NVAF on VKAs.

Methods: Retrospectively, we identified 911 consecutive patients with NVAF recently on VKAs who were attending the outpatient cardiology consultation of a tertiary hospital between January 2011 and February 2013. HAS-BLED and ATRIA were computed using the original criteria used in their development cohorts. Measures of performance for the risk scores were evaluated at predicting major bleeding (2005 International Society on Thrombosis and Haemostasis criteria) and intracranial hemorrhage (ICH).

Results: During 10±3 months of follow up, 30 (3.3%) developed major bleeding; 9 (1%) were ICH. Although both scores predicted major bleeding and ICH better than chance, their discriminative capacity was rather modest and did not differ significantly between each other regardless if they were considered as continuous (c-statistic ≤0.71) or categorical (c-statistic ≤0.65) variables. While as categorical variable, the HAS-BLED score was strongly associated with ICH (hazard ratio = 6.9; 95% CI: 1.8–28.1; p=0.007), the ATRIA risk score was not significantly associated with ICH (hazard ratio = 3.9; 95% CI: 0.96–15.5; P=0.06). The net reclassification improvement index numerically favored HAS-BLED for predicting major bleeding and ICH (+5.9% and +12%, respectively). In this cohort, diabetes mellitus (hazard ratio = 2.8; p=0.01) and chronic obstructive pulmonary disease (hazard ratio = 2.9, p=0.005) were also identified as independent predictors of major bleeding.

Conclusions: In this study, HAS-BLED outperformed ATRIA scoring system especially at predicting ICH in a real world cohort of patients with NVAF on VKAs. Diabetes mellitus and chronic obstructive pulmonary disease should be considered at bleeding risk stratification in these patients.

INFARCTION ACUTE PHASE STEMI

P4407 | BEDSIDE
Adherence to performance measures and in-hospital outcomes for myocardial infarction in China: findings from China Acute Myocardial Infarction (CAMI) registry
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Objectives: We sought to describe the hospital-level adherence to performance measures and in-hospital outcomes in a national sample of patients with acute myocardial infarction (AMI) in China.

Methods: From Jan. to 2013 to Sep. 2014, 16,113 ST-segment elevation myocardial infarction (STEMI) and 6,463 non-STEMI (NSTEMI) patients from 89 China hospitals were registered in the China Acute myocardial infarction (CAMI) Registry.

Results: Proportions of eligible participants receiving the following 10 performance measures were calculated: medications within 24 hours of admission (aspirin) and on discharge (aspirin, beta-blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers), PCI during primary percutaneous intervention (PPY12 antagonists), echo examination, reperfusion therapy, door to needle time (D2N) or door to balloon time (D2B). A composite adherence score, defined as the total number of successful interventions performed among eligible patients divided by the total number of possible interventions among eligible patients, was calculated.

Results: The provincial level hospitals had higher composite adherence score (0.67±0.20) than the prefecture level hospitals (0.66±0.21) and county level hospitals (0.61±0.25) on all performance measures (P < 0.0001). Among these performance measures, the rate of patients undergoing reperfusion therapy (thrombolytic therapy or PCI) in STEMI patients within symptom onset less than 12 hours was significantly different, with 80.4% in provincial level hospitals, 65.3% in prefecture level hospitals and 58.6% in county level hospitals (P < 0.0001). The mortality for provincial level, prefecture level and county level hospitals mortality groups for STEMI were 4.3%, 7.6% and 12.8% (P < 0.0001) and the mortality for NSTEMI was 4.9%, 6.1%, and 9.8% (P < 0.0001). Composite adherence score was inversely associated with risk-adjusted hospital mortality.

Conclusions: Although process performance was associated with hospital mortality, the NSTEMI patients are more often receiving guideline recommended therapy driven by in-hospital outcomes and improving STEMI patients' timely access to appropriate reperfusion therapy at a national level is a priority, especially in rural areas in China.

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P4408 | BEDSIDE
Lead aVR: the new armamentarium for culprit artery localization in acute inferior wall myocardial infarction; will it be the first point for artery localization?
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Background: Early discrimination of culprit artery in acute inferior ST elevation myocardial infarction (STEMI) caused by right coronary artery (RCA) and left coronary artery (LCX) lesions can guide the emergency department (ED) approach and prognosis. Existing criteria have poor sensitivity for LCX and poor specificity for RCA. If reliable simpler ECG patterns can be recognized, it will be possible to determine the culprit coronary artery earlier and facilitate the management.

Purpose: To study the change of STEMI segment deviation in lead aVR and its role in identification of infarct related artery in patients with acute inferior STEMI.

Methods: One hundred (100) consecutive patients admitted in our department as first acute inferior STEMI with symptoms of acute MI, 1 mm ST-segment elevation in ≥2 ECG leads, and suggestive of involvement of inferior coronary arteries and who subsequently underwent coronary angiography either as primary angioplasty or within 24 hrs of hospital admission was taken for study. We examined the relation between ST segment deviation in lead aVR and cul-
P4410 | BEDSIDE
Acute phase Glycemic Variability by continuous glucose monitoring system (CGMS) is associated with endothelial dysfunction in patients with ST-Elevation Myocardial Infarction

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Background: Endothelial dysfunction can predict cardiovascular outcomes in coronary artery disease. Previous study demonstrated glycemic variability might affect endothelial function. It remains unclear whether acute glycemic variability is associated with an increased risk of cardiac events in ST-elevation myocardial infarction (STEMI) patients.

Methods: This prospective study enrolled 70 patients with STEMI. CGMS provides glycemic excursion displayed at 5-minute intervals, 576 points during 48 hours. Endothelial function was assessed before discharge by measuring right brachial artery dilatation after 5 minutes of forearm ischemia flow mediated dilatation (FMD). Primary endpoint was measurement of endothelial function.

Results: Glycemic variability, as indicated by the mean amplitude of glucose excursion (MAGE), was measured and divided into 3 groups. The FMD values by MAGE tertiles (5.15mmol/L, 3.36–5.15mmol/L, 3.36–5mmol/L) had significant difference among 3 groups (figure). Blood glucose fluctuation was correlated with FMD, respectively p=0.02. Conclusion: Glycemic variability is significantly associated with impairment of endothelial function after coronary intervention for patients with STEMI. FMD might become the therapeutic target of medical intervention especially for blood glucose.

P4411 | BEDSIDE
Circulating corin concentrations are related to infarct size in patients after ST-segment elevation myocardial infarction

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Background: Corin, a transmembrane serine protease, partially sheds from the cardiomyocyte cell surface and enters the circulation, a process that might be enhanced by dissolving the setting of myocardial injury.

Objective: We sought to prospectively investigate the potential association between plasma corin concentrations and myocardial infarct size (IS) measured by cardiovascular magnetic resonance (CMR) in the first week after reperfused ST-segment elevation myocardial infarction (STEMI) and 4 months thereafter.

Methods: In this observational, single-centre study, IS was determined at base-line and 4 months after STEMI using late gadolinium contrast-enhanced CMR. Corin concentrations were determined from blood samples drawn at a median of 1.9 days (IQR 0.5–6.3) after STEMI and 1.3 days (IQR 0.5–6.3) after STEMI by an immunofluorescent assay.

Results: This study cohort included 50 patients (median age: 59 years (IQR 51–66 years); females: 7 (14%)). Corin concentrations (median = 1070 pg/ml, IQR 645–2117 pg/ml) were significantly associated with 4-month IS (r=0.366, p=0.009) but there was only a trend to correlation with baseline IS (r=0.249, p=0.084). Corin was significantly correlated with maximum high-sensitivity cardiac troponin T (hs-TnT) concentrations (r=0.346, p<0.014). A receiver operator characteristics (ROC) model including hs-TnT provided an area under the curve (AUC) of 0.95 (95% CI 0.89–1) for the prediction of large 4-month IS. Including corin instead of hs-TnT resulted in an AUC of 0.90 (95% CI 0.81–0.98).

Conclusion: Circulating corin at day 2 after acute STEMI is associated with 4-month IS as assessed by CMR.

P4412 | BEDSIDE
Outcome in patients with STEMI undergoing interhospital transfer: similar baseline characteristics and outcome despite a longer treatment delay group

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Background: Early reports showed that any delay in reperfusion with primary PCI was associated with a rise in mortality. On the other hand, taking care of sicker patients usually requires a longer time, so the delay can be the consequence rather than the cause of the worse prognosis. Moreover, the first medical contact-to-balloon (FMCTB) time may have a prognostic relevance as an index of the overall quality of care of the institution.

Purpose: We sought to assess the prognostic impact of FMCTB time in a single centre comparing patients arriving directly with patients transferred from spoke hospitals. The transfer requires a certain amount of time which is relatively independent of the patient’s risk profiles.

Methods: From January 2006 to December 2014, 1380 STEMI patients underwent primary PCI at our Centre, arriving directly (75%) or transferred from 3 spoke hospitals (25%). All STEMI patients were routinely transferred avoiding a selection bias.

Cost analysis of hospital stage of STEMI

<table>
<thead>
<tr>
<th>Cost analysis</th>
<th>STEMI, n=1380</th>
<th>STEMI transferred, n=3350</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>67±14±11.2</td>
<td>66±14±13.5</td>
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<tr>
<td>Females</td>
<td>26±7%</td>
<td>26±4%</td>
<td>0.963</td>
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<td>Diabetes</td>
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<td>20±6%</td>
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<td>Anterior MI</td>
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<td>36±1%</td>
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<td>TIMI Risk Index</td>
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<td>0.412</td>
</tr>
<tr>
<td>FMCTB time</td>
<td>77±62–97</td>
<td>104±89–132</td>
<td>0.001</td>
</tr>
<tr>
<td>In-hospital</td>
<td>180±123–290</td>
<td>231±148–398</td>
<td>0.001</td>
</tr>
<tr>
<td>Open vessel before PCI</td>
<td>32±3%</td>
<td>37±1%</td>
<td>0.183</td>
</tr>
<tr>
<td>Open vessel after PCI</td>
<td>95±7%</td>
<td>97±9%</td>
<td>0.093</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>7±1%</td>
<td>6±6%</td>
<td>0.743</td>
</tr>
</tbody>
</table>
Results: Transferred patients had a significantly longer FMCTB and total ischemic time, while other baseline characteristics and the outcome of the 2 groups of patients were similar (Table). Multivariate analysis identified age, total ischemic time, TIMI risk index, Killip class, open vessel before and after PCI, but not transfer, as significant predictors of mortality.

Conclusions: In our experience, patients with STEMI requiring interhospital transfer, as compared to non-transferred patients, had comparable baseline characteristics and similar mortality, although they experienced a longer treatment delay.

P4413 | BEDSIDE
Electrocardiographic findings leading to false ST elevation myocardial infarction activations at a percutaneous coronary intervention capable center

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Background: Electrocardiogram (ECG) interpretation is essential for diagnosing a ST Elevation Myocardial Infarction (STEMI). We report the EKG results of patients who presented with False STEMI activation.

Methods: Medical records of all patients presenting to our institution for percutaneous coronary intervention for possible STEMI from January 2012 to November 2014 were reviewed. A false STEMI activation was defined as a lack of clinical and ECG evidence of ongoing myocardial infarction.Inpatients undergoing cardiac catheterization without obvious culprit lesions were also included. The ECG findings were grouped into a) meeting STEMI criteria per American College of Cardiology/ American Heart Association, b) ST elevation not meeting STEMI criteria, c) new left bundle branch block (LBBB), d) new right bundle branch block (RBBB) without ST elevation, e) ST and/or T wave abnormalities suggesting myocardial ischemia, f) nonspecific ST/ T wave changes and g) paced rhythm.

Results: Of 643 STEMI activations, 29.7% (191/643) were false activations. Only 11% (21/191) met ECG criteria for STEMI. 40.3% (77/191) had ST segment elevations not meeting STEMI criteria. 12.6% (24/191) had LBBB morphology with no prior ECG available for comparison. 6.8% (13/191) were RBBB. 5.2% (10/191) showed ST and/ or T wave changes suggesting ischemia. 23.4% (44/191) showed nonspecific ST/ T wave changes. Among those, 31.8% (14/44) met diagnostic ECG criteria for left ventricular hypertrophy. There were 2 ECGs (1.1%) showing paced rhythm.

Conclusion: The vast majority of ECGs that led to False STEMI activation showed ST elevation that did not meet criteria for STEMI.

P4414 | BEDSIDE
An admission clinical index score for risk stratification of new-onset atrial fibrillation in STEMI patients undergoing primary PCI

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Background: Data relating high-sensitivity cardiac troponin T (hs-cTnT) to long-term myocardial function and infarct size in patients after first ST-segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI) are lacking.

Purpose: We aimed to evaluate the use of serial and peak concentrations of hs-cTnT for prediction of myocardial function as well as infarct size assessed by cardiac magnetic resonance imaging (CMR) one year following first STEMI.

Methods: Sixty-six patients (mean age 57±11 years, 12% females), reperfused by PCI for first-time STEMI, were enrolled in this single-centre, observational study. Serial hs-cTnT, creatine kinase (CK), high-sensitivity C-reactive protein (hs-CRP) and lactate dehydrogenase (LDH) levels were measured on admission as well as 12 h, and 24 h post-PCI. CMR imaging was performed within the first week and 12 months thereafter.

Results: Except for admission hs-cTnT, all single time point and peak hs-cTnT concentrations showed significant correlations with left ventricular ejection frac-
tion (LVEF: r=−0.404 to −0.517, all p<0.01) and infarct size (IS: r=0.421 to 0.700, all p<0.01) at baseline and 12 months follow-up. Peak concentrations of CK, hs-CRP and LDH were significantly associated with 12-month LVEF and IS (all p<0.05). In receiver-operator characteristic analysis, the under the curve (AUC) of peak hs-cTnT was 0.82 (95% CI 0.71 to 0.92) for the prediction of decreased LVEF (<55%) at 12 months and 0.89 (0.89, 95% CI 0.81 to 0.97) for the prediction of large IS (>8%) at 12 months. The combination of all four biomarkers resulted in an AUC of 0.82 and 0.92 for the prediction of reduced LVEF and large IS at 12 months, respectively.

Conclusions: Patients with first-time STEMI, serial and peak concentrations of hs-cTnT are closely correlated to long-term LVEF and IS. Combination of hs-cTnT with other traditional biomarkers did not add any significant prognostic value compared with hs-cTnT alone.

POST INFARCTION PERIOD | P4417 | BEDSIDE
Patterns of left ventricular remodeling during the first year after a repurposed myocardial infarction: a prospective MRI study
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Background: Left ventricular remodeling (LVR) is a major concern after a myocardial infarction.

Purpose: To study various patterns of LVR during the first year after a myocardial infarction, with the help of recent MRI approach.

Methods: 162 patients with a first ST-elevation MI admitted to our university hospital were prospectively enrolled. CMR was performed at baseline, and repeated at 3-month and 1 year follow-up in order to investigate left ventricular (LV) volumes and wall motion, infarction fraction, infarct size (IS), microvascular obstruction (MVO), and systolic wall stress (SWS).

Results: LVR (>10% increase end-systolic volume) occurred in 38 (23%) patients. 19 patients presented with early remodeling (ELVR) (>10% increase end-systolic volume during the first three months) and 19 others with late remodeling (LLVR) (>10% increase end-systolic volume between baseline and one year, excluding ELVR patients). In patients without remodeling (NoLVR), LV volumes and mass decreased and ejection fraction increased during follow-up. In ELVR patients, EF decreased during the first three months with no further variation (EF: 45.4%±9.9, 43.9%±9.6, 43.4%±10.4 at baseline, 3 months and 1 year, respectively). In LLVR patients, LV volumes remained stable during the first three months and then increased while EF presented a biphasic course per event (EF: 48.0%±11.4, 50.7%±11.1, 46.3%±11.2 at baseline, 3 months and 1 year, respectively). NoLVR and LLVR patients depicted similar infarct characteristics (Creatin kinase peak, infarct size, MVO) and similar baseline LV volumes and EF whereas ELVR patients presented larger infarct size, higher extent of MVO and greater creatin kinase peaks. In multivariate analysis, IS (OR=1.128 [95% CI: 1.067–1.193], p<0.001) was the sole independent predictor of ELVR. SWS at 3 months (OR=1.110 [95% CI: 1.002–1.228], p=0.045) and the non prescription of betablockers or angiotensin-converting enzyme inhibitors (OR=0.030 [95% CI: 0.003–0.346], p=0.005) were independent predictors of NoLVR.

Conclusion: Two clinical patterns of LVR were distinguished in our study. Initial infarct severity was the major determinant of early remodeling whereas SWS and long-term medications were the only determinants of late remodeling, intimating more general and chronic processes.

P4418 | BEDSIDE
The association between adherence to the Mediterranean diet and diabetes mellitus on the 10-year (2004-2014) acute coronary syndrome (ACS) prognosis; the Greeks study
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Background: The Mediterranean dietary pattern has been favorably associated with many health outcomes, onal glycemic profile, either as a component of metabolic syndrome or as a sole pathogenic factor undoubtedly increases the Cardiovascular Disease (CVD) risk.

Purpose: To evaluate the association between adherence to the Mediterranean Diet (MD) and history of diabetes mellitus, on the 10-year incidence among Acute Coronary Syndrome patients (ACS).

Methods: From October 2003 to September 2004 a sample of 6 Greek hospitals was selected and almost all consecutive 2,172 ACS patients were enrolled. In 2013–14, the 10-year follow-up (2004–2014) was performed in 1,918 participants (88% participation rate). Dietary habits were assessed through a validated food frequency questionnaire and adherence to MD was evaluated through the Med Diet Score (range 0–55). Higher values indicate greater adherence to the Mediterranean diet. The sample was classified in two categories: low Med Diet Score (<27) vs. moderate/high (≥27), Multiple logistic regression models were applied to evaluate the effect of adopting the Mediterranean dietary pattern in the 10-year ACS prognosis. Furthermore, stratified analysis was carried out including patient’s history of diabetes.

Results: The overall incidence of diabetes mellitus at baseline examination was 30% in males and 38% in females (p<0.001); whereas the 10-year ACS incidence was 40% in males and 32% in females (p<0.001). An inverse association was observed between adherence to the Mediterranean diet and recurrent cardiovascular events, after taking into account potential confounders (OR=0.802, 95% CI 0.644–0.999, p=0.049). However, the diabetes mellitus stratified analysis revealed that the adherence to the testing dietary pattern was inversely associated with ACS prognosis only among the non-diabetic patients (OR=0.795, 95% CI 0.613–1.032, p=0.085); whereas no significant association was observed in those with abnormal glucose homeostasis (p=0.360).

Conclusion: Moderate/high adherence to the Mediterranean dietary pattern seems to be protective against recurrent cardiovascular events, but only among diabetic ACS patients. The latter observation highlights a plausible interaction between history of diabetes and long-term nutritional habits in the ACS prognosis.

Acknowledgement/Funding: None to declare.
trials (PRAMI and CVLPRIT) have shown a superiority of complete in-hospital revascularisation as compared to culprit only. These trials have the potential to change the guidelines although they demonstrate no difference in mortality but in the composite end point, mainly driven by ischaemia.

**Aim:** To assess the role of stress imaging (CMR or echocardiogram) as gatekeeper to complete revascularisation in STEMI patients with moderate to severe bystander disease treated with Primary PCI (PPCI) of the culprit lesion.

**Methods:** Registry data collected on consecutive patients undergoing PPCI (Sept 2011–Sept 2013). A non-culprit lesion was considered to be moderate to severe if the stenosis was 50–75% in large proximal epicardial vessel or 70–90% elsewhere. Severe or critical bystander disease was excluded as the best treatment for those was deemed to be direct revascularisation without Fractional flow reserve (FFR). The diagnostic accuracy of stress echocardiogram was assumed 84% for detecting FFR >0.80. A stress imaging analysis model was created with the data collected from stress CMR or stress echocardiogram examinations and using the result in an FFR guided strategy. UK NICE and US CMS.Gov tariff for each investigation was used.

**Results:** 1,167 patients were included (74% males with a mean age 64 years). Significant MVD was present in 391 patients (33%), of which 298 patients (76%) underwent stress guided revascularization (n=157, 53% stress CMR, n=141, 47% stress echo). The remaining 93 patients with significant MVD (23%) either underwent direct revascularisation (severe or critical stenosis) or were lost to follow up.

In the stress CMR group, only 39% patients (61/157) had evidence of inducible myocardial perfusion defect, and in the stress echo group 55% (78/141 patients) had induced RWMA. In the cost-effectiveness analysis, using stress imaging as a gatekeeper to complete revascularisation led to a average saving of €302/patient (CMR) and €395/patient (echo) or €1341/patient (echo) (UK and US based cost model, respectively).

**Conclusions:** Our study demonstrated that in patients undergoing PPCI, maybe used to clarify the clinical severity of myocardial infarction.

### Glycosylated Apo J levels in acute myocardial infarction: implications in prognosis

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**Background:** Apolipoprotein J (Apo J) is a cytoprotective and anti-oxidant protein with an important function in lipid metabolism. We previously showed that in the early ischaemic phase at the onset of an acute myocardial infarction (AMI) there is a shift in Apo J glycosylation. Moreover, there are evidences of a protective role of Apo J against myocardial injury in the context of AMI. However, it is unknown whether Apo J glycosylation levels are potential markers in the prognosis after AMI.

**Purpose:** The aim of this study was to investigate if changes in glycosylated Apo J (Apo J-Glyc) levels during AMI are involved in the evolution and progression of the ischaemic event.

**Methods:** Apo J-Glyc levels were measured with a novel and original immunnoassay assay in serum samples from AMI-patients at the moment of admission (t=0h; N=227) and 3 days after the onset of the event (t=3d; N=68), and compared to an age and gender matched group of control subjects without any type of cardiovascular disease (N=144).

**Results:** AMI-patients at admission had a 20% decrease in Apo J-Glyc levels with respect to control non-ischaemic patients (P < 0.0001). Multiple lineal regression analysis (including drug treatment, gender, presence of diabetes and LDL-cholesterol, HDL-cholesterol and total cholesterol levels), showed that only the presence of the ischaemic event remained as an independent factor for Apo J-Glyc levels (r=0.428; P < 0.0001). Apo J-Glyc levels at admission were able to discriminate the presence of AMI with an area under the ROC curve (AUC) of 0.752 (95% CI: 0.703–0.801; P < 0.0001) and were inversely correlated with the ischemia time (r=-0.207; P = 0.007) and with the GRACE risk score (r=0.268; P = 0.0002). Follow-up of AMI-patients 3 days after the event revealed a progressive decrease of Apo J-Glyc levels (15% reduction vs. t=0h; P < 0.0003). Furthermore, Apo J-Glyc levels 3 days after the event showed a predictive value for cardiac shock presentation (AUC: 0.766; 95% CI: 0.617–0.914; P = 0.006) and mortality (AUC: 0.744; 95% CI: 0.597–0.891; P = 0.006) in AMI-patients.

**Conclusions:** These results indicate that Apo J-Glyc is a novel biomarker of ischaemic event. Moreover, the continuous decrease in Apo J-Glyc levels predicts a worsening in the evolution of the cardiac event, likely acting as a prognostic marker.

**Acknowledgement/Funding:** Plan Estatal de I+D+I 2013-2016 SAF2013-42962-R (LB) FEDER “Una manera de hacer Europa”; ISCIII RD12/00420227 (LB)

### Influence of face cooling (diving reflex) on heart rate variability and double product in patients after myocardial infarction

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**Background:** Patients after myocardial infarction (MI) are at high risk of new cardiovascular and arrhythmic events. Heart rate variability (HRV) is used to identify patients at risk for cardiovascular events or death. Cold stimulus applied to the face induces cardiovascular responses, notably bradycardia, known as diving reflex. **Purpose:** The aim of this study was to assess the influence of face cooling (diving reflex) on heart rate variability and double product in patients after myocardial infarction.

**Methods:** 51 patients after MI were studied, in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 55.3 years. Patients were randomly divided in the face cooling group (29 patients) and control group (without face cooling: 22 patients). Patients of similar age, sex and site of infarction. All patients were exposed to 25 degrees C ambient air for 30 min., they had their blood pressure taken, as well as, continuously monitored ECG for 5 min, in the lying position. Cooling group patients had cold water bags of 2 degrees C water put on their faces. They had their blood pressure taken and monitored ECG for 5 min again. Control group patients had the same procedure, but without face cooling. Out of 5 min. continuous monitored ECG four parameters of the "time domain" HRV were assessed: SDNN, RMSSD, N50 and HRV index.

**Results:** 51 patients after MI were studied, in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 55.3 years. Patients were randomly divided in the face cooling group (29 patients) and control group (without face cooling: 22 patients). Patients of similar age, sex and site of infarction. All patients were exposed to 25 degrees C ambient air for 30 min., they had their blood pressure taken, as well as, continuously monitored ECG for 5 min, in the lying position. Cooling group patients had cold water bags of 2 degrees C water put on their faces. They had their blood pressure taken and monitored ECG for 5 min again. Control group patients had the same procedure, but without face cooling. Out of 5 min. continuous monitored ECG four parameters of the "time domain" HRV were assessed: SDNN, RMSSD, N50 and HRV index.

**Conclusions:** The study demonstrated that face cooling significantly decreased
both heart rate and double product, that is myocardial oxygen uptake, at rest. Face cooling also significantly increased HRV parameters, which represent vagal activity. Face cooling could be possibly used in the treatment of ischemic chest pain.

**P4424 | BEDSIDE**

The influence of pre-hypertension on long-term major adverse cardiac events in patients with acute myocardial infarction and preserved left ventricular systolic function

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Background: We evaluated the independent prognostic value of pre-HT on long-term MACE after acute MI with preserved LV systolic function.

Methods: Using data from Korea Working Group on Myocardial Infarction, a total of 2538 patients who were diagnosed with acute myocardial infarction, had no history of previous hypertension and whose LV ejection fraction (EF) was equal or higher than 45%. The eligible patients were classified into two groups according to initial systolic blood pressure (sBP): optimal group (sBP<120 mmHg and diastolic BP (dBP) < 80 mmHg; n=1314, 51.8%) vs pre-HT group (120<sBP<140 mmHg or 80<dBP<90 mmHg; n=1224, 48.2%). Predicted MACE was all cause mortality, repeated MI, revascularization and new onset heart failure. In addition, we investigated the predictive value of pre-HT for MACE with multivariable Cox regression analysis.

Results: Patients in pre-HT group were younger, less male, and prescribed beta-blockers more. The initial sBP was 104.4 vs 124.2 mmHg in each group (p<0.001). Their angiographic findings were not different. Total incidence of MACE was similar between the two groups, which was 15.8% and 14.5% in optimal and pre-HT group, respectively (p=0.413). Among individual component of MACE, only target vessel revascularization rate was marginally higher in pre-HT group (0.3% vs 1.0%, p=0.06). After adjusting confounding factors, pre-HT was not predictor of 12-month MACE (HR 0.914, p=0.459). Only initial LVEF was a significant predictor (HR 0.982, 95% CI 0.967–0.998).

Conclusion: We found no association between pre-HT and long-term MACE in patients with acute myocardial infarction.

**POST INFRINGEMENT PERIOD II**

**P4425 | BEDSIDE**

Prognostic value of plasma galectin-3 levels for in-hospital and long-term complications of patients with right ventricular myocardial infarction

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The prognosis of patients (pts) after coronary artery bypass surgery (CABS) has been noted in many studies, but only few studies analyzed prognosis of pts with acute myocardial infarction (AMI) after prior CABS. The primary aim of the POP study (PostOperative Prognosis study) is analyze, follow-up and making scores using clinical, angiographic, and procedural variables available 30-day after intervention. The aim of this study was to present early and late prognosis of pts with AMI and prior CABS. The study population consisted of 924 pts with AMI after prior CABS (post bypass group) and control group of 1182 pts with AMI and without prior CABS, who were followed from April 1988 to January 2015. At baseline post bypass group was slightly younger (p=0.0323), with more men (p=0.0001) and with more pts with previous angina (p=0.0318) and previous AMI (p=0.0001). Control group of pts had more hypertensives (p=0.0212), smokers (p=0.0026) and heredities (p=0.0124). Post bypass group had in prior therapy more beta-blockers (p=0.00122) and anticoagulants (p=0.0056). Other baselines characteristics were similar in both groups of patients. Indexes of infarct size were lower in post bypass group (p=0.0065). There were more VF (p=0.0086) in post bypass group and AV block rhythm disturbances (p=0.0086) in control group of pts with patients with mortality was similar (p=0.4324). Approximately 9 years after discharge, post bypass pts had more new coronary events (p=0.0001), heart failure (p=0.0196), recurrent CABS (p=0.0001), reinfarction (p=0.0001) and unstable angina (p=0.0001) than did control pts. Cumulative mortality was better in control group than in post bypass group (p=0.0396). Multivariable proportional hazards analysis showed that previous angina (p=0.0014), diabetes (p=0.0086) and age (p=0.0184) were undependable prediction factors for survival. Use of digitals and diuretics, together with previous angina influenced on survival too (p=0.0174) as well as male gender, older pts and diabetes together, influenced worse survival in post bypass group of pts.

Conclusion: Patients with AMI after prior CABS had smaller infarct, but more reinfarction, reoperation, heart failure and angina. Previous angina, diabetes and age undependable as well as use of digitals, diuretic and angina together and male gender, older pts and diabetes together, influenced worse survival in post bypass group of pts.

**P4426 | BEDSIDE**

Clinical impact of left ventricular spontaneous echo contrast in patients with acute anterior wall myocardial infarction


Background: This study is designed to investigate the clinical impact of LV spontaneous echo contrast (SEC) and association with LV thrombus (LVT) formation in patients with acute anterior wall myocardial infarction (ant-AMI) and underwent percutaneous coronary intervention (PCI).

Methods: 36 ant-AMI patients with LV SEC were enrolled and divided into 2 groups depending on future development of LVT. We compared the demographic and procedural characteristics and clinical outcome of the two groups.

Results: Median clinical follow-up period was 80 (2–267) months. In 9 (23.7%) patients, LVT developed median 40 (3–690) days after ant-AMI. Although 15.8% of LV SEC patients were NSTEMI, LVT developed only in STEM1. No embolic events occurred in all LV SEC patients even in patients with future LVT formation, whereas LV SEC with future LVT formation was associated with CHF hospitalization during post-MI follow-up. In STEM1 patients with LV SEC, LVT formation was related to poorer LV systolic function and more decline of hemoglobin than in patients without future LVT (Table). Male gender and smoking were conversely related to LVT formation. STEM1 patients with SEC and future LVT formation who had undergone primary PCI were associated with longer door-to-balloon time, lower initial TIMI flow and more frequent thrombus aspiration procedure than those of no LVT.

Conclusions: Patients with LV SEC after ant-AMI had higher risk of LVT formation. Male gender and smoking were associated with future LVT formation.
has prognostic value in patients with heart failure and acute coronary syndrome. However, relationship between galectin-3 and complications after RV MI is still unknown.

**Purpose:** To evaluate the significance of galectin-3 as a predictor of complications at 2.6-year follow-up in patients with RV MI on the background of the posterior Q-MI.

**Methods:** The study involved 155 patients (60% males and 40% females) with acute RV MI on the background of the posterior Q-MI aged 64.11±0.78 years. Galectin-3 levels were determined with enzyme immunoassay on day 2 of MI. Follow-up was 2.6±0.4 years. Study endpoints were: unstable angina (UA); recurrent myocardial infarction (Re-MI); stroke; and death.

**Results:** Study endpoints reached 62 (40%) patients: UA - 51 (32.9%), Re-MI - 16 (10.3%), stroke - 9 (5.8%) patients, 14 people (9.0%) died. Patients with completed follow-up period had significantly higher concentration of galectin-3 than those of patients without complications (34.33±0.58 mg/ml vs 27.16±0.52 mg/ml, p<0.0001). Multivariable analysis demonstrated that galectin-3 level is an independent risk factor for paroxysmal atrial fibrillation (AF) and cardiogenic shock in acute period of RV MI. It was proved that galectin-3 level is a predictor of Re-MI during 2.6 years of follow-up.

**Regression summary for Galectin-3**

<table>
<thead>
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<th>B ± Std. Err. of B</th>
<th>p-level</th>
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</thead>
<tbody>
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</tr>
<tr>
<td>Cardiogenic shock</td>
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<td>Paroxysmal AF</td>
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<td>Renifaction</td>
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<tr>
<td>Age</td>
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</tr>
</tbody>
</table>

**Conclusion:** Evaluation of galectin-3 level in patients with RV MI on the background of the posterior Q-MI may be useful as an additional marker of life-threatening complications in acute period of MI and as a predictor of Re-MI during long-term follow-up.

**P4428 | BEDSIDE**

**Clinical impacts of high-sensitivity C-reactive protein reduction for secondary prevention in Asian patients with one-year survivor after acute myocardial infarction**


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**Background:** Reduction of inflammation using statins after acute coronary syndrome (ACS) patients is associated with significant improvement in long-term prognosis. However, there are few convincing data about secondary prevention in Asian acute myocardial infarction (AMI) patients.

**Objectives:** The aim of this study was to investigate the clinical impacts of high-sensitivity C-reactive protein (hs-CRP) reduction for secondary prevention in stabilized Asian AMI patients after statin therapy.

**Methods:** Between February 2008 and November 2011, 1,031 AMI patients who had baseline low-density lipoprotein cholesterol (LDL-C) levels <70 mg/dL, hs-CRP level ≥1 mg/L, and underwent successful percutaneous coronary intervention (PCI) with stent at three large national university hospitals were enrolled in the present study. They were divided into 2 groups at the approximate median reduction of hs-CRP reduction during one-year (<20% reduction from baseline n=510, >80% reduction n=521). The entire study population completed the 2-year follow-up period.

**Results:** During the 2-year follow-up period, cardiac death or myocardial infarction (MI) occurred in 22 patients (2.1%). More hs-CRP reduction group included higher risk patients such as history of hypertension, systolic heart failure, and pre-procedural total occluded lesion. After multivariate analysis, less hs-CRP reduction group exhibited worse outcomes after multivariate analysis [Hazard ratio (HR) 3.05, 95% confidence interval (CI) 1.07–8.64, p=0.036]. In patients with LDL-C reduction <50%, cardiac death or MI rates were significantly different in the 2 groups (HR 4.18 95% CI 1.13–15.4, p=0.032). However, no significant differences were existed in whose LDL-C level reduced over 50% in one-year after statin therapy (OR=0.19–22.8, p=0.575).

**Conclusions:** For secondary prevention, hs-CRP reduction decreased the risk of cardiac origin death or recurrent MI among stabilized Asian AMI patients. The clinical impact was prominent especially in patients who did not achieve LDL-C reduction goal.

**Acknowledgement/Funding:** Korean Health Technology R&D Project (HI13C1527)

**P4429 | BEDSIDE**

**Clinical impacts of high-sensitivity C-reactive protein reduction for secondary prevention in Asian patients with one-year survivor after acute myocardial infarction (AMI) patients.**

**Methods:** We studied 375 consecutive AMI patients (either ST or non-ST segment elevation) within 12 hours of symptoms’ onset. UA and creatinine levels were daily measured throughout hospitalization and their peak values were recorded in each patient. WRF was defined as ≥0.3mg/dl increase in creatinine during hospital stay. Primary end-point was 1 year mortality.

**Results:** Mortality rate at 1 year was 10.9%. Optimal value for predicting 1 year mortality was 1.1 mg/dl for UA elevation. Based on the presence of WRF and UA elevation (1.1 mg/dl) AMI patients were classified in those with both WRF and UA elevation (9.1%), WRF only (8.3%), UA elevation only (27.5%) and those with neither WRF nor UA elevation (controls, 55.2%). AMI patients with both UA elevation and WRF experienced increased 1 year mortality compared to those with UAE elevation only (38.2 vs 11.7%, log-rank p<0.001) and controls (38.2 vs 2.9%, log-rank p<0.001). Patients with WRF only had increased 1 year mortality compared to those with UA elevation only and controls (32.3 vs 11.7 vs 2.9%, log-rank p=0.003 and <0.001, respectively). Finally, patients with UA elevation only had increased 1 year mortality compared to controls (11.7 vs 2.9%, log-rank p=0.002) (Figure 1). In multivariate Cox regression analysis, EF (HR 0.929, p<0.001) and co-existence of WRF and UA elevation (HR 8.605, p<0.001) were independent predictors of 1-year mortality.

**Conclusions:** In-hospital WRF and UA elevation >1.1mg/dl have a synergistic adverse effect on 1-year outcome in AMI patients. Among them WRF appear as a stronger predictor of adverse outcome.
P4431 | BEDSIDE
The long-term prognosis of patients diagnosed as type 2 myocardial infarction does not differ from that of patients with myocardial injury

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Introduction: The differentiation between patients (pts) with type 2 myocardial infarction (T2MI) and pts with troponin (cTn) values above the decision limit, indicating myocardial injury but otherwise not fulfilling the diagnostic MI criteria remains a clinical challenge.

Purpose: To describe the clinical features and the long-term survival of pts with T2MI and those with myocardial injury.

Methods: During 2010–2011 we prospectively studied unselected pts admitted to a 1000-bed university hospital, having cTnl measured on clinical indication. The diagnosis of a T2MI was according to the universal MI definition including established criteria for myocardial oxygen supply/demand imbalance. A cTnl value > 30 ng/L (CV < 10%) was considered the decision limit. Pts were followed for up to 4 years with all-cause mortality as the clinical endpoint.

Results: Within the one-year period of inclusion a total of 1577 consecutive hospitalized pts with cTnI values > 30 ng/l were considered. Of these 119 were classified as T2MI, and 1089 were found to have myocardial injury. No difference in the median age between the two groups was observed: 78 (IQR 67–84) yrs vs. 81 (IQR 69–84) yrs. 1093 (70%) pts were prescribed statins at discharge. The predictive accuracy of uACR was good (Area Under the Curve (AUC), 0.725; 95% CI 0.676–0.774) and was better compared to urine NGAL (long axis, 4 chamber and 2 chamber) views. P who did not present adequate image loops for analysis were excluded. Clinical follow-up (FU) time of at least 12 months was performed to assess the occurrence of composite end-point of death and hospital admission for HF. For statistical analysis we used chi-square and t-student test, Cox regression analysis, Roc and Kaplan-Meier curves.

Conclusions: The use of uACR can easily be applied in the clinical setting, allows for robust risk assessment and offers the potential to improve the management of AMI patients at risk for acute kidney injury.

P4432 | BEDSIDE
Statin non-prescription at discharge and long-term mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary interventions


Background: Guidelines uniformly recommend statin therapy at discharge to all patients following ST-elevation myocardial infarction to reduce the risk of subsequent cardiovascular events.

Objective: We sought to investigate the impact of statin non-prescription at discharge on long-term mortality in patients who underwent urgent coronaryography for planned primary PCI.

Methods: From January 2009 to December 2010, in a single high-volume center, 1949 consecutive patients underwent urgent coronaryography for myocardial infarction and survived hospitalization period. Long-term mortality was compared between 149 (7.6%) pts without statin prescription at discharge and 1800 (92.4%) pts with statins.

Results: Statin non-prescribers were older (61.7±13 vs 59±11; p<0.02), had less hyperlipidemia (42% vs 64%; p<0.02), higher rate of baseline TIMI 3 flow (20% vs. 13%; p<0.01), but lower rate of TIMI 3 flow in infarct related artery post PCI (87% vs. 94%; p<0.01) and were more likely a CADILLAC high risk patients (37.8% vs. 21.6%; p<0.01). At a mean follow-up of 48±20 months, non-prescribers had significantly higher mortality than patients on statins (37.6% vs. 13.5%; p<0.001). After multivariable adjustment using Cox regression model, statin non-prescription remained independent predictor of long-term mortality not only in CADILLAC high risk patients (OR 2.5; 95% CI 1.4–4.6; p<0.01) but also in CADILLAC low/medium risk patients (OR 2.49; 95% CI 2.01–4.13; p<0.001) (figure 1 and 2).

Conclusion: Incidence of statin non-prescription at discharge is low and long-term survival benefit of statin therapy was seen in all CADILLAC risk strata.

P4433 | BEDSIDE
Strong predictive value of left ventricular global longitudinal strain on mortality and heart failure admissions following ST segment myocardial infarction

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Purpose: We retrospectively analysed consecutive patients (P) with STEMI and those with myocardial injury Network (AKIN), the Acute Dialysis Quality Initiative [Risk, Injury and Failure (RFI)LE] criteria and the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Blood and urine sampling for neutrophil gelatinase-associated lipocandin (NGAL), interleukin-18 (IL-18), cystatin-C, and uACR assessment was performed during admission.

Results: The predictive accuracy of uACR was good (Area Under the Curve (AUC), 0.725; 95% CI 0.676–0.774) and was better compared to urine NGAL (P<0.007), urine (P<0.001) and serum Cystatin-C (P<0.001). ROC analysis identified concentrations of >66.7 μg/mg as having the best diagnostic accuracy. The use of uACR exhibited good discriminating ability independent to possible confounders and additive regarding the use of novel biomarkers.

Conclusions: The use of uACR can easily be applied in the clinical setting, allows for robust risk assessment and offers the potential to improve the management of AMI patients at risk for acute kidney injury.
Results: 155 P (mean age 58±14.9 years, 80% male) were included with a median FU of 509 days and 16 P reached the composite end point (5 deaths and 11 HF hospitalizations). Significant prognostic value was found for LV-GLS (AUC 0.836; HR: 1.46; 95% CI: 1.20–1.78; p<0.001). There was a trend associated with E/e' ratio (95% CI 0.99–1.24; p=0.054) and left ventricular ejection fraction [LVEF] (95% CI 0.89–1.00; p=0.07). Other possible predictors held non-significant results towards the end-point, mainly: E/e' ratio (95% CI 0.51–4.54; p=0.39), BNP on admission (95% CI 0.99–1.03; p=0.88), GRACE score (95% CI 0.99–1.04; p=0.21) and TIMI score (95% CI 0.82–1.36; p=0.69). Multivariate analysis showed that LVEF remained independently associated with the composite end-point (HR: 1.85; 95% CI: 1.28–2.09; p<0.001). From the ROC curve analysis, the best cut-off value to predict the combined end-point was LV-GLS worse than −11% with AUC 0.842.

Conclusions: Semiautomatic LV-GLS is a rapidly accessible tool to assess LV function and provides strong prognostic value for death and heart failure hospitalizations following STEMI. In our population, LV-GLS had greater accuracy to predict outcomes than LVEF, E/e' and E/A ratios, BNP on admission, GRACE and TIMI scores. LV-GLS worse than −11% is an excellent cut-off value to predict poorer outcome after STEMI.

CPR CARDIOPULMONARY RESUSCITATION

P4434 | BEDSIDE

Improved survival after out-of-hospital cardiac arrest most substantial in younger patients - results from a statewide quality improvement initiative in North Carolina during 2010-2013

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Background: Bystander cardiopulmonary resuscitation (CPR), first responder defibrillation rates, and survival to discharge in out-of-hospital cardiac arrest patients increased significantly following a quality improvement initiative in North Carolina (NC), USA; during 2010–2013. We assessed how these changes varied according to patient age.

Methods: From the CARES registry, we identified out-of-hospital cardiac arrests of presumed cardiac cause and not witnessed by emergency medical services from counties with complete case capture in NC (n=17), population=3.0 million during 2010–2013 and excluded cases with missing age (n=11) and age <18 (n=142).

Results: Of 6,234 patients, 965 (15.5%), 1,938 (31.1%), 1,983 (31.8%) and 1,348 (21.6%) were 18–49, 50–64, 65–79 and >80 years of age. Lower proportions of witnessed arrest (p=0.003) and shockable rhythm (p=0.001) were seen with increasing age. Bystander CPR rates increased in all age groups during 2010–2013 (33.1 to 49.2% for age 18–49, p=0.001; 41.1 to 45.1% for age 50–64, p=0.11; 37.4 to 53.4% for age 65–79, p<0.001; and 40.4 to 50.8% for age >80, p=0.003); similar was seen for first responder defibrillation rates (33.3 to 47.8% for age 18–49, p=0.034; 40.1 to 46% for age 50–64, p=0.55; 45.2 to 49.8% for age 65–79, p=0.03; and 37.3 to 50% for age >80, p=0.23). Survival only increased in younger patients (see Figure) and only among those who received bystander CPR (7.2 to 21.9% for age 18–49, p=0.028; and 10.9 to 19.9% for age 50–64, p=0.003); minimal changes were seen in cases who did not receive bystander CPR (12.3 to 11.3% for age 18–49, p=0.86; and 7.9 to 8.5% for age 50–64, p=0.75).

Conclusions: Bystander and first responder intervention rates increased in all age groups, but survival only improved in younger patients.

P4437 | BEDSIDE

Does hyperglycaemia predict the prognosis in patients after cardiac arrest? The higher the glucose level, the worse the outcome?

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Background: Hyperglycaemia is known to be associated with adverse outcomes for patients after acute myocardial infarction. However, little is currently known regarding in patients after cardiac arrest.

Purpose: We assessed the hypothesis that higher glucose levels are associated with worse outcomes in patients after cardiac arrest in the current therapeutic hypothermia era.

Methods: Patients who were resuscitated and treated with targeted temperature management were enrolled in this study. Blood glucose was measured at the time of terminating advanced cardiac life support in the hospitals. The study patients were divided into four groups according to the plasma glucose levels: Q1 (<11.4 mmol/l; N=59), Q2 (11.5–15.2 mmol/l; N=60), Q3 (15.3–19.4 mmol/l; N=59), and Q4 (>19.5 mmol/l; N=60), and their clinical characteristics and 30-day mortality were assessed.

Results: Among the study patients (N=238), the median age was 62 years (interquartile range, 52–71 years), 178 patients (75%) were male, 125 (53%) had initial recorded rhythms that were shockable, 145 (60%) underwent immediate coronary angiography, and 77 (32%) underwent subsequent coronary revascularisation. The age, sex, and rates of witness to arrest, and bystander-initiated cardiopulmonary resuscitation were similar between the groups. The rates of initial recorded rhythms that were non-shockable (58%, 30%, 42%, and 60%) and the time intervals from collapse to the return of spontaneous circulation (median, 42 min [interquartile range, 21–52 min], 24 [16–43], 36 [24–48], and 42 [25–58]) showed J curve associations with the glucose levels (61%, 33%, 51%, and 71%, respectively). With Q2 as the reference value, Q1 (odds ratio, 1.82 [95% confidence interval, 1.04–3.03]) and Q4 (1.91 [1.09–3.43], P=0.02) were independently associated with the 30-day survival by Cox proportional hazard regression analysis.

Conclusions: In patients after cardiac arrest, the outcomes, severity of illness, and glucose level showed J curve associations. Plasma glucose of 11.5–15.2 mmol/l, which is usually considered as hyperglycaemia, was associated with the most favourable outcomes.
Out-of-hospital cardiac arrest with no obvious extra cardiac cause: impact of coronary angiography on early survival

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Background: Out-of-hospital cardiac arrest (OHCA) is mainly driven by coronary artery disease. However, the functional prognosis remains poor with a very high inhospital mortality, and less than 10% of patients will survive without neurological damage. Accordingly, early coronary angiogram (CA) has been proposed in OHCA patients in order to improve survival.

Aim: To identify the impact of coronary angiogram on survival without neurological sequelae in OHCA patients with no obvious extra-cardiac cause.

Methods: In a prospective study between January 2011 and December 2013, we analyzed clinical and biological data in OHCA patients referred in two centers with CA facilities. Uni- and multivariate analysis were used to identify factors associated with in-hospital survival.

Results: 125 patients were included, with 60% survival rate. CA was performed in 108 (86%) patients and coronary angiography realized in 85 (68%) patients. Univariate analysis identified factors associated with hospital survival: age (p<0.002), duration of no-flow (2.7±4 vs 5.6±4.6 min, p<0.0003), initial shockable rhythm (p<0.001), dosage of adrenaline bolus (p<0.0003), APACHE II score (p<0.0001), lactate level (p<0.0001), and leftventricular ejection fraction at admission (p=0.0005). The added value of coronary angiography on survival was significantly better (p<0.001) than the one of CA (p=0.02).

In a multivariate analysis, APACHE II score (p=0.002), level of lactates at admission (p=0.006), initial shockable rhythm (p=0.011) and coronary angioplasty (p=0.014) are both independent predictors of survival. However, only APACHE II score (p=0.001) and not coronary angioplasty (p=0.18) was associated with a good neurological outcome.

Conclusions: Parameters reflecting pre-hospital care (APACHE II score and re-suscitation delays) were the most important factors predicting survival and neurological prognosis. Survival could be influenced by coronary angiography but triage for OHCA patients is mandated to select those who require immediate coronary angiography. Further studies with larger groups of patients are necessary to confirm the role of CA in OHCA.

Vitamin D deficiency is associated with severe shock in patients with sudden cardiac arrest

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Background: Vitamin D deficiency is associated with various cardiovascular diseases, including sudden cardiac arrest (SCA). Severe shock is related to morbidity and mortality in patients resuscitated from SCA. This study investigated the association of vitamin D deficiency with severe shock in patients with SCA.

Methods: We enrolled patients who were successfully resuscitated from out-of-hospital cardiac arrest of presumed cardiac cause. Severe shock was defined as hypotension requiring mechanical circulatory support such as extracorporeal life support devices or inotropic support. Vitamin D level was measured as plasma 25(OH)D concentration and severe vitamin D deficiency was defined as 25(OH)D ≤ 10 ng/mL.

Results: A total of 96 patients (67 men (70%), mean age 55±15.8 years) were included in this study. First monitored rhythm was shockable rhythm in 59 patients (62%) and non-shockable rhythm in 37 (38%). Bytander coronary angiography (CP) was performed in 78 (81%) and mean arrest time and CP time were 28.9±17.9 and 26.0±17.2 minutes, respectively. Severe shock was observed in 27 patients (28%). The Mean vitamin D level was 10.0±5.2 ng/mL and severe vitamin D deficiency was diagnosed in 56 patients (58%). Vitamin D level was significantly lower (7.2±4.1 vs. 11.2±5.2 ng/mL, p=0.001) and vitamin D deficiency was observed more frequently (82 vs. 49%, p=0.004) among patients with severe shock. Patients with severe shock were likely to have more left ventricular systolic dysfunction (LVF<40%, 78 vs. 44%, p=0.002) and to be obese [body mass index (BMI) = 24 kg/m², 74 vs. 51%, p=0.038]. In multivariate logistic analysis, vitamin D deficiency was the significant independent predictor of severe shock after SCA (OR 4.83, 95% CI 1.56–14.91, p=0.006) with left ventricular systolic dysfunction (OR 4.83, 95% CI 1.66–14.91, p=0.004) after adjusting for confounding variables such as first monitored rhythm, bystander CPR, baseline renal function, and BMI.

Conclusion: Vitamin D deficiency was strongly associated with severe shock in patients resuscitated from SCA.

DNA deoxyribonucleic acid damage in humans successfully resuscitated from cardiac arrest

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Background: Cardiac arrest is a highly stressful event with a transient whole body ischaemia and common ischaemic-reperfusion injury in successfully resuscitated victims. The prognostication of outcome remains limited.

Purpose: To investigate whether cardiac arrest may induce severe deoxyribonucleic acid (DNA) damage in successfully resuscitated humans and evaluate its prognostic value.

Methods: The prospective study (1/2013–1/2014). In successfully resuscitated patients from non-traumatic out-of-hospital cardiac arrest (n=41; 64±14 years; men 73%, arrest of cardiac aetiology 76%; witnessed arrest 88%) the most severe DNA damage (double strand breaks) in lymphocytes sampled at admission were analysed using phosphorylation of histone H2AX (γH2AX). Data records: according to the Utstein protocol. The prognostic outcome: in-hospital mortality/discharged alive.

Results: 68% (28/41) of patients were discharged alive, 32% (13/41) died in a hospital (Fig). Regarding DNA: 83% (34/41) of patients had DNA damage, 17% (7/41) had intact DNA. Of patients discharged alive (n=28): DNA damage was in 86% (24/28). Of patients who died in hospital (n=13): DNA damage was in 100% (13/13). Of patients with DNA damage (n=34): 71% (24/34) were discharged. From patients with intact DNA (n=7): 57% (4/7) were discharged. Length of hospitalization was 13 (1;110) days. Among Utstein parameters the differences in DNA results was only for asystole (damage vs intact; 18% vs 57%; P=0.048).

DNA damage is not suitable for prediction of poor outcome (AUC 0.389/95% CI 0.195–0.569).

Vitamin D deficiency was strongly associated with severe shock in patients resuscitated from SCA.
Conclusions: This study for the first time demonstrates the severe DNA damage in successfully resuscitated patients. Data showing better prognosis of patients with DNA damage contrast with the authors’ hypothesis.

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POST INFARCTION PERIOD III

P4442 | BEDSIDE
Results of stem cell therapy in anterior STEMI patients with severe systolic dysfunction. Pilot study. Romanian experience
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Background: Stem cell therapy seems to be a promising adjuvant treatment for patients with ST-segment elevation myocardial infarction (STEMI) and low left ventricular ejection fraction (LVEF). It is a major health care problem, and cardiac progenitor cell therapy holds potential for treating myocardial ischemia. After STEMI, myocardial regeneration could be promoted through interactions between the injected stem cells and resident cells which stimulate endogenous repair mechanisms.

Methods: A group of 18 patients with anterior myocardial infarction with elevated ST segment (STEMI) and LVEF <40% were divided into 2 groups: the autologous bone marrow stem cell group (ABMSC) and the control group. After obtaining the informed consent the first group was treated at 7 to 10 days after myocardial infarction by means of mononuclear corona artery injection: all the patients were treated in accordance with up to date guidelines. Mononuclear cells were obtained by iliac crest puncture, separated by density gradient and administrated after 5 hours. Patients were followed for 12 months by the same paraclinical methods and imagistic by echocardiography 2D, 3D and speckle tracking analysis.

Results: During 12 months no adverse effects were observed following administration of stem cell therapy. LVEF recovery at 1 year follow-up is concerned and with statistic significance in treated group: for 2D measurements, LVEF increasing 9%, p<0.001; vs. 6.72%, p=0.77 in control group; for 3D measurements, LVEF increasing 8.41%, p=0.02 in ABMSC group vs. 5.7%, p=0.28 in control group; the improvement in global longitudinal strain (GLS) was greater in stem cell treated patients than in the control group with absolute value 2.75 vs 1.12 (from -8.2 to -11.25 vs. -9.7 to -10.9). Tests applied failed in proving a significant difference between the two groups. After 12 months patients treated with stem cells had a increased ventricular end-diasstolic volume and ejection fraction estimated both by biplane Simpson method 2D and 3D ultrasound. These data were supported by speckle tracking analysis at 12 month after STEMI. Coronary angiography showed permeability of the artery responsible for myocardial infarction in both cases.

Conclusions: At 12 months we observed improved ejection fraction in patients treated with stem cells, evaluation performed both by echocardiographic methods (2D, 3D) and speckle tracking analysis. Our results are similar with those from literature, but larger studies are required for more accurate data.

P4443 | BEDSIDE
Could pulmonary hemodynamic impact diffusion lung capacity in patients with ST elevation myocardial infarction?
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Some data suggest that lung dysfunction presents in early stages of myocardial damage but little data exist that explain pathological mechanisms behind this phenomenon.

Aim of the study: To estimate the pulmonary circulation effects on alveolar-capillary membrane conductance in patients with myocardial infarction.

Methods: Patients with ST segment elevation myocardial infarction hospitalized within 24 hours from symptoms onset were included in the study. The study protocol was approved by the local IRB. Every patient voluntarily signed the informed consent before being included in the study. Transthoracic cardiac echo was done on 10th hospital stay day and diffusion capacity of lung for carbon monoxide (DLCO) was measured on 10th to 14th days. The statistical analysis was done with statistical software package SPSS for Windows, version 13.0. Quantity data are presented as mean and standard deviation for median and lower and upper quartiles. Relationships between 2 numerical variables were calculated with a linear regression analysis. All the p values described are 2-sided and a p<0.05 was considered statistically significant.

Results: 107 patients (mean age 56.1±9.3 yrs) were included in the study, of which 88 (82%) males. Univariate analysis showed that there were significant relationships between pulmonary pressure and DLCO. Patients with low DLCO (i.e., <80%) had markedly higher mean pulmonary pressure (mean PP): 16.7 (14.4;19.9) mm Hg versus 14.0 (10.7;16.7) mm Hg in patients with normal mean range (i.e., 80–120%), p<0.002. Moreover, in the patients with DLCO <80%, pulmonary hypertension was seen more than 2 times frequent as compared to the patients with “normal” DLCO (27% and 12%, respectively, p=0.04).

We conducted a regression analysis which yielded the linear regression equation: 
DLCOcor, % = 109.5 − 1.8 x mean PP , mm Hg (F=21.0; R2=0.17; p<0.001). It can be suggested that DLCO might be inversely associated with pulmonary pressure and for each 1 mm Hg increase in mean pulmonary pressure alveolar-capillary membrane conductance decreased by 1.8%. The further analysis, in which myocardial structure and remodeling variables were included in the model, confirmed that pulmonary pressure has an impact on diffusion lung capacity with mean pulmonary pressure and left atrium (LA) volume being in the final model: DLCOcor, % = 121.9 − 0.5 x LA volume, ml − 1.2 x mean PP, mm Hg (F=18.6; R2=0.27; p<0.001).

Conclusions: It can be assumed that even a slight pulmonary pressure increase might be associated with a DLCO drop.

P4444 | BEDSIDE
Renal dysfunction strongly predicts adverse short and long term survival in patients undergoing reperfusion for STEMI

Background: Reperfusion therapy (RT) in ST elevation myocardial infarction (STEMI) reduces mortality and long-term complications. The benefit of RT in those renal insufficiency remains less well validated.

Methods: We tested the hypothesis that renal insufficiency (GFR <60 cc/min) would significantly impact survival following RT for STEMI in a large community based registry. Patients presenting within 2 hours of symptom onset at non PCI capable hospitals received IV fibrinolytic therapy unless contraindicated, while those presenting beyond 2 hours had delayed primary PCI after transfer to the referral center. We report survival as a function of RT and renal function.

Results: 1871 patients with STEMI were evaluated; 1439 had normal renal function (GFR >60) while 432 had renal impairment. Patients with renal impairment were older, more likely to be female and slightly higher rates of diabetes those with normal renal function (p<0.01). There were no differences in location of the STEMI on the presenting ECG or in the timing of and mode of reperfusion (lysis vs PCI) between the groups. Patients with renal dysfunction had significantly higher in–hospital mortality (16% v 4%, p<0.001) and rates of stroke (3% v 1%, p<0.001) but no difference in rates of re-infarction (2%). Mortality at 1 month (18.6% vs 4.2%), 6 months (23.9% vs 6.2%), 12 months (28.2% vs 7.3%), 24 months (33.1% v 9.1%), 60 months (55.1% v 17.4%) and 84 months (60.9% v 23.1%) was substantially higher in the renal dysfunction group (p<0.001).

Conclusion: Patients with STEMI who have underlying renal insufficiency have significantly worse short and long term survival despite prompt RT compared with those with normal renal function. Renal failure remains a challenging risk to mitigate in treatment of STEMI.

Acknowledgement/Funding: Mayo Clinic

P4445 | BEDSIDE
In hospital mortality for prehospital STEMI patients directly admitted to cath-lab beyond 120 min
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Background: Improving timely access to life saving reperfusion therapy is well recognized as major goal of STEMI care. Primary PCI is the recommended reperfusion therapy if performed by an experienced team within 120 min. of FMC.

Purpose: To assess the impact of delay on in-hospital mortality of STEMI patients transported for pPCI.

Methods: Data from an ongoing prospective registry that includes all STEMI <12h managed by MIUCs in a metropolitan area, from 2003 to 2013. Ambulance triage and direct transfer to pPCI capable hospital by-passing ED. Comparison of in-hospital mortality for group 1 with FMC to cath-lab−<120 min, and for group 2 with FMC to cath-lab−>120 min. data were compared using Chi 2 test.

Results: 10,210 patients were included in the registry during the period. 2.454

Table 1

<table>
<thead>
<tr>
<th>Group 1 −&lt;120 min</th>
<th>Group 2 −&gt;120 min</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>6,645</td>
<td>1,111</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>122 (1.8%)</td>
<td>44 (4.1%)</td>
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patients (24%) received prehospital fibrinolysis and 7,756 patients (76%) were directly admitted to the cath-lab for pPCI. Main results are shown in table 1.

**Conclusion:** Increase of in-hospital mortality for unselected STEMI patients transported from scene to cath-lab is strongly correlated to time to pPCI beyond 120 min, out of recommended delay. A system delay <120 min remains a major goal to achieve for prehospital teams.

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**P4446 | BEDSIDE**

**Infarct size assessment after spontaneous, guide wire or angioplasty induced reperfusion in acute myocardial infarction**

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**Methods:** Between October 2012 and August 2013, all patients admitted for STEMI were included and obtained successful reperfusion (TIMI 3 flow). Three groups were defined: spontaneous reopening of the IRA (group 1), reopening reperfusion induced in acute myocardial infarction (STEMI).

**Purpose:** To evaluate impact of reperfusion obtained spontaneously, after guide wire crossing or after PCI in the infarct size (IS) and clinical outcomes in patients admitted for STEMI.

**Results:** We included 74 consecutive patients. Procedural characteristics and scar score at 7 days and secondary endpoints evaluated 30 days ischemic clinical outcomes.

**Results:** We included 74 consecutive patients. Procedural characteristics and pain duration were not different in the 3 groups. Group 1 (n=24) exhibited a significantly smaller IS (p=0.01) in comparison with both groups 2 (n=28) and 3 (n=22). Groups 2 and 3 showed not different IS (p=0.34) (figure). Group 1 presented less microvascular obstruction (n=1, 4.17%; p=0.01) when compared to groups 2 and 3 (respectively 35.71%, n=9 vs 38.10%, n=8; p=0.20). Results after stratification on IRA remained unchanged. Group 1 had significantly less major cardiovascular adverse events, (n=0, 0%) compared to groups 2 (n=5, 27.8%) and 3 (n=4, 26.7%) (p=0.05) with no difference between latter two groups (p=1).

**Conclusion:** While spontaneous reperfusion was associated with a better prognosis and a reduced IS, reopening of the occluded IRA by obtaining across the guide wire was not associated with IS reduction compared with PCI induced reperfusion.

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**P4447 | SPOTLIGHT**

**The Zwolle risk score as a guide to early discharge**

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**Background:** Patients with ST elevation myocardial infarction (STEMI) are a heterogeneous group with varying length of hospital stay. The Zwolle percutaneous coronary intervention (PCI) score is an externally validated score and may help with early discharge of low risk PCI patients.

**Purpose:** The aim of this study was to use the Zwolle score to identify patients who potentially could be suitable for early discharge.

**Methods:** We retrospectively analysed all STEMI patients presenting to our University Hospitals over a 1 year period (January 2013 to December 2013). All patients were scored according to the Zwolle and length of stay calculated.

**Results:** 309 patients (age 63±8 years, 39% female, left ventricular ejection fraction (LVEF) 38±5%) with chronic ischemic cardiomyopathy underwent strain echocardiography and CMR within 3±1 days. LVEF and global circumferential strain variables by echocardiography compared to CMR. The role of myeloperoxidase and monocyte chemoattractant protein-1 in the improvement of left ventricular function after ST-segment elevation myocardial infarction

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**Purpose:** To examine an association between the improvement of left ventricular (LV) function and the concentration of selected chemokines among patients with and without metabolic syndrome (MeS) treated with primary percutaneous coronary intervention (pPCI) for ST-elevation myocardial infarction (STEMI).

**Material and methods:** The study population comprised 69 patients (mean age 53.0±14.5 years, 83% men) with first STEMI and single pPCI. We selected 33 patients with MeS according to the criteria of the International Diabetes Federation.

**Aim:** To determine the predictive value for better LV systolic function in patients with MeS.

**Methods:** Baseline MPO and MCP-1 are the predictors of LV function improvement in patients with STEMI. In patients with MeS increased level of MPO had a very good predictive value for the occurrence of EF improvement. However in patients without MeS only increased concentration of MCP-1 had a good predictive value for better LV systolic function.

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**P4448 | BEDSIDE**

**Prediction of mortality by strain echocardiography compared to CMR**

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**Background:** Cardiac magnetic resonance (CMR) has been established as a powerful predictor of mortality. However, application is limited by general availability and various contraindications. This study evaluated the predictive value of layer specific myocardial deformation analysis for mortality in patients with chronic ischemic left ventricular dysfunction.

**Methods:** 309 patients (age 63±8 years, 39% female, left ventricular ejection fraction (LVEF) 38±5%) with chronic ischemic cardiomyopathy underwent strain echocardiography and CMR within 3±1 days. LVEF and global circumferential strain parameters and global myocardial scar to relevant clinical variables was determined by echocardiography.

**Results:** The concentration of MPO –118.45 ng/ml had a very good predictive value (AUC=0.922, p<0.001) for the improvement of EF but only in patients with MeS. Among patients without MeS the concentration of MCP-1= 176,13pg/ml had a good predictive value (AUC=0.804, p<0.001) for the better LV function after 1-year follow-up.

**Conclusions:** Baseline MPO and MCP-1 are the predictors of LV function improvement in patients with STEMI. In patients with MeS increased level of MPO had a very good predictive value for the occurrence of EF improvement. However in patients without MeS only increased concentration of MCP-1 had a good predictive value for better LV systolic function.


Gender differences on the 10 year (2004–2014) acute coronary syndrome (ACS) incidence rates, among cardiac patients: a classification analysis

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**Background:** The increased risk of cardiovascular disease (CVD) among women, even in younger ages (< 40 years) and the worse disease prognosis compared with men, has been recently gaining a scientific interest, in the research field.

**Purpose:** To evaluate potential differences in the major cardiometabolic risk factors, among Acute Coronary Syndrome (ACS) male and female patients.

**Methods:** From October 2003 to September 2004 a sample of 6 hospitals was selected and almost all consecutive 2,172 ACS patients were enrolled. In 2013–14, the 10-year follow-up (2004–2014) was performed in 1,918 participants (88% participation rate). Age, sex, Body Mass Index (BMI), current smoking, Medical etScore categories (<27 vs. >27), physical activity, history of CVD, hypertension, hypercholesterolemia and diabetes mellitus were evaluated in relation to the development of 10-year CVD incidence, in each sex subgroup, based on hierarchical classification analysis using Fisher linear discriminant function.

**Results:** The 10-year incidence was 40% in males and 32% in females (p < 0.001). The classification of CVD risk factors was not the same in the two gender groups while only some of them led to a significant association concerning the ACS prognosis. Thus, in males the predominant risk predictors were diabetes (Wilks’ L=0.997, p=0.079) and current smoking (Wilks’ L=0.997, p=0.083); while history of CVD, hypercholesterolemia, BMI, MedIDetScore and physical activity were in the second highest rank. Respectively, in females, physical inactivity (Wilks’ L=0.992, p=0.071), low adherence to the Mediterranean diet (<27) (Wilks’ L=0.993, p=0.086) and current smoking (Wilks’ L=0.993, p=0.108) were the most commonly observed characteristics. Age specific analysis confirmed that the aforementioned ranking was irrespective of participants’ age.

**Conclusions:** The present analysis revealed the gender differences in the prevalence of the major CVD risk factors and the 10-year ACS prognosis. Women’s lifestyle habit modifications, like unhealthy diet, physical inactivity and increased smoking prevalence, contribute to the development of cardiovascular disease and impose a substantial clinical and public health burden which should not be underestimated or ignored.

**Acknowledgement/Funding:** None to declare.

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**Impact of proportion of rapid eye movement sleep on all-cause mortality and stroke in patients with acute myocardial infarction**


**Background:** Deteriorated haemodynamics are associated with increased mortality in patients with ST elevation Myocardial Infarction (STEMI). Beta-blockers may worsen haemodynamics. The association between chronic beta-blocker treatment and haemodynamics in patients with STEMI treated by primary PCI is not well studied.

**Methods:** In 5014 consecutive patients with STEMI treated with primary PCI, the association between chronic beta-blocker treatment (before the index STEMI) and risk of either cardiogenic shock (CS) or pre-shock is studied. CS was defined as systolic blood pressure < 90 mm Hg. Pre-shock was defined as a Shock Index (SI, the ratio of heart rate and systolic blood pressure) > 0.7. Adjustments were made for differences in baseline variables.

**Results:** A total of 1141 patients (22.8%) had chronic beta blocker treatment. CS was observed in 265 patients (5.3%), pre-shock in 1038 Patients (20.7%). There was a non-significant trend for reduced risk of CS in patients with chronic beta blocker treatment (adjusted OR 0.81, 95% CI 0.50–1.31). Chronic beta blocker treatment was significantly associated with a reduced risk of SI > 0.7, adjusted OR 0.77 (95% CI 0.60–0.99); p-value 0.04.

**Conclusion:** In STEMI, chronic beta blocker treatment does not increase the risk of either shock or pre-shock. Even, chronic beta blocker treatment may reduce the risk of hemodynamic deterioration. Early beta blocker treatment for STEMI should be further studied.

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**Effect of chronic beta-blocker treatment on admission haemodynamics in STEMI patients treated with Primary Angioplasty**

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**Purpose:** Addressing the increasingly recognized, yet unmet clinical need for...
rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTnT) T at presentation in combination with hs-cTnT 1h-algorithm versus hs-cTnT 2h-algorithm.

Methods: In a prospective international multicentre diagnostic study enrolling 1697 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. The 2h-algorithm was defined as 0h<4ng/l and 1h<14ng/l and the combination LOD and 1h algorithm was defined as LOD <5ng/l or 0h<12ng/l and A<0<1h<3ng/l. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial ECG, STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 16% of patients. The safety was very high and comparable with both algorithms (2h algorithm: NPV 100%, 95% CI 99.7–100% versus LOD+1h-Algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns).

Regarding efficacy, 2h-algorithm allowed rule-out in 64% of patients versus 60% with 1h-algorithm + LOD (p=0.018).

Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI. The 2h-algorithm has a slightly higher efficacy; however the combination of LOD+1h-algorithm has the obvious advantage of allowing rule-out already after 1h.

P4455 | BEDSIDE
Can we utilize pharmaco invasive strategy in patients with chest pain needle time over 3 hours?
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Background: The STREAM study utilized 3 hours as the maximum time to implement Pharmaco Invasive Strategy (PIS). In this period of time there is scarce real world information about PIS in the literature.

Methods: We analyzed 1147 consecutive STEMI patients who were treated by PIS between January 2010 and December 2014, network of 12 ER, 22 advanced ambulances and one PCI hospital organized as a Registry (NCT 02090712). We have included patients until 12 hours of symptoms as per guidelines. Sixty one patients were excluded because there was no complete record of pain onset or time to tenecteplase (TNK) dosage. Rescue coronary angiography was performed if fibrinolysis failed. Patients were divided as follows: Group 1 (427) had chest pain-needle time (CPNT) until 3 hours from the initial symptoms; Group 2 (442) had CPNT between 3 and 6 hours; Group 3 (278) had CPNT greater than 6 hours.

All events from first medical contact until hospital discharge were analysed. The primary end point was intra hospital death and co-primary a composite of inhospital death, shock, congestive heart failure and reintervention. Group 1 was considered gold standard to time of treatment and all groups were compared to it.

Results: Ages varied between 18 and 93 years. Age was significantly lower in group 2 than group 1 (p=0.003) and 3 (p=0.003). Men were more frequent in group 1 than the other groups (77% in group 1 vs 65,4% in group 2, p=0.001; 66,4% in group 3, p=0.003). Diabetes mellitus was more prevalent in group 3 than in group 1 (38,2% vs 26,9%, p=0.002). Other demographics and risk factors were non significantly different among the 3 groups. In relation to hospital follow up, group 1 and 2 have the same event rate. Cardiogenic shock was more frequent in group 3 than group 1 (14,2% vs 8,7%, p=0.02). We observed major bleeding (BARC) in 2,3% in group 1, 3,8% in group 2 and 4,6% in group 3 without significance. We observed combined events in 27,9% in group 1, 29% in group 2 (p=0.7) and 30,6% in group 3 (p=0.48). And death for all causes was 4,2% in group 1, 4,5% in group 2 (p=0.87) and 11,5% (p=0.001).

Conclusions: PIS mortality increased significantly for those treated with CPNT beyond 3 hours; however the results of those treated from >3 to 6 hours were not different from those treated with CPNT less than 3 hours, for mortality and the combined co-primary events, suggesting that PIS could be safely employed until 6 hours.

P4456 | BEDSIDE
Troponin T elevation in acute aortic syndromes: frequency and impact on diagnostic delay and misdiagnosis
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Background: Despite troponin assay being a part of the diagnostic work up in many conditions with acute chest pain, little is known about its clinical implications in Acute Aortic Syndromes (AAS).

Purpose: To evaluate frequency, impact on diagnostic delay, inappropriate treatments, and prognosis of troponin elevation in AAS.

Methods: Data were collected from a prospective metropolitan AAS registry (398 patients diagnosed between 2000 and 2013). Cardiac troponin test, using either standard or high sensitivity (HS) assay, was performed according to standard protocol used in chest pain units. The following time intervals were recorded: 1) symptoms onset to presentation; 2) hospital presentation to final AAS diagnosis; 3) symptoms onset to final AAS diagnosis.

Results: Troponin T values were available in 248 patients (60%) of the registry population; the overall frequency of troponin positivity was 28% (ranging from 16% to 54%, using standard or HS assay respectively, p=0.001). Troponin positivity was frequently associated with Acute Coronary Syndromes (ACS)-like ECG findings, and with a twofold increased risk of long in-hospital diagnostic time (OR 1.92, 95% CI 1.05–3.50, p=0.03). The combination of positive troponin and ACS-like ECG abnormalities resulted in a significantly increased risk of in-hospital delay/coronary angiography/antithrombotic therapy due to a misdiagnosis of ACS (figure). However, troponin positivity was not associated with in-hospital mortality (OR 1.63, 95% CI 0.86–3.10, p=0.131).

Conclusions: Troponin positivity was a frequent finding in AAS patients, particularly when a HS assay was employed. Abnormal troponin values were strongly associated with ACS-like ECG findings and with in-hospital diagnostic delay but they did not influence in-hospital mortality.

P4457 | BEDSIDE
Combined cardiac and lung ultrasound protocol for differential diagnosis of acute dyspnea in the emergency department
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Objectives: To combine Echo and LUS into a “thoracic FAST exam”, a rapid ultrasound protocol to be used to examine acutely dyspneic patients immediately after arrival in the emergency department (ED). To use the protocol for diagnosing left sided AHF, and to examine it’s yield in differential diagnosis of acutely dyspneic patients.

Methods: We included 99 cognitively intact adult patients presenting with dyspnea at rest in our ED. Patients with mitral stenosis and pulmonary fibrosis were excluded. LUS of 2–3 pulmonary fields and pleurars bilaterally, medial E/e’ and visual estimation of the right side of the heart was performed. Other alarming findings were reported if seen. The patients were classified as having AHF if having E/e’ >15 and either bilateral B-lines (BBL) or rightsided/bilateral pleural fluid (PF) on LUS.

Results: According to the protocol, 53 (53,5%) of the 99 patients had AHF, and 46 (46,5%) had an alternative diagnosis. The mean E/e’ was 21,14 (sd 4,30) for AHF patients, and 9,75 (sd 2,96) for the control group (p<0.001). In the AHF group 51
Methods:
Purpose:  With hs-cTn levels below the 99th percentile is unknown. The ability to rule out myocardial infarction (MI). However, major adverse cardiac events (MACE) were independent predictors of MACE with odds ratios of 30.61 (95% CI 99.4 to 99.9%) for the primary outcome across all patients (Figure).

Background: High sensitivity cardiac Troponin (hs-cTn) profoundly increases the ability to rule out myocardial infarction (MI). However, major adverse cardiac events (MACE) were independent predictors of MACE with odds ratios of 30.61 (95% CI, 99.4 to 99.9%) for the primary outcome across all patients (Figure). As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial hs cTn assay, STEMI patients were excluded from the analysis.

Results: Myocardial infarction was the final diagnosis in 18.7% of patients. With hs-cTn, the safety was very high and comparable with both algorithms (dual marker strategy: NPV 99.8%, 95% CI 99.0–99.9% versus below LOD and 1h-algorithm: NPV 99.8%, 95% CI 99.0–99.9%, p=0.002). Regarding efficacy, dual marker strategy allowed rule-out in 47.2% of patients versus 57.4% with the LOD and 1h-algorithm (p=0.002). Using hs-cTnI, the safety was very high and comparable with both algorithms (dual marker strategy: NPV 96.0%, 95% CI 94.3–97.2% versus LOD and 1h-algorithm: NPV 99.2% (95% CI 98.2–99.9%, p=0.001).

Conclusion: The combination of LOD and the 1h algorithm allows a better rule-out of AMI than the dual marker strategy, irrespective of the underlying hs-cTn assay. Both strategies show a comparable effectiveness with ruling-out around half of the population.

Background: Takotsubo cardiomyopathy (TTC) typically affects postmenopausal women and clinically presents with chest pain, ST-segment elevation, elevated cardiac enzymes and apical left ventricular (LV) wall motion abnormalities that mimic “apical-anterior” acute myocardial infarction (AMI). This study assessed whether admission clinical evaluation helps in differential diagnosis between the two conditions.

Methods: The study compared at-admission clinical, ECG and echocardiographic findings of 31 women (median age 67 years, IQR 62–76) with typical TTC and 30 women (median age 73 years, IQR 61–81) with apical-anterior AMI due to acute occlusion of the middistal left anterior descending coronary artery.

Results: Women with TTC significantly more often showed PR-segment depression (OR=37.2, 95% CI: 3.4–424, p=0.002) and ST-segment elevation in lead II (42% versus 10%, p=0.01) than those with AMI. At multivariate analysis, PR-segment depression (OR=37.2, 95% CI: 3.4–424, p=0.002) and maximum ST-segment elevation ≥2mm (42% versus 37%, p=0.001) and ST-segment elevation in lead II (42% versus 10%, p=0.01) than those with AMI. At multivariate analysis, PR-segment depression (OR=37.2, 95% CI: 3.4–424, p=0.002) and maximum ST-segment elevation ≥2mm (42% versus 37%, p=0.001) and ST-segment elevation in lead II (42% versus 10%, p=0.01) than those with AMI.

Conclusions: At-admission ECG (but no clinical, laboratory and echocardiographic features) allows differential diagnosis between TTC and apical-anterior AMI in postmenopausal women. The combination of PR-segment depression and maximum ST-segment elevation predicted TTC with greater accuracy than traditional ECG parameters such as localization of ST-segment elevation and reciprocal ST-segment depression.

P4459 | BEDSIDE
High-sensitivity cardiac troponin on presentation to rule out acute myocardial infarction

Methods:
Purpose:  Direct comparison of the safety and efficacy of two previously defined strategies: combination of copeptin and hs-cTnI on presentation for acute myocardial infarction: combination of copeptin and hs-cTn.

Results:  Myocardial infarction was diagnosed on the index presentation in 656 patients (64±16 years, 57% men) presenting with suspected acute coronary syndrome between June 2013 and January 2014. All patients had serum troponin concentrations measured using a high-sensitivity cardiac troponin I assay on presentation. The primary outcome was defined from routine data as a composite of myocardial infarction or index presentation, and recurrent myocardial infarction or cardiac death at 30 days. We evaluated the negative predictive value (NPV) for the primary outcome of a range of troponin concentrations on presentation.

Methods: In a prospective multicentre trial we identified 4,886 consecutive patients (64±16 years, 57% men) presenting with suspected acute coronary syndrome between June 2013 and January 2014. All patients had serum troponin concentrations measured using a high-sensitivity cardiac troponin I assay on presentation. The primary outcome was defined from routine data as a composite of myocardial infarction or index presentation, and recurrent myocardial infarction or cardiac death at 30 days. We evaluated the negative predictive value (NPV) for the primary outcome of a range of troponin concentrations on presentation.

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and was similar for men and women. Use of this threshold identified 2,296 patients (47%) at low risk of acute coronary events.

Conclusions: Cardiac troponin concentrations less than 5 ng/L on presentation correctly ruled out fatal and non-fatal cardiac events at 30 days in more than 99% of patients with suspected acute coronary syndrome. Implementation of this approach could allow almost half of all patients with suspected acute coronary syndrome to be safely discharged and would have major benefits in reducing unnecessary hospital admissions.

P4464 | BEDSIDE
Hybrid coronary revascularization in 100 patients with multivessel disease: what can we expect?
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Introduction: Hybrid coronary revascularization (HCR) arises as a combined approach of surgical and percutaneous coronary intervention (PCI). This strategy allows the best of two traditionally isolated treatment options in multivessel coronary artery disease (CAD).

Purpose: We aim to assess the safety and clinical outcomes of patients submitted to HCR.

Methods: From May 2008 to December 2014 one-hundred consecutive patients underwent two-staged coronary revascularization (PCI after coronary artery bypass grafting), in our hospital, after Heart Team evaluation. Death, myocardial infarction and repeated target vessel revascularization (MACE) were analyzed in index hospitalization and at follow-up.

Results: Mean age was 67±10 years and 66% of patients were male. HCR was performed after an acute coronary syndrome in 47% of the population and two-thirds of the patients had preserved left ventricular ejection fraction. In all cases an arterial graft to the left main was performed. Forty-nine percent of patients also underwent other arterial or veins grafts. CABG was carried out off-pump in 76% of patients. PCI occurred 5±3 days after surgery, with 100% of angiographic success and using drug-eluting stents (67%), bare-metal stents (32%) or both (1%). No in- or out-hospital deaths were reported. At a mean follow-up of 22±14 months, eighty-three patients were evaluated and overall population freedom from MACE was 97%; one case died from pneumonia and two had non-STEMI, treated with conservative approach. No cardiac death occurred.

Conclusions: Hybrid coronary revascularization may be considered a viable option in patients with multivessel CAD. In our experience HCR has a good outcome at short and mid-term follow-up. In spite of the lack of large randomized controlled trials with long term follow-up, it seems reasonable to consider that this strategy can have an important role in CAD treatment.
P4464 | BEDSIDE
Prognostic impact of contrast volume on the basis of renal function and CHA2DS2-VASc score in patients with coronary artery disease

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Purpose: To investigate the association among clinical outcomes, CHA2DS2-VASc score, and contrast volume on the basis of renal function in patients undergoing percutaneous coronary intervention (PCI) with coronary artery disease (CAD).

Methods: A cohort of 2489 patients (69.8±10.8 years old, 77% male) who underwent PCI for CAD was analyzed from CAS (Cardiovascular Assessment Study) multi-center registry. We divided patients into 3 groups according to tertile of contrast media volume/e-GFR ratio (CV/GFR): Low (<2.21: n=829), Mid (2.22–3.30: n=830), and High (3.31–≤: n=830). We then re-divided these into low, mid, and high tertiles of creatinine (Cr) and e-GFR. The c statistic of the MACE prediction model changed from 0.583 to 0.654 (p=0.036). The c statistic of the MACE prediction model changed from 0.583 to 0.654 (p=0.036) after the addition of CHA2DS2-VASc as a continuous variable (35%, CI: 21.9–58%).

Results: Among the total cohort, 24.4% had significant coronary stenosis, 64% had CAD and 36% had zero CAC. Patients with CAC were older (p<0.001), with a greater number of males (p<0.001) than those with zero CAC. In patients with CAC, all risk factors were more prevalent in those with significant coronary stenosis than in patients without, with obesity proving to be the most important (QR=2.94). However, in patients with zero CAC, obesity was the only discriminator of significant coronary stenosis. Similarly, multivariate analysis identified smoking, diabetes, obesity and family history (but not dyslipidaemia or hypertension) as independent predictors of significant coronary stenosis in CAD patients but only obesity was predictive in those with zero CAC (p<0.001 for all).

Conclusion: In symptomatic patients with CAC, most risk factors were predictive of significant stenosis, the most important being obesity, although hypertension and dyslipidaemia were not predictive. In patients with zero CAC, obesity was the sole independent predictor of stenosis. These results highlight the need for stringent management of metabolic syndrome.

P4467 | BEDSIDE
Risk stratification using the CHADS2 score in patients with coronary heart disease undergoing percutaneous coronary intervention

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Purpose: Risk stratification using the CHADS2 score in patients with coronary heart disease (CHD) without AF. Recently, CHADS2 score is used for prediction of stroke in patients with atrial fibrillation (AF). However, clinical validation of CHADS2 score for prognostic stratification in coronary heart disease (CHD) without AF remains uncertain.

Methods: In this study, we evaluate whether CHADS2 score could predict clinical outcome in CHD without known AF.

Results: One-year follow-up was completed in 1,632 patients (95.2%). Cumulative incidence of MACE was 139 cases. In Kaplan-Meier analysis, incident of MACE was significantly higher in patients with CHADS2 score ≥3 compared to Patients with CHADS2 score <3 (p=0.001; HR: 12.9% 99% CI: 7.4–22.3% vs. 1.7% 99% CI: 0.001–3.02% (Figure). In multivariate Cox regression analysis, CHADS2 score was an independent predictor for MACE (hazard ratio 1.18, 95% confidence interval 1.01–1.38, p=0.040).

Conclusions: This study demonstrated that CHADS2 score could provide prognostic information in CHD without known AF.
P4469 | BEDSIDE
Lower burden of coronary disease in treated patients with HIV.
A retrospective single centre study
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Background: Treated HIV has been associated with accelerated vascular disease including a higher incidence of coronary artery disease and myocardial infarction, partly due to a higher burden of traditional risk factors and metabolic complications of anti-retroviral treatment. It is not well established whether HSV vasculopathy, in a contemporary group of treated patients is a diffuse multi-vessel process or secondary to vulnerable high-risk plaque.

Purpose: We sought to quantify the burden of coronary artery disease in a group of well treated patients with HIV using invasive and non-invasive data from coronary angiograms in patients presenting for investigation of suspected coronary ischemia.

Methods: Demographic and angiogram data from 160 males who presented acutely with STEMI/NSTEMI or unstable angina (73 patients with HIV and 87 age and clinical presentation matched HIV negative controls) were obtained from our hospital (a major public teaching hospital). The sample was pooled and coronary vessel patency was calculated using the Gensini Angiographic Scoring System by an experienced cardiologist blinded to HIV status. The statistical software package SPSS v22 was used to analyse the data to assess the relationship between HIV status, traditional risk factors and coronary vessel patency.

Results: The two groups were matched for age and there was no difference in cholesterol profiles, rates of smoking or hypertension. Statin use was higher in patients with HIV (59% vs 33% p<0.001). There was a significant difference (p=0.004) in mean Gensini score, between the HIV positive group (22.72) compared to HIV negative group (36.55) of 10.83 (95% CI 0.83, 20.82). The mean number of vessels affected was lower in the HIV positive group (1.97) compared to the control (2.26). With a mean difference of 0.29 however, this was not significant (p=0.034).

Conclusion: HIV treated patients demonstrated a lower burden of coronary disease in a group of well treated, virally suppressed, aged matched patients with HIV and similar traditional risk factors.

P4470 | BEDSIDE
Novel association factor in spontaneous coronary artery dissection and recurrences
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Introduction and purpose: Spontaneous coronary artery dissection (SCAD) is a rare but challenging clinical entity of unknown etiology. Patients with hypothyroidism may have a higher risk of arterial wall injury. Our primary objective was to see the relationship between hypothyroidism and SCAD.

Methods and results: A total of 38 patients registered in our Hospital from 2000 to 2014 were retrospectively enrolled. The definition of spontaneous coronary artery dissection (SCAD) was based on the presence of medial dissection or intramural hematoma that was recognized by angiography and according with the classification proposed by Saw. Finally, 38 patients diagnosed as SCAD (male/female 16/22, age 54±12 years) were included in the analysis. The clinical presentation was myocardial infarction in 87% of patients. 10% SCAD developed after disruption of a coronary artery aneurysm, partly due to a higher burden of traditional risk factors and metabolic complications of anti-retroviral treatment. It is not well established whether HSV vasculopathy, a contemporary group of treated patients is a diffuse multi-vessel process or secondary to vulnerable high-risk plaque. These findings may represent more aggressive risk factor management in our cohort, including statin use, lowering the burden of coronary vascular disease.

P4471 | BEDSIDE
Clinical characteristics and outcomes of acute myocardial infarction in young Korean adults

Background: Although many efforts for reducing cardiovascular disease, there is no significant change in the incidence of young patients who were diagnosed as AMI.

Purpose: This study aims to investigate the clinical features, angiographic find- ings, and outcomes of young AMI patients.

Methods: We analyzed major adverse cardiac events (MACE) in the Korea Acute Myocardial Infarction Registry from November 2005 to 2010. The regist ered patients were divided into two groups; young age group (<45 years) and old age group (≥65 years).

Results: The young age group included 1,248 patients (39.6±4.3 years) and the old age group included 9,759 patients (74.5±6.5 years). Male gender, smoking, family history, and dyslipidemia were more frequently observed in the young age group than in the old age group (96.6% vs. 57.5%, P<0.001; 86.9% vs. 45.7%, P<0.001; 15.5% vs. 4.8%, P<0.001; 13.4% vs. 9.5%, P<0.001). Young Korean adults with AMI had a shorter symptom-to-door time (17.4±7.2 min vs. 24.2±7.7 min, P=0.002), but a longer door-to-balloon time (111.1±106.8 min vs. 101.8±52 min, P=0.043). The young age group showed a favorable prognosis compared with the old age group by the Kaplan-Meier survival analysis (long-rank, P<0.001).

Conclusion: Young Korean adults with AMI have similar clinical outcomes compared to old age patients, and therefore, they should be treated aggressively like the elderly patients.

P4472 | BEDSIDE
Clinical impact of beta-blocker on long-term clinical outcomes in patients with coronary chronic total occlusion

Background: Limited data are available on efficacy of β-blockers for secondary prevention in patients with coronary chronic total occlusion (CTO).

Purpose: We investigated the association of β-blockers therapy with long-term clinical outcomes in CTO patients.

Methods: From March 2003 to February 2012, a total of 1,228 CTO patient treated with either percutaneous coronary intervention (PCI) or medical therapy alone were enrolled. We classified patients into β-blocker group (n=674) and non-β-blocker group (n=554) according to the use of β-blockers at discharge. Propensity-score matching analysis was also performed in 475 pairs. The primary outcome was cardiac death.

Results: During a median follow-up duration of 3.8 (interquartile range: 1.9–5.9) years, cardiac death occurred in 40 (5.9%) of the β-blocker group versus 29 (5.2%) of the no-β-blocker group (p=0.88). After propensity-score matching analysis, there were no significant differences in the rates of cardiac death (hazard ratio [HR]: 1.16, 95% confidence interval [CI]: 0.79–1.53, P=0.585), major adverse cardiac events, defined as the composite of cardiac death, myocardial infarction, or repeat revascularization (HR: 1.15, 95% CI: 0.87–1.51, P=0.32).

Conclusions: β-blockers therapy at discharge was not associated with favorable long-term clinical outcomes in stable CTO patients treated with either PCI or medical therapy alone.
Background and introduction: Patients with type 2 diabetes mellitus (T2DM) exhibit a typical pattern of dyslipidemia with low HDL cholesterol, high triglycerides and a low LDL cholesterol to apoB ratio. A high triglycerides, low HDL cholesterol and a low LDL-C/apoB ratio predict incident T2DM among non-diabetic patients with established coronary artery disease (CAD).

Methods: We enrolled 655 non-diabetic patients with angiographically proven stable CAD. Prospectively, the incidence of T2DM was recorded over a mean follow-up period of 6.1±3.7 years. Diabetes was diagnosed according to ADA criteria.

Results: From our non-diabetic coronary patients, 358 (54.7%) at baseline had normal fasting glucose (NFG) <100 mg/dl. During follow-up, T2DM was newly diagnosed in 17.4% of our patients. Baseline IFG compared to NFG was associated with a strongly increased risk of T2DM (26.6% vs. 9.8%; adjusted OR 3.34 [2.17–5.16]; p<0.001). Low HDL cholesterol, high triglycerides, and a low LDL-C/apoB ratio after multivariate adjustment including fasting glucose significantly predicted incident diabetes in the total study cohort (OR 0.65 [0.49–0.86]; p=0.003, 1.40 [1.13–1.74]; p=0.002 and 0.54 [0.41–0.71]; p<0.001, respectively) and also when we separately analyzed patients with IFG (OR 1.42 [1.03–1.96]; p=0.032 and 0.56 [0.39–0.79]; p=0.001, respectively) and NFG (OR 0.62 [0.40–0.96]; p=0.034, 1.38 [1.03–1.86]; p=0.033 and 0.49 [0.32–0.76]; p=0.001, respectively).

Conclusion: We conclude that among patients with angiographically proven stable CAD the incidence of diabetes is high, particularly among those with IFG. Importantly, high triglycerides, low HDL cholesterol and a low LDL-C/apoB ratio significantly predict incident diabetes independently from baseline glycemia.

P4474 | BENCH Impact of diabetes on 2-year clinical outcomes in patients with acute myocardial infarction: Korean registry of DIABETIC (diabetic acute myocardial infarction disease) I.C. Kim¹, S.H. Hur¹, Y.K. Cho¹, H.J. Yoon¹, C.W. Nam¹, J.W. Bae², W.J. Kang³, K.B. Kim¹, H.S. Kim³ on behalf of DIABETIC Investigators. ¹Keimyung University Hospital Dongsan Medical Center, Internal Medicine, Division of Cardiology, Daegu, Korea, Republic of; ²Chungbuk National University Hospital, Cardiovascular Center, Cheongju, Korea, Republic of; ³Seoul National University Hospital, Cardiovascular Center, Seoul, Korea, Republic of

Background: We established diabetic acute myocardial infarction (AMI) cohort in order to extend knowledge of AMI with diabetes mellitus (DM) and to provide a better understanding of clinical consequences following AMI in DM patients.

Methods: Korean registry of DIABETIC (Diabetic Acute Myocardial Infarction Disease) is a prospective, observational study where consecutive AMI patients with DM were enrolled from 22 hospitals in South Korea between April 2010 and June 2012. In order to compare clinical outcomes between diabetic and non-diabetic AMI, we retrieved non-diabetic AMI from KAMIR cohort (3,178 patients from Korea Acute Myocardial Infarction Registry) on the basis of a 1:1 propensity score matching (PSM) by age and gender. The primary end point was the incidence of major adverse cardiac events (MACE, a composite of all-cause death, recurrent MI, and target vessel revascularization) at 2-year follow-up.

Results: In diabetic cohort, patients were older (64.9±9.8 vs. 62.2±13.1, p<0.001), left ventricular ejection fraction was lower (50.8±11.8 vs. 54.0±10.9, p<0.001), estimated glomerular filtration rate was lower (73.5±31.9 vs. 84.6±28.8, p<0.001) and there were more female patients (34.2% vs. 23.4%, p<0.001). Patients with DM were more likely to have other comorbidities such as hypertension (66% vs. 43.7%, p<0.001) and hyperlipidemia 27.1% vs. 12.5%, p<0.001) with more history of prior MI (5.5% vs. 2.3%, p<0.001). After PSM analysis, the 2-year incidence of MACE was significantly higher in DM (9.2% vs. 3.6%, p<0.001).

Conclusions: AMI patients with DM in Korea had worse clinical characteristics and more accompanied with comorbidities. In this PSM comparison with non-diabetic AMI, DM increases the risk of MACE in AMI patients at 2-year follow-up.

P4475 | BENCH Eastern European patients undergoing percutaneous coronary intervention: factors that impact in-hospital and one year outcome. Results from the first Jordanian PCI Registry (JoPcR 1)

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Background: and Introduction. There is paucity of studies which evaluate the in- hospital and long-term outcome of Eastern Middle Eastern population undergoing percutaneous coronary interventions (PCI) for acute coronary syndrome (ACS) or chronic stable angina (CSA), and the factors that predict mortality in such patients.

Purpose: The aim of this prospective multicenter study was to evaluate incidence of major cardiovascular events during admission, at 1 and 12 months in Middle Eastern patients undergoing PCI and the factors that predict mortality in such patients.

Methods: We enrolled 2426 consecutive patients (from December 2012 to February 2014) who underwent PCI for ACS (N=1870, 77%) or CSA (N=556, 23%). Mean age was 56±11 yr, 25% were <50 yr of age and 14% were >70 yr of age. Women comprised 21% of the study group, 62% had hypertension, 53% were diabetics, and 44% were current smokers. Dual antiplatelet therapy was prescribed in 99.8% of the patients. Cardiovascular mortality rates during hospitalization and after 1 and 12 months were 0.78%, 1.2%, and 1.98%; respectively. Stent thrombosis occurred in 9 patients (0.37%) during hospitalization, and in 57 (2.4%) at 1 year. Rates of readmission for ACS and target vessel/lesion repeat PCI at 1 year were 5.3% and 4.6%, respectively. Of 23 variables evaluated for potential impact on outcome; 5 were significantly associated with increased 1 year cardiovascular mortality: diabetes (odds ratio [OR] 4.0), heart failure on admission (OR 5.5), chronic stable angina (CSA), and diabetes mellitus (DM). Patients with DM had increased risk of death (OR 2.4, p<0.001). Effective glycaemic control (HbA1c < 7.5% at hospital admission) and hospitalisation after diabetic medication initiation significantly decreased MACE rates at 1 year (p<0.001). Following discharge, patients with DM had lower rates of antithrombotic therapy (p<0.001) and were more likely to be readmitted to hospital (p<0.001) compared to non-diabetic patients.

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P4476 | BENCH New onset diabetes mellitus at mid-term follow-up after acute myocardial infarction is related to increased prevalence of decreased renal function

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Background: The prevalence of new onset diabetes mellitus (newDM) in relation to microvascular complications after hospital discharge due to acute myocardial infarction (AMI) is little known.

Aim: To evaluate the occurrence of newDM at mid-term follow-up in patients after AMI and to invasively monitor the prevalence of decreased renal function.

Methods: The single-centre observational and prospective study encompassed consecutive AMI patients treated invasively who completed check-up visits on an outpatient basis at least 6 months after hospital discharge. At follow-up visit (FU) median duration was 7 months) 341 subjects without antidiabetic medication were selected and screened for newDM with respect to 2013 ESC guidelines for diabetes mellitus. NewDM group was compared to control group consisted of remaining patients. Renal dysfunction was defined on the basis of GFR estimated according to the abbreviated Modification of Diet in Renal Disease Study Group Equation proposed by the National Kidney Foundation.

Results: NewDM was diagnosed in 45 subjects (13.2%). NewDM patients, when compared to controls, had higher prevalence of decreased renal function at FU
Heart and Lung Project (MHLP), a community-based study of asymptomatic general populations >45 years. The enrolled subjects underwent a complete routine peripheral blood laboratory examination, including high-sensitivity C-Reactive Protein (hsCRP) measurement. Individual body mass index (BMI) was calculated according to standard formulas. Computed Tomography (CT) Calcium Score was obtained and CAC density was determined according to previously described Agatston score-derived formulas.

Results: Multiple regression statistical analysis showed independent positive correlations of CAC density score with blood levels of gamma-glutamyltransferase (GGT) (P=0.0011), creatinine (P=0.0047) and triglycerides (P=0.0088), as well as with age of subjects (P <0.0001) and circulating monocyte number (cells/ml) (P <0.0001). On the other hand, CAC density score exhibited independent inverse correlations with blood high-density lipoproteins (HDL) (P=0.0426 and platelet number (P=0.0179).

Conclusions: Our results demonstrate for the first time that the blood monocyte number represents a powerful inflammation marker independently associated with the CAC density score in a wide population of asymptomatic subjects, so suggesting a key functional role of this leukocyte subset in the histopathological process of arterial calcification.

P4479 | BEDSIDE
Coronary CT angiography in patients with a zero agatston score: results from the German cardiac CT registry
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Background: The absence of coronary calcification has been shown to be associated with a favorable prognosis in asymptomatic individuals, but it is unclear whether the lack of coronary calcium permits to rule out coronary stenoses and avoid further diagnostic workup in symptomatic patients. We report the clinical phenotype, symptom status, risk profile and in the vast majority of patients CAD, is excluded with no need for risk stratification for CAD or for detection/exclusion of obstructive CAD (97.1%). 43% of patients with a zero Agatston score were asymptomatic. In 70.8% of patients a previous stress test was performed, out of these 56.9% were normal, 24.7% were indicative of ischemia and 18.4% were inconclusive. The mean mean of traditional cardiovascular risk factors was 2.0, the mean cholesterol level was 215 mg/dl, the mean LDL-level was 132 mg/dl, mean triglycerides level was 116 mg/dl and the mean Framingham 10 year risk was 5.1±5.1%. Coronary CT angiography was performed in 1665/ 2016 patients (82.6%, mean heart rate 60.7±10.8 bpm, 94% in sinus rhythm) with a mean effective radiation dose of 3.2 mSv. In 80.2% of patients CAD was excluded, in 17.5% non-obstructive CAD (stenosis >50%) was detected and in 2.3% obstructive lesions (stenosis ≥50%) were identified. Following coronary CT angiography, ischemia testing was recommended in 1%, invasive coronary angiography in 2.7%, changes in medication in 10.8% and early hospital discharge in 18.8%.

Conclusion: Patients with an Agatston score of zero show a low cardiovascular risk profile and in the vast majority of patients CAD, is excluded with no need for further downstream testing. Albeit seldom, significant coronary stenoses are detectable in a small percentage of patients without coronary calcifications.

P4478 | BEDSIDE
Temporal trends in clinical features and outcomes in the elderly following percutaneous coronary intervention

Background: Accompanied by aging society, percutaneous coronary intervention (PCI) has been widely performed in the elderly patients for the past few decades. However, a paucity of published data examining clinical features and outcomes is available.

Methods: We analyzed data of patients with the age of 70 to 85 following PCI in Juntendo University (Tokyo, Japan) from 1985 to 2010. The patients were divided into three groups according to the timing of PCI (March, 1985–December, 1997; plain old balloon angioplasty (POBA)-era, January, 1998–July, 2004; bare metal stent (BMS)-era, August, 2004–December, 2010; drug-eluting stents (DES)-era). Primary endpoint was a composite of all-cause mortality and acute coronary syndrome assessed at three-year after the initial procedure.

Results: A total of 1070 patients were examined (POBA-era; 184, BMS-era; 364 and DES-era; 519). Mean age and BMI, a prevalence of diabetes, hypertension and dyslipidemia were higher in DES-era. Lipid profiles were better and prescription rates of evidenced-based medicine including aspirin, statin and beta-blocker were higher in DES-era. Kaplan-Meier estimation for 3-year all-cause mortality and acute coronary syndrome was not different between the groups (Figure 1).

Conclusions: Despite the higher risk profiles of the older patients in the current DES-era, long-term clinical outcomes following PCI were similar among POBA-, BMS- and DES-eras.

P4477 | BEDSIDE
CLINICAL ADVANCES IN COMPUTED TOMOGRAPHY ANGIOGRAPHY
P4477 | BEDSIDE
Circulating monocytes are strongly associated with coronary artery calcification (CAC) density in a population of asymptomatic subjects
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Background: Coronal artery calcification (CAC) is an active and regulated inflammatory process in the natural history of atherosclerosis, strongly associated with clinical conditions conferring a high risk of cardiovascular disease (CVD). However, a clearly established association between the spreading of CAC and the circulating level of inflammatory/metabolic markers is still lacking. We aimed to investigate the relationships between CAC density score and peripheral inflammatory/metabolic parameters in a wide population of asymptomatic subjects.

Methods: We evaluated 1606 subjects from the population of the Montignoso
were lost to follow-up. After a median follow-up of 6.1 years, MACE occurred in 0% of normal, 6% of non-obstructive, 30% of obstructive and 39% of revascularised patients (all comparisons p < 0.003, except obstructive versus revascularised non-significant). Multivariate Cox analysis identified obstructive stenosis and CACS as independent MACE predictors (p < 0.001). Area under receiver operating characteristic curve was higher for CCTA than CACS: 0.804 (0.742–0.866) vs. 0.738 (0.644–0.832).

Conclusion: Low-dose 64-slice CCTA with prospective ECG triggering has an excellent prognostic performance with a warranty period of at least 6 years for patients with normal coronary arteries.

P4482 | BEDSIDE

Relation between quantitative coronary CTA and myocardial ischemia by adenosine stress CT myocardial perfusion imaging

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Objectives: The purpose of this study was to assess the relation between coronary stenosis severity and plaque characteristics by quantitative coronary computed tomography angiography (QCT) and myocardial ischemia diagnosed by adenosine stress CT myocardial perfusion imaging (CTP).

Background: The relation between stenosis severity measured by invasive coronary angiography and ischemia has been well established. Coronary CTA and CTP provide anatomic and functional information in one cardiac imaging technique. The association between percentage lumen area stenosis and plaque characteristics measured by QCT and ischemia by CTP is unclear.

Methods: We evaluated 84 patients who underwent both coronary CTA and CTP. All coronary artery plaques were analysed by CQCT. Vessels without atherosclerosis were excluded. Luminal area stenosis severity and additional plaque characteristics (section length, mean plaque burden, remodeling index) were determined.

Subsequently, the presence of myocardial ischemia was assessed by CTP using a summed difference score of ≥1 on a 17 myocardial segment model. Vascular territories were linked to the three coronary arteries.

Results: Atherosclerosis was present in 146 coronary arteries. 33 (21%) vascular territories, had myocardial ischemia. Lumen area stenosis percentage (p < 0.001), mean lesion burden (p < 0.001), lesion length (p < 0.033), maximal plaque thickness (p < 0.021), dense calcium volume (p < 0.005) were significantly higher in ischemic territories.

Conclusion: Lumen area stenosis severity measured by QCT is incrementally related to ischemia as detected by CTP. However, in a substantial amount (41%) of high-grade stenoses (≥81% luminal narrowing) no ischemia is detected on CTP.

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P4483 | BEDSIDE

Diagnostic accuracy of first-pass myocardial perfusion imaging without stress in comparison with invasive FFR

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Background: Coronary computed tomography angiography (CCTA) alone could not evaluate whether a stenosis causes ischemia. Previously, we have reported that CCTA plus first pass CT-myocardial perfusion imaging (MPI) without stress, which requires no additional radiation exposure and contrast medium, could provide excellent diagnostic performance compared with CCTA alone in patients without history of CAD. However the clinical feasibility of first pass CT-MPI without stress is still controversial. Thus we further evaluated the diagnostic accuracy of first pass CT-MPI without stress compared with invasive fractional flow reserve (FFR) in patients without history of CAD.

Methods: A total of 54 patients suspected CAD underwent both CCTA, first pass CT-MPI without stress and invasive FFR. CT-MPI imaging was created using same raw data used for CCTA. The thresholds of diagnostic ischemia were defined as invasive FFR ≥0.80.

Results: In 54 patients, 67 coronaries were evaluated with first pass CT-MPI and invasive FFR. First pass CT-MPI showed perfusion abnormalities in 26 (39%)
vehicle territories among 67 vascular territories. With invasive FFR, 20 (30%) coronaries had significant coronary stenosis, as FFR <0.80. The area under the receiver-operating curve for first pass CT-MPI was 0.758 (95% confidence interval [CI]: 0.627 to 0.889) for invasive FFR (p=0.001). First pass CT-MPI without stress showed sensitivity 0.75, specificity 0.77, positive predictive value 0.58 and negative predictive value 0.88 for detecting vascular territories with significant coronary stenosis as determined with invasive FFR <0.80.

Conclusion: First pass CT-MPI without stress shows excellent diagnostic accuracy compared with invasive FFR as the reference standard. This technique could complement CCTA for diagnosing CAD.

P4485 | BEDSIDE
Cardiovascular plaque predicts severity of coronary atherosclerosis in asymptomatic diabetics: a prospective study
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Objective: To evaluate the association of carotid plaque and carotid IMT measurements in asymptomatic diabetics with or without coronary atherosclerosis.

Methods: As part of a ongoing trial (PROCEED-Progression of coronary atherosclerosis in diabetics: Evaluation of CT coronary angiography and novel biomarkers to evaluate the effects of intensive or standard statin therapy with/without eicosapentanoic acid on the progression of coronary calcium score (CCS), This trial demonstrated that annual progression rate of Agatston score was similar among groups and 40% (95% CI: 9–61%) in all patients irrespective of a significant plaque compared to 12% in previous study. No significant difference was noted in quadrant progression of CCS with standard statin therapy and the presence of statin therapy. Therefore, it is of interest to find factors involving CAC progression. Among several cardiovascular risk factors, the number of coronary plaque positive cell was reported to be associated with vascular function and cardiovascular risk.

Purpose: To examine the number the number of CD34 positive cell and annual progression of CAC in the PEACH trial.

Methods: The PEACH trial was a multicenter, prospective and randomized trial evaluating the effects of intensive or standard statin therapy with/without eicosapentanoic acid on the progression of coronary calcium score (CCS).

Results: The number of CD34 positive cell was 70% in the entire study population, 71% in the same group and 145 (59%) were males. Patients with microvascular disease (MVD) were 117 (47%), carotid plaque prevalence 115 (46%), mean CIOMT was 0.72±0.19 mm, duration of diabetes 13.76±7.8 yrs and waist hip ratio 0.95±0.09.

A total of 31 (12.5%) patients were found to have obstructive coronary plaque (<70% stenosis) and the prevalence of carotid plaque was 22 (71%) in the same group.

On binary logistic regression analysis, age (Odds ratio 1.0, CI 1.009–1.107, P = 0.001), hypertension (Odds ratio 5.932, CI 1.37–25.6, P = 0.017) and carotid plaque (Odds ratio 3.2, CI 1.43–7.4, P = 0.003) were significantly associated with obstructive coronary plaque. Of the other factors, duration of diabetes (Odds ratio 1.05, CI 1.006–1.104, P = 0.004) and family history of CAD (Odds ratio 2.1, CI 1.4–7.4, P = 0.07) are significantly associated.

On multi variate predictors, the area under the curve increased to 0.84 from 0.65 for duration of diabetes, hypertension, BMI, waist hip ratio, family history of CAD and current smoking.

Conclusion: Presence of carotid plaque was a strong predictor of obstructive coronary plaque in asymptomatic diabetes. The early detection of carotid plaque will help us to further risk stratify patients from traditionally available risk scoring algorithms (FRE, Quirk et) in predicting severity of coronary artery disease.

P4486 | BEDSIDE
The number of circulating CD34 positive cell is an independent predictor of the annual progression of coronary calcium score determined by MDCT: Results from the PEACH trial
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Background: The PEACH trial was a multicenter, prospective and randomized trial to evaluate the effects of intensive or standard statin therapy with/without eicosapentanoic acid on the progression of coronary calcium score (CCS).

Methods: The PEACH trial evaluated 156 patients with CCS of 1 to 999, hypercholesterolemia, and no history of cardiovascular disease from 27 sites in Japan from May 2010 to August 2011. Patients were assigned into three groups of pta- vastatin 2mg/day alone, or 4mg/day alone, and 2mg/day + eicosapentanoic acid 1800mg/day. MDCT and a blood test were performed again at one year follow-up. The number of circulating CD34 positive cell was counted with flow cytometry.

Results: Correlation analyses among circulating biomarkers revealed that the annual change in CAC was significantly associated with the baseline number of CD34 (r = −0.19, p = 0.037), but not with age, gender, body mass index, baseline levels of LDL-cholesterol, triglyceride, hsCRP, uric acid, serum creatinine, and adiponectin. On the other hand, the number of CD34 positive cells was significantly correlated with age, gender, body mass index, baseline value of LDL-cholesterol and HDL-cholesterol. Multiple logistic analysis demonstrated that lower CD34 positive cell number (<0.84) (Odds ratio: 7.0, 95% confidential interval: 1.26–38.5, p = 0.01) and CD34 positive cell number >2.74, 95% confidential interval: 1.23–6.12, p = 0.01) were independent predictors of the CAC progression, even after adjustment of age >60 years, hypertension, diabetes, and current smoking.

Conclusion: The substudy demonstrated the lower number of circulating CD34 positive cell is a novel predictor of CAC progression in patients with hypercholesterolemia under statin therapy.

P4487 | BEDSIDE
Non-invasive assessment of coronary everolimus-eluting bioresorbable vascular scaffolds using multi detector-computed tomography - comparison to invasive coronary angiography
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Background: Multi detector-computed tomography (MDCT) permits visualization of coronary arteries as well as coronary artery stenoses. However, although clinically desirable, the assessment of coronary artery stent patency with MDCT is time-consuming and frequently impaired by artefacts caused by high-density stent material. As being made of non-radiopaque material, recently introduced everolimus-eluting bioresorbable vascular scaffolds (BVS) promise significantly better assessability in MDCT than conventional coronary stents.

Methods: Dual source-Computed Tomography (DSCT, Siemens Somatom Definition, i.v.-injection of 70–85ml of contrast agent at 8ml/s) was performed in 18 patients (mean age 58±7y) with previously implanted BVS (n=32; all ABSORB, Abbott Vascular) at a mean interval of 7 months after scaffold implantation. This was followed by conventional coronary angiography with MDCT of the entire coronary tree. Each BVS was evaluated by two readers in consensus. They were classified evaluable or unevaluable by visual estimation, and evaluable BVS were further separated as to the presence of relevant restenosis/occlusion.

Acknowledgement/Funding: British Cardiac Research Trust
Results: Mean diameter of the BVS implanted was 2.9±0.1 mm, and mean length was 20.7±1.3 mm. BVS were located in LAD (n=14), RCA (n=8), RCX (n=4), diagonal branches (n=2) and marginal branches (n=2), respectively. Out of 32 coronary scaffolds, 30 (94%) were determined assessable. Assessability was impaired by motion artefacts in two scaffolds (one BVS in RCA and one in a diagonal branch), but no BVS was classified unassessable due to beam-hardening artefacts, partial volume effects or other artefacts caused by scaffold components. Regarding unassessable scaffolds as being potentially stenotic, 28 BVS were correctly determined to be patent, 2 scaffold occlusions were detected accurately, and 2 false positive findings occurred. Consequently, the overall diagnostic accuracy was 94%, revealing a sensitivity of 100% and a specificity of 93%. Positive and negative predictive values were 50% and 100%, respectively.

Conclusion: In contrast to conventional coronary artery stents, MDCT allows for comprehensive intracoronary lesion characterization with good diagnostic accuracy independent of scaffold diameter or length. Only a small number of BVS is unassessable in MDCT, which is due to motion artefacts.

TECHNICAL DEVELOPMENTS IN COMPUTED TOMOGRAPHY ANGIOGRAPHY

P4488 | BEDSIDE
Bail out intravenous esmolol for heart rate control in cardiac computed tomography angiography

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Background: Adequate heart rate (HR) control is paramount for optimal cardiac CT image acquisition. The primary safety endpoint (SEP) was HR < 65 bpm just after scouting. The primary efficacy endpoint (EEP) was HR < 65 bpm during contrast image acquisition. The primary safety endpoint (SEP) was symptomatic hypotension (SBP < 90 mmHg) or bradycardia (HR < 45 bpm) up to hospital discharge.

Methods: From August 2011 to June 2014, individuals submitted to cardiac 64-MSCT in single institution were analyzed. Those in sinus rhythm, with no contra-indications for beta-blockers and HR > 60 bpm on presentation, received 50–200 mg of oral metoprolol at least 1 hour before CTA. Intravenous (IV) bolus esmolol 1–2 mg/kg were administered (and repeated if necessary) whenever HR was > 65 bpm just after scouting. The primary efficacy endpoint (EEP) was HR < 65 bpm during contrast image acquisition. The primary safety endpoint (SEP) was symptomatic hypotension (SBP < 90 mmHg) or bradycardia (HR < 45 bpm) up to hospital discharge.

Results: From 947 CCTA cases performed during the study period, IV esmolol (mean dose 1.54 mg/kg) was used in 130 (14%) patients; 84 (64%) of which were pre-medicated with oral metoprolol. HR > 65 bpm was achieved in 82 of the 130 patients (63%). For the whole population, this resulted in a significant increase in primary EEP (86% to 95%, p < 0.001). For esmolol-treated patients initial and during contrast injection HR > 74±12 bpm and 63±5 bpm, respectively (p < 0.001). During CCTA a HR above 80 bpm was observed in 5 (4%) patients. Esmolol drove 95% of patients to be imaged with a HR below 65 bpm.

Conclusion: In our population, quantification of CAC allowed the optimization of the protocol including CTA for patients with CAC ≥ 100 and CT-IP if CAC < 100 showed the highest AUC (0.81, 95% CI 0.73–0.89). The protocol showed high negative predictive values or false negatives (“worst case scenario”). An integrated protocol including CTA and CT-IP for uninterpretable segments was tested (CT-IP).

Results: 95 patients were included in the analysis (62±8 years, 68%males). Inclusion of CAC was associated with a significant increase in the AUC of the models including CTA-ID and CTP for prediction of hSCAD. The model including CTP and CAC showed the highest AUC (0.92, 95% CI 0.86–0.98). The protocol including CTA and CTP if CAC > 100 showed the highest AUC (0.81, 95% CI 0.73–0.89).

Conclusion: In this large cohort of asymptomatic individuals with no previous history of coronary revascularisation, a substantial proportion of patients had CAC score >0. In contrast to previously held assumption, Asians are not at higher risk of having coronary calcification, compared with white subjects, although Afro-Caribbean subjects appear to have lower risk than Asians.

P4490 | BEDSIDE
Coronary artery calcium quantification in the optimization of a comprehensive cardiac CT protocol for the diagnosis of hemodynamically significant coronary artery disease


Background: High coronary artery calcium (CAC) undermines the role of coronary CT angiography (CTA) in the investigation of obstructive coronary artery disease (CAD). Myocardial CT perfusion (CTP) may represent an opportunity to overcome this limitation. The aim of this study was to explore the role of CAC in the optimization of a protocol including coronary CTA and CTP for the detection of hemodynamically significant CAD (hsCAD).

Methods: Symptomatic patients with intermediate pretest probability of CAD were prospectively recruited and underwent both cardiac CT and invasive coronary angiography (ICA). Normal reference range of CAC score was published for White, Non-Chinese Asian (non-Chinese) and Chinese.

Results: Among 180 symptomatic patients, 156 (87%) had coronary calcification (CAC > 0) and 14 (8%) had calcification score ≤ 10. The AUC for CTA was 0.76 (95% CI 0.65–0.87) for the detection of hsCAD. The AUC for CTP was 0.76 (95% CI 0.65–0.87). Inclusion of CAC was associated with a significant increase in the AUC of the models including CTA-ID and CTP for prediction of hsCAD. The model including CTP and CAC showed the highest AUC (0.81, 95% CI 0.73–0.89). The protocol including CTA and CTP if CAC ≥ 100 showed the highest AUC (0.81, 95% CI 0.73–0.89).

Conclusion: In this large cohort of asymptomatic individuals with no previous history of coronary revascularisation, a substantial proportion of patients had CAC score >0. In contrast to previously held assumption, Asians are not at higher risk of having coronary calcification, compared with white subjects, although Afro-Caribbean subjects appear to have lower risk than Asians.
value to predict hemodynamic relevant stenoses >70% in ICA (Sensitivity 90.9%, specificity 89.3%) with an AUC of 0.97 (p < 0.0001, 95% CI 0.95–0.99). Minimal lumen diameter cut-off was 1.2 mm (sensitivity 90.9% and specificity 85.25) with an AUC of 0.92 (p < 0.0001, 95% CI 0.88–95). Maximal area and diameter stenoses (%) showed lower AUC values with 0.89 and 0.87 respectively.

Conclusion: Minimal lumen area of <1.8 mm² is the most accurate cut-off for high-grade CT stenoses in proximal coronary vessels and may add information to identify hemodynamic relevant stenoses that require revascularization in invasive angiography.

P4492 | BEDSIDE Impact of calcium distribution for predicting successful revascularization of chronic total occlusion: assessed by multi-detector computed tomography
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Background: In previous reports, the amount of calcification, tortuosity and actual length of the occluded segment which are established predictors of the success of percutaneous coronary intervention for chronic total occlusion (CTO-PCI) are all better characterized by multi-detector computed tomography (MDCT). However, there is little data regarding whether the distribution of intraluminal calcification is related to the success of CTO-PCI as observed by MDCT. So we investigated that in this study.

Methods and results: This was a retrospective, non-randomised study carried out in a single facility. Two hundred three patients with de novo 216 CTO lesions who underwent 64-slice MDCT prior to CTO-PCI were investigated. The lesions were divided into two groups according to procedural success (190 lesions in the PCI-success group, 26 lesions in the PCI-failure group). The degree and location of calcification was evaluated by cross-sectional lumen views along the occluded segment. We defined the calcium that occupied the center of the vessels as centric calcification. Regarding lesion characteristics, the rate of blunt stump, that of bending 45°, that of calcification >50% of cross-sectional area, and that of centric calcification were significantly higher in the PCI-failure group than in the PCI-success group (58% vs. 17%, p < 0.01, 64% vs. 28%, p < 0.01, 50% vs. 21%, p < 0.05, and 58% vs. 18%, p < 0.01, respectively). CTO length and total calcification length were significantly longer in the PCI-failure group than in the PCI-success group (33.4 ± 17.1 mm vs. 24.8 ± 13.3 mm, p < 0.05, and 12.7 ± 15.5 mm vs. 6.7 ± 7.9 mm, p < 0.01, respectively). The multivariate analysis revealed that the independent predictors of failed CTO-PCI were blunt stump (Odds ratio [OR] 7.04, p < 0.01, CI 2.46–21.6), bending >45° (OR 4.43, p < 0.05, CI 1.35–15.2), and centric calcification (OR 10.9, p < 0.05, CI 1.41–105.0).

Conclusion: The calcium distribution of occluded segments assessed by MDCT can deliver important information for predicting procedural outcomes in PCI of CTO.

P4494 | BEDSIDE Feasibility of coronary computed tomography angiography using multi slice slice computed tomography (CT) scanners for the detection of percutaneous coronary intervention (PCI) patients
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Objective: New generation dual-source multi slice computed tomography (CT) scanners allow low radiation dose in coronary computed tomography angiography (CTA). Purpose of this study was to evaluate the image quality and radiation dose of low dose cardiac CTA using automated attenuation-based selections of tube parameters in daily clinical practice.

Methods: Patients were referred to the heart center due to suspected coronary artery disease (CAD). CTA was performed using a 192-slice dual-source CT scanner. Images were recorded by prospectively electrocardiogram (ECG)-triggered high-pitch acquisition (“turbo flash”) mode (collimation 2×192×0.6 mm; 50 mAs contrast agent, Ultrasound 370; flow 50 ml/s). Automated attenuation-based selections of individualized tube parameters were used. Image quality (4-point rating score from 0 = nondiagnostic to 3 = excellent) and radiation dose were evaluated.

Results: 66 patients and 198 coronary arteries (mean age 59±14 years, 24 females) were analyzed by CTA. Mean heart rate was 61±6 bpm after application of intravenous betablocker up to 20 mg metoprolol prior CT scan. Mean radiation dose was 0.98±0.65 mSv. Tube parameters were 48±25 mAs and 84±110 kV. Subjective image quality was 2.4±0.3. 3 studies (9 coronary arteries, 4.5%) could not be interpreted due to poor image quality. Relevant coronary artery disease (stenosis ≥50%) was estimated by CTA in 8 patients (14 coronary arteries) who were referred to invasive coronary angiography. In 7 patients (13 coronary arteries) CTA findings were proofed in one patient LAD stenosis was overestimated in CTA.

Conclusion: The combination of prospectively ECG-triggered high-pitch acquisition mode and automated attenuation-based selections of individualized tube parameters is a powerful and reliable tool to assess coronary arteries in third generation 192-slice dual-source computed tomography with low radiation dose.

P4495 | BEDSIDE Epicardial fat density evaluated with MDCT is associated with cardio-metabolic risk factors
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Background: The volume of epicardial adipose tissue (EAT) determined with CT is shown to be associated with cardiovascular risks such as metabolic syndrome and the severity of coronary artery disease (CAD). Recently, several basic studies showed that perivascular fat could affect the vascular lesion by paracrine effects and the increase in vasa vasaorum. However, clinical significance of epicardial fat quantity in risks of cardiovascular disease remains unknown.

Purpose: To investigate the association between the quality of EAT determined as CT attenuation and cardio-metabolic risk factors.

Methods: Patients with CAD undergoing coronary bypass surgery (n=50) and non-CAD undergoing valvular surgery (n=50) were included (51% mean male age: 50 years). The EAT density in each subject was identified as a median value of CT attenuation (−190 to −30 Hu). The EAT volume, visceral fat (VAT) and subcutaneous fat (SAT) areas were also quantified.

Results: The EAT density in CAD group was lower than that in non-CAD group (vs. −78 vs. −70 to −70 vs. −77 to −64 Hu, p < 0.01), expressed median (25th percentile to 75th percentile) of 75th percentile. Of all patients, EAT density was correlated with EAT volume (r=−0.27, p=0.01) and the number of metabolic syndrome’s components.
P4498 | BEDSIDE
Improved visualization of the coronary arteries using model-based iterative reconstruction for cardiac CT
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Purpose: To evaluate the image quality characteristics of coronary CT angiography (CTA) images reconstructed with standard filtered back projection reconstruction (FBF), hybrid iterative reconstruction (HIR) and model-based iterative reconstruction (IMR) techniques.
Methods: Patients: 252 patients (39 male, age 64.7±9.3 years, BMI 28.2±5.6kg/m2) who underwent 256-slice coronary CTA were reconstructed with standard filtered back projection reconstruction (FBF), hybrid iterative reconstruction (HIR) and IMR. Two readers evaluated the datasets qualitatively and quantitatively. A four-point scale was used to rate overall image quality from 1-excellent to 4-poor, non-diagnostic. Image noise was graded from 1-no image noise to 4-severe noise, while image sharpness was evaluated on a five-point scale. Mean image noise (SD) and contrast-to-noise ratio (CNR) were measured in proximal and distal coronary segments.
Results: Qualitative analysis showed that IMR improves image quality and image sharpness as compared to FBF and HIR (p<0.0001 all). Image noise was significantly lower with IMR as compared to FBF and was further reduced with IMR as compared to HIR (p<0.0001 all). The mean image noise as measured in the ascending aorta was lowest with IMR (42.1±10.7 vs. 28.7±12.7 vs. 12.9±2.7; FBF vs. HIR vs. IMR, respectively; p<0.001 all), while mean attenuation did not differ among the three reconstruction methods (517.1±93.3 vs. 517.9±93.1 vs. 517.7±93.1 HU, p=1.0 all). Proximal CNR in FBF, HIR and IMR was 17.4±5.8 vs. 23.5±8.4 vs. 25.2±12.0 (p<0.001 all), while distal CNR was 16.2±5.0 vs. 23.2±7.4 vs. 55.2±12.4, respectively (p<0.001 all).
Conclusion: IMR significantly improves image quality accompanied by a substantial increase in CNR and decrease in image noise in coronary CTA.

P4499 | BEDSIDE
Paced QRS morphology is closely correlated with the right ventricular pacing lead position: a study by cardiac computed tomography
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Background: The rightward lead position on the left anterior oblique projection by fluoroscopy is often used as a marker of lead positioned in the right ventricular (RV) septum. Nonetheless, whether the lead is truly located in the septum remains unclear.
Purpose: The purpose of this study was to investigate the association between paced QRS morphology and the RV lead position revealed by computed tomographic angiography.
Methods: Consecutive 36 patients who underwent cardiac CT after pacemaker implantation were enrolled. The lead position was confirmed by using both tomographic images and 3-dimen sional reconstruction. A paced QRS morphology was obtained by 12-lead ECG.
Results: Thirty leads were aimed to be positioned in the right ventricular septum among 51 leads (33%) that were confirmed to be placed in the septum by CT. QRS duration was significantly shorter in the septal group (137±13 msec) than those in the apex group (162±18 msec, p=0.006) and in the free wall group (188±31 msec, p<0.001). QRS duration was significantly associated with body mass index, HDL-cholesterol, adiponectin, and oxidized LDL-cholesterol. Paced QRS duration showed a negative correlation with body mass index (r=−0.20, p=0.04) and area under curve (AUC) of left atrial appendage area (LAA) on post CPVI was 0.7.
Conclusion: Paced QRS duration is significantly associated with body mass index and the presence of CAD (odds ratio of lower LAA duration: 0.187, 95% CI 1.03 to 7.12, p=0.04) after adjustment of age, gender, hypertension, diabetes mellitus, dyslipidemia, and current smoking.

P4500 | BEDSIDE
Assessment of the coronary sinus vein with multi-detector computed tomography angiography - implications for mitral valve resharpening in patients with functional mitral valve regurgitation
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Background: There are few treatment options for functional mitral valve regurgitation (FMR), which is caused by mitral annulus dilatation. Recently introduced annuloplasty devices are percutaneously implanted into the coronary sinus vein (CS), reshaping the mitral valve annulus. However, data on CS length, diameters and its location in relation to the left circumflex artery (RCA) are crucial for device implantation. Multi detector-computed tomography (MDCT) is well applicable for that purpose by providing an assessment of the CS in any arbitrary plane with high spatial resolution.
Methods: Thirty patients (15 female, mean age 75±5y) with at least moderate FMR underwent contrast-enhanced, retrospectively ECG-gated dual-source CT (Siemens Somatom Definition, injection of 70 – 90ml of contrast) as part of a planning procedure prior to percutaneous mitral valve annuloplasty. Curved multiplanar reformat (cMPR) of the CS were rendered, and sinus vein length, proximal and posterior caliber (0.76±0.29 mm) of left PV were the thickest point among LAAWTH around each PV at 12 sites (1–12 o’clock) by a radiologist who did not know clinical information. Reconnected PVs were applied with reconnected PVPs were compared with their LAAWT. The location of RV lead confirmed by CT.

P4501 | BEDSIDE
Left atrial antral wall thickness around pulmonary veins is associated with stroke and the reconnection of pulmonary venous potential after catheter ablation on atrial fibrillation
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Background: Circumferential pulmonary vein isolation (CPVI) is most important strategy of catheter ablation on atrial fibrillation (AF). However, the reconnection of PV is a main mechanism of AF recurrence. Although it is important to understand left atrial antral wall thickness (LAAWT) prior to catheter ablation, its clinical implications were not well known.
Purpose: The purpose of this study was to investigate the association between left atrial antral wall thickness around pulmonary veins and potential after catheter ablation of AF , the LAAWT was measured around each PV at 12 sites (1–12 o’clock) by a radiologist who did not know clinical information. Reconnected PVs and intact PVs were compared with their LAAWT.
Methods: Patients: Thirty patients (15 female, mean age 75±5y) with at least moderate FMR underwent contrast-enhanced, retrospectively ECG-gated dual-source CT (Siemens Somatom Definition, injection of 70 – 90ml of contrast) as part of a planning procedure prior to percutaneous mitral valve annuloplasty. Curved multiplanar reformat (cMPR) of the CS were rendered, and sinus vein length, proximal and posterior caliber (0.76±0.29 mm) of left PV were the thickest point among LAAWTH around each PV at 12 sites (1–12 o’clock) by a radiologist who did not know clinical information. Reconnected PVs and intact PVs were compared with their LAAWT.
Results: The mean LAAWT was 0.6±0.3 mm. The LAAWTHs at anterior roof (0.75±0.27 mm) of right superior PV (RSPV), posterior side (0.74±0.49 mm) of right inferior PV (RIPV), and posterior side (0.76±0.29 mm) of left PV were the thickest point among LAAWTH around each PV. The left PVs were thicker (0.67±0.24 vs. 0.60±0.25 mm, p<0.001) and had more reconnected PVs (57.1 vs. 50.0%, p<0.009) than right PVs.
Male patients with higher LAAWT (0.65±0.26 vs. 0.58±0.20 mm, p<0.001), and patients with diabetes (0.67±0.28 vs. 0.63±0.24 mm, p<0.025) or heart failure (0.69±0.23 vs. 0.63±0.25 mm, p<0.005) had thicker LAAWT than those without. In contrast, patients with stroke (0.53±0.18 vs. 0.65±0.29 mm, p<0.001) or high
Purpose: We sought to evaluate the agreement between TEE and CTA for mitral valve assessment in any arbitrary plane with high spatial resolution.

Methods: Transoesophageal echocardiography (TEE) is the recommended modality prior to percutaneous edge-to-edge mitral valve repair. Nevertheless, CTA may be used to evaluate mitral valve geometry.

Conclusion: The assessment of the CS with MDCT prior to percutaneous mitral valve annuloplasty is feasible and yields information on the course of the CS as well as specific values for CS dimensions. These values are normally distributed, and they correlate with the LV-EDD in patients with relevant FMR.

Results: Mean LV-EF of all patients was 41±4%, mean LV-EDD was 61±2mm. The CS length ranged between 66 and 131mm (mean 98±4mm, median 94mm), enclosing 38% of the mitral valve circumference on average (range 25–50%). Mean ostial CS diameter was 15±10.6mm (range 9–22mm, median 15mm), and mean distal CS diameter was 4.9±0.2mm (range 3–7mm, median 5mm). In 70% of all patients (n=21) the CS took a course superior to the RCX. There was no difference in mean CS length between men and women (99±6mm vs. 97±4mm, p=0.65), and there was no correlation between LV-EDD or LV-EF and CS length (r=0.11, p=0.6 and r=0.3, p=0.16). However, mean ostial CS diameters varied significantly between men and women (16.5±0.9mm vs. 13.7±0.7mm, p=0.04), whereas distal CS diameters did not (5.3±0.3mm vs. 4.5±0.3mm, p=0.12). LV-EDD correlated with distal CS diameters (r=0.45, p=0.05) and showed a trend for correlation with ostial CS diameters (r=0.4, p=0.07). There was no correlation of LV-EDD with CS diameters [ostial; r=0.17, p=0.47, distal; r=0.3, p=0.16]. However, all CS parameters were normally distributed.

Conclusion: Assessment of the CS with MDCT prior to percutaneous mitral valve annuloplasty is feasible and yields information on the course of the CS as well as specific values for CS dimensions. These values are normally distributed, and they correlate with the LV-EDD in patients with relevant FMR.

Results: RVM fibrosis was observed in 14 subjects (23%) on CT (CTEPH 22%; PAH 29%; P=0.91). CT attenuation of RVM in the late phase was significantly greater in subjects with RVM fibrosis than in those without (P=0.025). ROC curves of CT attenuation of RVM in the early and late phase, and ratio of CT attenuation of RVM in the early phase/late phase showed AUCs of 0.55, 0.70, and 0.65, respectively. The best cutoff points of 79.5 HU (sensitivity of 50% and specificity of 69% for CT attenuation of RVM in the early phase, P=0.59), 99.5 HU (sensitivity of 50% and specificity of 88% for CT attenuation of RVM in the late phase, P=0.025), and 1.41 (sensitivity of 29% and specificity of 94% for ratio of CT attenuation of RVM in the early phase/late phase, P=0.092) were used to distinguish subjects ± RVM fibrosis.

Conclusion: Quantitative measurement of CT attenuation of RVM in the late phase may be able to detect presence of RVM fibrosis in PH subjects.

Results: The mean ostial CS diameter was 15±10.6mm (range 9–22mm, median 15mm), and mean distal CS diameter was 4.9±0.2mm (range 3–7mm, median 5mm). In 70% of all patients (n=21) the CS took a course superior to the RCX. There was no difference in mean CS length between men and women (99±6mm vs. 97±4mm, p=0.65), and there was no correlation between LV-EDD or LV-EF and CS length (r=0.11, p=0.6 and r=0.3, p=0.16). However, mean ostial CS diameters varied significantly between men and women (16.5±0.9mm vs. 13.7±0.7mm, p=0.04), whereas distal CS diameters did not (5.3±0.3mm vs. 4.5±0.3mm, p=0.12). LV-EDD correlated with distal CS diameters (r=0.45, p=0.05) and showed a trend for correlation with ostial CS diameters (r=0.4, p=0.07). There was no correlation of LV-EDD with CS diameters [ostial; r=0.17, p=0.47, distal; r=0.3, p=0.16]. However, all CS parameters were normally distributed.

Conclusion: Assessment of the CS with MDCT prior to percutaneous mitral valve annuloplasty is feasible and yields information on the course of the CS as well as specific values for CS dimensions. These values are normally distributed, and they correlate with the LV-EDD in patients with relevant FMR.

Purpose: Right ventricular myocardial (RVM) fibrosis may be a significant indicator of prognosis in pulmonary hypertension (PH).

Background: Recently, an innovative imaging technique has been developed to display in real time a virtual multi-planar reconstruction obtained from contrast-enhanced

Conclusion: AVAng and RootAng correlate with aortic dilatation patterns and also aortic dissection. These angles may explain the differential shear stresses seen along the 2 curvatures in aortic pathologies.

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Background: Management of adult congenital heart disease (ACHD) patients requires advanced imaging techniques to assess its complex morphological and functional features.

Recently, an innovative imaging technique has been developed to display in real time a virtual multi-planar reconstruction obtained from contrast-enhanced...
Multidetector-computed tomography (MDCT) corresponding to the same cross-sectional image from echocardiography (Smart Fusion, Toshiba). The aim of this study is to assess the usefulness of this fusion imaging in ACHD patients.

Methods: This study consisted of consecutive 46 patients (28 women, 58±16 years with ACHD who underwent TTE and MDCT. All patients underwent echocardiography within a week of MDCT. Both MDCT and echocardiographic images were displayed simultaneously in the same screen side by side and then, MDCT images act in synchronization with echocardiography.

Results: Fusion imaging was safe and feasible in all patients with ACHD. Cardiac chamber size and maximum size of the defect was accurately measured. This integrated fusion imaging also revealed unexpected and incremental findings and exclusively provided correct anatomical classification or clarified suspected abnormal findings on echocardiography.

Example cases (figure): 1. Guidance for Doppler coronary flow assessment. 2. To clarify the etiology of unorinary severe tricuspid regurgitation. 3. To identify anomalous pulmonary venous connection undiagnosed by echocardiography. 4. Assessment of RVOT stenosis; precise location and grade.

Conclusions: This novel cardiac fusion imaging is clinically useful. Especially, integrated anatomical and functional multi-modality imaging provides incremental role over echocardiography in complex anatomy, and allows functional information in ACHD patients.

P4504 | BEDSIDE

Left atrial appendage sizing for percutaneous occlusion with amplatzer cardiac plug: a multimodality imaging approach

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Background: The morphology of the LAA and the LAA ostium are extremely complex and heterogeneous. Accurate sizing of the landing zone is crucial for the optimal choice of the device size. Cardiac CT has been shown to provide accurate measurement of the LAA. Transesophageal echocardiography (TOE) and selective LAA angiography can provide discordant results during the procedure, and there is no consensus about the most reliable imaging modality.

Aim of the study: Compare the sizing of the LAA using a multimodality imaging approach.

Methods and results: We retrospectively included 45 patients (aged 67.6±6.2 years) who underwent LAA occlusion using the Amplatzer® cardiac plug (ACP). Mean diameter of the landing zone (average of the smallest and largest diameters) was determined using the different imaging modalities: MPR for cardiac-CT and 3D TOE, multiple angle view at 0, 45, 90 and 120° using 2D TOE, and monoplanar projection (RAO30° cranial 20°) for angiography. We also compared the mean diameter derived from the area of the landing zone, with the diameter derived from the average of min and max diameters measured by CT.

High intra and inter observer reproducibility were found for diameter (r=0.93 and 0.87, p<0.01 respectively with mean difference of -0.1mm [-1.9; +1.8] and -0.2mm [-2.9; +2.5] respectively) and area measurement (r=0.94 and 0.88, p<0.01 respectively with a mean difference of 0 cm² [-0.15; +0.16] and 0 cm² [-0.9; +0.9], respectively) of the landing zone by CT.

20% mean difference in diameter was weakly correlated with CT (r=0.35, -1.4mm [-5.7; +8.5]).

Conclusions: We found significant variability in the sizing of the LAA landing zone, using different imaging modalities. 3D data set provided by Cardiac-CT and 3D TOE looks interesting to get a complete overview of LAA anatomy. Multiple angle view from 0 to 120° are mandatory when using 2D TOE. Monoplanar LAA selective angiography seems not accurate for LAA sizing and may be avoided when non invasive imaging modalities are available.
P4507 | BEDSIDE

Clinical utility of stress dynamic myocardial perfusion imaging using 256-slice computed tomography detecting myocardial ischemia: comparison with echocardiographic assessment of coronary flow reserve

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Background: Myocardial perfusion imaging using computed tomography (CT) is useful for the evaluation of myocardial ischemia. Using adenosine triphosphate (ATP) stress transluminal Doppler echocardiography, coronary flow velocity reserve (CFVR) ≤2.0 was a promising value to detect myocardial ischemia in left anterior descending coronary artery (LAD) territory.

Purpose: To evaluate the ability of ATP stress dynamic myocardial CT perfusion (CTP) for detecting myocardial ischemia in LAD territory.

Methods: Forty-seven patients with stable angina were prospectively enrolled (mean age 70 years). Myocardial ischemia was assessed from the CTP images using gray and color scale based on the concentration of contrast agent in the myocardium (Figure). LAD bed by CTP was confirmed from three-dimensional fusion imaging with CT angiography and perfusion.

Results: CTP imaging detected myocardial ischemia in the LAD region of 21 patients. The mean CFVR in regions with myocardial ischemia assessed by CTP was lower than in those without myocardial ischemia (1.8 ± 0.5 vs 2.9 ± 0.8, p < 0.01). CTP could diagnose CFVR ≤2.0 with 87.2% diagnostic accuracy (sensitivity 89.5%, specificity 85.7%, positive predictive value 81.0%, negative predictive value 92.3%).

Conclusions: ATP stress CTP imaging adds incremental diagnostic capability to CT angiography in evaluating myocardial ischemia in the LAD region. This method may expand clinical utility to detect ischemic region in whole myocardium compared to echocardiographic CFVR technique.

P4508 | BEDSIDE

First real-world clinical experience with non-invasive fractional flow reserve derived from coronary computed tomography angiography

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Background and introduction: In clinical trials, non-invasive fractional flow reserve derived from standard coronary CT angiography (CTA) datasets (FFRct) has shown superiority to both coronary CTA and invasive coronary angiography for the diagnosis of lesion-specific ischemia using FFR as the reference standard.

Purpose: We aimed to evaluate the diagnostic performance of FFRct in a real-world clinical setting.

Methods: FFRct analysis was performed in patients with atypical angina and intermediate pretest risk of coronary artery disease and intermediate coronary stenosis (40–70%) at coronary CTA. Routine 82Rb PET (positive if any regional perfusion <1.6 ml/g/min or regional tracer distribution significantly altered between rest and adenosine-stress) was performed in a subset of the study cohort. FFRct/FFR ≤0.80 was considered diagnostic of ischemia. FFR was performed if FFRct was <0.80 or 82Rb PET was positive.

Results: Between April and November 2014, 123 consecutive patients were enrolled (mean age 60±12 years, 67% males, mean BMI 29 (range 46–76), mean Agatston score 91 (range 0–1133; 23% with score 0). FFRct analysis could not be performed in 4 (3%) patients. In 25 (21%) patients FFRct was ≤0.80. In 6 out of 106 (6%) patients the 82Rb PET result was positive, of whom FFRct ≤0.80 in 5 (83%). FFR was performed in 22 patients (27 vessels) with FFRct ≤0.80 (Table). In 20 of these, 82Rb PET was performed (Table). Mean (range) FFRct in false positive vessels was 0.78 (0.74–0.80).

Conclusions: FFRct is an efficient gatekeeper to the cath lab in stable patients with intermediate coronary stenosis. FFRct and PET results show significant discordance. The relative diagnostic value of FFRct and conventional ischemia testing needs further delineation.

P4509 | BEDSIDE

Appropriate and inappropriate use of cardiac computed tomography in a large volume centre

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Introduction: Appropriateness criteria have been proposed as a way to promote the rational use of several tests in Cardiology. The purpose of this study was to assess the appropriateness of cardiac CT according to international criteria in a large volume centre.

Methods: The clinical data from 1868 consecutive patients (1046 men, age 60±12 years) undergoing cardiac CT between May 2012 and May 2014 were collected in a prospective registry. The indication and appropriateness of each test were categorized according to the 2010 Appropriateness Criteria issued by the Society for Cardiovascular Computed Tomography (SCCT).

Results: The most frequent indications for cardiac CT were suspected coronary artery disease (CAD) in patients with a previous positive, inconclusive or doubtful exercise ECG (37%, n=694), suspected CAD with no previous testing (16%, n=269), and pre-ablation of atrial fibrillation (13%, n=236) - Figure. Globally, the indications for cardiac CT were classified as appropriate in 64% of cases, inappropriate in 12%, and uncertain in 11%. A further 12% could not be classified according to the SCCT criteria.

The most frequent reasons for inappropriate referral were an exercise ECG with low risk findings (6%, n=110), asymptomatic individuals with low or intermediate cardiovascular risk (2%, n=40), and symptomatic patients with coronary stents <3mm in diameter (1%, n=21). There were no significant differences in the proportion of inappropriate test results in relation to referring physician’s specialty and type of institution.

Conclusion: Even though there is room for improvement, only a small proportion of cardiac CTs were considered inappropriate, dismissing concerns that this test might be largely misused in clinical practice.

P4510 | BEDSIDE

Coronary CT angiography in patients with low-risk acute chest pain: quantitative analysis of plaque parameters

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Background: Coronary CT angiography (CTA) is recommended in the workup of patients presenting to the emergency department (ED) with low to intermediate risk acute chest pain.

Purpose: We analyzed CT data for quantitative plaque parameters between patients with non-obstructive and invasively confirmed obstructive coronary artery disease (CAD).

Methods: Coronary CTA data sets of consecutive 151 ED patients (mean patient age 51±14 years, 67% males) without known CAD presenting with acute chest pain in 5 (83%) patients were recognized and measured myocardial fractional flow reserve (FFR). There were 13 stenotic lesions with FFR below 0.8 which were considered coronary significant stenosis. Sensitivity, specificity, positive predictive value, and negative predictive value of the CT myocardium image analysis to identify coronary significant stenosis with use of FFR as the standard reference were 92%, 90%, 92%, and 91%, respectively.

Conclusions: FFR is an efficient gatekeeper to the cath lab in stable patients with intermediate coronary stenosis. FFRct and PET results show significant discordance. The relative diagnostic value of FFRct and conventional ischemia testing needs further delineation.
Injury after CTO revascularization.

In this study, we investigated 111 non-calculated or mild calcified lesions from 103 patients using 64-slice MDCT before percutaneous coronary intervention (PCI) and assessed by IVUS. EAT thickness was measured using the short-axis view of a curved multiplanar reconstruction image of coronary CT and defined as the sum of the peripheral thickness of the visceral layer of the pericardium to the coronary artery and the surface of the heart to the coronary artery. EAT thickness ratio was calculated as EAT thickness across the obstructive lesion divided by EAT thickness across the reference vessels and was assigned into two groups: I (<112%) or II (≥112%) EAT thickness ratio groups.

Conclusions: There were no significant differences in the baseline clinical characteristics between the two groups. IVUS analysis showed that the group II had a higher prevalence of attenuated plaque (45.3% vs. 20.7%, p=0.008) and a higher percentage of plaque burden (79.9% vs. 76.2%, p=0.004). From coronary CT analysis, the group II had a higher prevalence of napkin-ring sign (36.9% vs. 17.2%, p=0.01) and lower plaque hourglass units (48.9 vs. 63.4, p=0.009). Patients of the group II who had both MDCT-detected napkin-ring sign and IVUS-detected EAT thickness ratio ≥112% had a higher prevalence of transient slow flow phenomenon during PCI (47.1% vs. 2.7%, p=0.0002).

Conclusions: A large EAT thickness ratio as measured by multidetector computed tomography has a significant association with vulnerable plaques. MDCT and IVUS can provide important information to predict slow flow phenomenon during PCI.
lack detection of functional significance. Fractional flow reserve (FFR) determined by invasive angiography is useful in prediction of functional significant stenosis.

**Purpose:** We investigated the relationships lesion morphologies assessed by CCT and FFR values.

**Methods:** We assessed 58 coronary lesions with 54 patients undergoing CCT and invasive angiography with FFR measurement. Lesion length, minimum lumen diameter, (MLD), minimum lumen area (MLA), % area stenosis, lesion vessel area, plaque burden [vessel-lumen area]/vessel area < 100, remodeling index (RI), and minimum CT-density within the plaque at the culprit site were measured by CCT. Optimal cutoff values of CCT parameters for prediction of functional significant coronary lesions (FFR ≤ 0.75) were calculated.

**Results:** FFR was < 0.75 in 12 lesions (20.7%). Lesions with FFR ≤ 0.75 showed smaller MLD (mm) (2.7 ± 0.8 vs. 0.75 ≤ 0.05), smaller MLA (mm²) (5.7 ± 0.3 vs. 0.75 ≤ 0.05), larger plaque burden (%) (65.17 ± 0.05 vs. 56.85 ± 0.05, P = 0.12), larger RI (1.19 ± 0.05 vs. 0.98 ± 0.05, P = 0.06), and lower CT-density (HU) (29.9 ± 49.45 vs. 45.31 ± 63), respectively. Those without cutoff had no statistically significant difference between the two groups. Furthermore, the logistic regression analysis showed that FFR ≤ 0.75 was associated with 1.9 mm MLD, 3.5 mm² MLA, 58% plaque burden, 0.83 RI, and 29 HU for minimum CT-density. The stepwise multiple regression analysis showed that MLD [3.5 mm² (odds ratio 39.4, 95% confidence intervals 3.12–497.38, P = 0.005) and minimum CT-density [<= 29 HU] identified by CCT (odds ratio 13.4, 95% confidence intervals 1.36–132.29, P = 0.03) were independent predictors for FFR ≤ 0.75.

**Conclusion:** Noninvasive assessment by CCT measurements, not only lesion morphologies but also plaque quality, may be useful to identify functionally significant coronary lesions.

**EXCITATION-CONTRACTION COUPLING AND CONTRACTILE REMODELLING**

P4515 | BENCH

Rosuvastatin attenuates the tgf-beta1-induced proliferation and differentiation of cardiac fibroblast through RUNX3 activation

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**Background:** Rosuvastatin has been reported to play a role in cardiac remodeling, which is related to the proliferation and differentiation of cardiac fibroblasts (CFs). However, little is known about the effect of rosuvastatin on CFs.

**Purpose:** The study aimed to investigate the effect of rosuvastatin on the proliferation and differentiation of CFs induced by TGF-beta1, and the potential role of RUNX3 in the process.

**Methods:** CFs, isolated from Sprague–Dawley rats, were induced by TGF-beta1 treatment for 24h. RUNX3 down- or up-regulation in CFs was performed by small RNA interference (RNAi) or lentiviral transfection (LT), respectively. CFs, with or without regulation, were cultured with rosuvastatin or PBS followed by TGF-beta1 stimulation. The proliferation of CFs was measured by BrdU, MTT assays and flow cytometry. The differentiation of CFs was analyzed by expression of -smooth muscle-actin (α-SMA).

**Results:** Rosuvastatin inhibited the expression of α-SMA in CFs. Overexpression of RUNX3 induced CFs proliferation by rosuvastatin were observed by both BrdU assay and α-SMA expression level. However, little is known about the effect of rosuvastatin on CFs.

**Conclusion:** Rosuvastatin inhibits the proliferation and differentiation of CFs in response to TGF-beta1 stimulation by activating the RUNX3 and repressing α-SMA expression, with the subsequent down-regulation of α-catenin/catenin D1 cascade.

P4516 | BENCH

Mitochondria play an important role in the regulation of the nuclear Ca concentration

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**Background and purpose:** Cardiac myocytes release huge amounts of Ca for each contraction. In addition, Ca within myocytes is an important second messenger for important cellular processes as the regulation of nuclear gene transcription, apoptosis and mitochondrial metabolism. Mitochondria are able to take up Ca. Therefore, they are able to shape the cytosolic Ca transient. The amplitude of nuclear Ca transients is an important factor for the regulation of gene transcription. It consists of a passive component of Ca diffusion from the cytosol and an active component through Ca release in the nucleus via IP3 receptors. Here, we investigated whether mitochondria, by Ca buffering and shaping of the passive component of the nuclear Ca transient, are able to influence the nuclear Ca transient and thus nuclear gene transcription. To answer these questions mitochondrial, nuclear and cytosolic Ca was measured using confocal microscopy.

**Results:** The treatment of electrically stimulated cardiac myocytes with blockers of mitochondrial Ca uptake (Ru360: mitochondrial Ca unporter (mCU), dantrolene: mitochondrial RYR (mRYR)) alone did not alter mitochondrial Ca content. Before, we were able to show that IP3 mediated Ca release from the SR resulted in an increase in mitochondrial Ca. Thus, we studied the myocytes with mitochondrial blockers added to the bathing solution. Addition of Ru360 and dantrolene to electrically stimulated myocytes treated with angII resulted in an increase of cytosolic and nuclear Ca concentration. Interestingly when dantrolene was added, the nuclear Ca content increased proportionally compared to the cytosolic Ca concentration, indicating that mitochondrial Ca uptake through the mRYR1 is somehow relevant for the regulation of Ca concentration, despite their involvement in diabetic microvascular complications.

**Conclusion:** Mitochondrial Ca uptake is an important factor for the fine tuning of the cytosolic Ca transient. For the regulation of the nuclear Ca transient, mitochondrial Ca uptake via the mRYR1 plays an important role.

P4517 | BENCH

The role of nitric oxide synthase (NOS) and its essential cofactor tetrahydrobiopterin (BH4) in diabetic cardiomyopathy

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**Background:** Little evidence has emerged to demonstrate whether NOS dysfunction and a reduction in the tetrahydrobiopterin (BH4) cofactor play a role in the pathology of "diabetic cardiomyopathy", despite their involvement in diabetic microvascular complications.

**Purpose:** To investigate if oxidative stress, characteristic of diabetic vascular dysfunction, also contributes to the phenotype of type 1 diabetic cardiomyopathy, and explore the mechanisms underlying the potential benefits of local BH4 augmentation.

**Methods:** Type 1 diabetes was induced in male mice by daily streptozotocin injection (42–45mg/kg, 5 consecutive days). To enhance local BH4 and therefore NOS activity, transgenic mice expressing BH4 were generated. In contrast to mice with the wild-type allele and no BH4, mice with the BH4 expressing allele displayed prolonged relaxation. However, both the cardiomyocyte and global cardiac dysfunction were prevented by mGCH1 overexpression. Unlike isolated aortas from diabetic mice, diastolic dysfunction was not associated with increased oxidative stress, as evidenced by unchanged superoxide production and no reduction in BH4 or NO bioavailability. Unchanged expression profiles excluded the possibility of either Ca2+-handling protein downregulation or inflammation as a basis for the cardiomyopathy, while the absence of fibrosis and lipid deposition also discounted structural remodelling. Reductions in LV mitochondrial ATP flux did however demonstrate altered energy metabolism in WT diabetic hearts, which, crucially, was prevented in mGCH1-Tg mice. Metabolic changes were accompanied by increased expression of UCP3 in WT diabetic mice and the GLUT1 transporter in both mGCH1-Tg groups. Interestingly, protein changes were also evident after only 4 weeks of diabetes, prior to the development of any cardiomyopathy.

**Conclusions:** We propose that impaired myocardial metabolism, and not oxidative stress, precedes and underlies the later development of LV diastolic dysfunction observed in type 1 diabetes. Moreover, we demonstrate that local augmentation of BH4 prevents the cardiomyopathy, potentially through improving energy availability.

P4518 | BENCH

BMP7 ameliorate cardiac fibrosis through inhibiting endothelial-to-mesenchymal transition in viral cardiomyopathy

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**Background:** Emerging evidence has indicated that endothelial-to-mesenchymal
Effect of adenosine agonists and antagonist on infarct size and haemodynamics in MI rats

<table>
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Effect of adenosine agonists and antagonist on infarct size and haemodynamics in MI rats.
P4522 | BENCH
Effect of remote ischemic preconditioning on platelet activation and reactivity induced by percutaneous coronary intervention
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Background: In this study we assessed whether remote ischemic preconditioning (RIPC) may reduce platelet activation induced by coronary angiography (CA) and for percutaneous coronary interventions (PCI).

Methods: We studied 30 patients (67±11 years, 27 males) undergoing CA for suspect stable angina. Patients received ASA (100 mg) and clopidogrel (300 mg) short episodes of forearm ischemia, or sham forearm ischemia (controls), immediately before CA. Blood samples were collected at baseline at the end of the procedure and 24 hours later. Platelet activation was assessed by flow cytometry by measuring monocyte-platelet aggregates (MPAs), platelet CD41 and CD62 in the platelet gate. ADP stimulation increased platelet variables at baseline, but did not further increase platelet activation during the procedure in both groups. PCIs were performed in 10 patients (6 in the RIPC group and 4 in controls), but had no effect on platelet activation compared to CA alone.

Results: Basal values of platelet variables were similar in the 2 groups. Platelet activation increased during the procedure in both groups, persisting after 24 hours. However, compared to controls, RIPC patients showed a lower increase in platelet variables, including MPAs (p<0.009; figure), CD41 (p=0.005) and CD62 (p<0.05) in the MPA gate and CD41 (p<0.05) and CD62 (p=0.014) in the platelet gate. ADP increased platelet variables at baseline, but did not further increase platelet activation during the procedure in both groups. PCIs were performed in 10 patients (6 in the RIPC group and 4 in controls), but had no effect on platelet activation compared to CA alone.

Conclusions: Preventive RIPC reduces the increase of platelet activation during CA, with or without PCIs. The lack of significant effects by RIPC on platelet response to ADP stimulation during CA/PCI in this study was likely related to the administration of an ADP antagonist (clopidogrel) to all patients.

P4523 | BENCH
Cardioprotective effects of dipeptidyl peptidase-4 (DPP-4) inhibitors independently of DPP-4
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Background: Dipeptidyl peptidase-4 (DPP-4) inhibitors, novel oral hypoglycemic agents, not only improve impaired glucose tolerance in diabetes, but also have pleiotropic extra-pancreatic effects such as preconditioning effect for myocardial ischemia-reperfusion injury. We hypothesized that some beneficial extra-pancreatic effects of DPP-4 inhibitors may be brought independently of DPP-4.

Purpose: We investigated the anti-remodeling effects of DPP-4 inhibitors after myocardial infarction (MI) by use of DPP-4-deficient rats.

Methods: MI was induced by ligation of coronary artery in 8-week old Fischer 344 rats with inactivating mutation of DPP-4. Control (FC) rats were subjected to sham operation. After MI induction, rats were randomly separated into three groups, which were orally administered DPP-4 inhibitor, sitagliptin (FS; 50 mg/kg/day), linagliptin (FL; 5 mg/kg/day), or vehicle (FB) in drinking water for 4 weeks. After 4 weeks of administration, a transverse echocardiographic study was performed to estimate left ventricular (LV) function. MI-induced interstitial fibrosis in marginal region of infarction was assessed by Sirius red staining. Intestinal macrophage infiltration was assessed by immunohistochemical staining with F4/80. Protein and gene expression levels in marginal area of infarction were evaluated by western blotting and quantitative RT-PCR.

Results: Administration of both DPP-4 inhibitors did not affect hemodynamic status including blood pressure and heart rate, body weight, and infarct size. Although LV systolic function such as ejection fraction was similar among the FV, FS and FL groups, LV diastolic function such as E/e’ was significantly improved in the FL group compared with the FV group. LV diastolic function in the FS group also tended to be increased. Intestinal fibrosis in marginal region and macrophage infiltration were significantly lower in the FS and FL groups than those in the FV group. Fibrosis-related gene expressions, such as collagen I and transforming growth factor-beta 1 were significantly suppressed in marginal area of the FL and FS rats compared with the FV rats. Inflammation-related expressions tended to be suppressed in the FL rats compared with the FV rats.

Conclusion: Administration of DPP-4 inhibitors attenuated MI-induced cardiac remodeling in DPP-4 deficient rats via DPP-4-independent pathways.
Cardioprotective effect of inorganic phosphate in a
P4528 | BENCH
Urocortin-1 preserve XIAP and CD40-ligand to reduce
ischemia/reperfusion-induced cardiac myocyte apoptosis via
the activation of ERK1/2 through EPAC
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Background: Urocortin-1 (Ucn-1) is a potent endogenous peptide that protects
heart from ischemia and reperfusion (I/R) injuries. Ucn-1 is known to improve
post-ischemic cardiac performances, which include recovery of heart contraction,
 prevention from intracellular Ca2+ overload and cardiac cell death. However, Ucn-1
role in the transcription of specific genes related to survival signaling pathway
has not been fully defined.

Purpose: The aim of this study was to determine the pathways implicated in the
improvement of cardiomyocytes survival induced by Ucn-1.

Methods: To determine hemodynamic parameters, rats were perfused in the
isolated Langendorff system and were exposed to 40 min of ischemia followed by
80 min of reperfusion in the presence or not of Ucn-1. The signaling pathways involved
in Ucn-1 effects were examined by the use of inhibitors of PKA, Epac and the Extra-
sential Signal–Regulated Kinases 1/2 (ERK1/2). Furthermore, we used isolated
cardiac myocyte subcultured from ischemia followed by 18 h of reperfusion to
study the cell survival and apoptosis. Annexin-V/PI staining, microarray, west-
ern blotting and qRT-PCR approaches were used to explore the implication of
Epac, ERK1/2, BAD, CD40-ligand (CD40-lg) or X-linked inhibitor (XIAP) in Ucn-1
regulation of cardiac myocyte survival.

Results: We found that Ucn1 application before ischemia and at the onset of
reperfusion fully recovered heart contractility and prevented the increase of
Left End Ventricular Diastolic Pressure (LVEDP). These beneficial protective effects
were independent of protein kinase A (PKA) but were significantly reduced when
hearts were co-treated with the inhibitors of Epac and ERK 1/2. Moreover, Ucn-1
protected cardiac myocyte from reoxygenation injury, as evidenced by the aug-
mentation of cell survival and the decrease of cell necrosis. Ucn-1 stimulated the
increase of the expression of BAD, CD40-lg and XIAP proteins that are implicated
in apoptosis and cell survival. Finally, we determined that Ucn-1 regulated CD40-
lg and XIAP through the activation of ERK1/2 signaling pathway.

Conclusions: Our data confirm that Ucn-1 efficiently preserved hearts hemody-
namic parameters and protected heart and cardiac myocyte from I/R damage by
the regulation of signaling pathways involved in cell survival and apoptosis which
improve Bad expression independently of ERK1/2 signaling pathway.

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0041; P10-1082-2012; P10-CVI-6095

Cardiovascular mortality is a major driver of global mortality.
P4530 | BENCH
Physical exercise exerts beneficial effects on walking capacity and polarization state of circulating monocytes and muscular macrophages in a mouse model of intermittent claudication
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Background and introduction: Physical exercise (PE) therapy is indicated to improve walking capacity in patients with intermittent claudication (IC) due to atherosclerotic stenosis of lower extremity arteries. The effect of PE on arterial stenosis on walking capacity is unknown.

Purpose: To determine the protective effects of PE prior to peripheral arterial stenosis in a mouse model of IC.

Methods: Atherosclerotic C57BL/6 ApoE−/− mice were allowed free access to an voluntary wheel running (WR; daily average running distance: 4.2±1.6 km) or remained sedentary (SED) for 5 weeks before unilateral iliac artery ligation. Thereafter, two of the groups were kept sedentary for 5 weeks. Maximal running distance and time until exhaustion were determined using a treadmill running test. Hindlimb perfusion was assessed using laser Doppler imaging. Real-time RT-PCR was used to quantify inflammatory phenotype (M1 versus anti-inflammatory M2 macrophages) in hindlimb quadriceps muscle. Flow cytometry was employed to analyse blood circulating monocyte subsets (Ly6Chigh inflammatory macrophages versus Ly6Clow resident monocytes).

Results: Maximal walking distance and time were significantly improved by 23% and 13%, respectively, in WR mice compared to SED mice at 5 weeks post-arterial ligation. Compared to SED mice, ischemic hindlimb perfusion in WR mice was significantly increased at week 3 (40%), week 4 (50%) and week 5 (28%) post-arterial ligation. In WR mice, mRNA expression of M2 marker CD206 in ischemic muscle significantly increased (1.7-fold versus non-ischemic muscle at week 5 post-arterial ligation) whereas no significant change was observed in SED mice. M1 marker CD11c mRNA expression did not significantly differ between ischemic and non-ischemic muscle both in WR and SED mice. WR significantly increased the resident monocyte Ly6Clow subset in the circulation (45% versus SED mice at 5 weeks post-arterial ligation).

Conclusion: PE prior to peripheral arterial stenosis ameliorates impaired walking capacity subsequent to arterial stenosis. Underlying potential mechanisms include increased production of the ischemic hindlimb perfusion and a positive effect on circulating monocytes and local muscular macrophages polarization state. Our findings support the role of PE in primary prevention of IC.

P4532 | BEDSIDE
Cystatin C is not causally associated with diabetes or the metabolic syndrome
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Background: The prevalence of incident diabetes is 3.6% per year in patients with established cardiovascular disease (CVD). The association between high cystatin C and the development of diabetes is not well understood. Our recent studies indicate that NADPH oxidase (Nox) proteins, specifically Nox4, augment cardiac function and metabolic effects. Here, we examine whether Nox4 contributes to the development of diabetes.

Methods: To identify pathways that might be driving Nox4-dependent effects on substrate handling we performed metabolomics on heart tissue from cardiac-targeted Nox4-overexpressing mice, Nox2-overexpressing mice and controls using 2D-DIGE.

Results: Proteomics identified glycolysis and fatty acid oxidation as the most enriched pathways altered by Nox4. Metabolomics also indicated significant differences in metabolites related to these pathways (e.g. 2.2 fold increase in acetate:carbonatine concentration, p=0.002). Nox4 hearts demonstrated a significantly increased capacity for FAO compared to wild-type hearts (3.6 fold increase, p=0.01), which was sustained under pressure-overload. Cardiac energetics under basal or pressure-overload indicated that a reliance on FAO was not detrimental to cardiac function. Extracellular flux analyses confirmed the Nox4-dependent effects in augmenting FAO in isolated cardiomyocytes.

Conclusion: Nox4 is a master regulator of metabolic specificity, especially enhancing FAO in the murine heart. This may help to explain the cardioprotective effects of Nox4 but also provides insight into novel ROS-mediated mechanisms that can regulate metabolism.

P4533 | BEDSIDE
Platelet to lymphocyte ratio as a novel indicator of inflammation associated with the presence and severity of metabolic syndrome
M. Akboga1, U. Canpolat1, M. Yuksel2, C. Yaya1, O. Turak1, O. Ozek1, T. Topaloglu1, D. Aras1, D. Ozturk1, A. Ali1

Background: The platelet to lymphocyte ratio (PLR) has been proposed as a marker to identify inflammation in the presence of metabolic syndrome (MetS). While, recent studies suggest that sCD40L and Th17 cells may play key roles in the pathogenesis of MetS.

Methods: To examine the association between high levels of laminin and increased risk of future development of MetS, we estimated the effect size of the strongest genome wide association study derived cystatin C SNP (major allele of rs13038305) on plasma cystatin C and incidence of the metabolic syndrome (MetS) among the first 2,369 subjects who participated in the re-examination study of the population-based Malmö and Diet Cancer Cardiovascular cohort (MDD-C-re-exam).

Results: The association of the rs13038305 and incident MetS (610 cases of MetS and 2300 controls) was similarly investigated in the whole MDD-C-re-exam. We also attempted to replicate our previously shown association of cystatin C with incident MetS in subjects from the MDD-C-re-exam (147 cases and 709 controls) that were not included in our previous report.

Conclusion: We were able to replicate our previously shown association between high levels of cystatin C and increased risk of future development of MetS. However, a causal involvement of cystatin C in the aetiology of MetS or diabetes seems unlikely since genetic elevation of plasma cystatin C was not significantly related to incidence of these diseases.

Acknowledgement/Funding: Supported by grants from the Swedish Medical Research Council, the Swedish Heart and Lung Foundation.
Results: MetS (+) group revealed significantly higher PLR and C-reactive protein (CRP) levels as compared to MetS (−) group (p < 0.05). There was a graded relationship between number of MetS components and PLR (p < 0.05). Also, PLR was positively correlated with CRP level (r = 0.163, p < 0.001). In multivariate regression analysis, PLR [1.121 (1.113–1.135), p < 0.001], CRP [1.044 (1.029–1.060), p < 0.001] and age [1.030 (1.017–1.043), p < 0.001] were remained as independent predictors for the presence of MetS.

Conclusion: Our findings showed that increased PLR was significantly associated with both the presence and severity of MetS which was linked to systemic inflammation on the basis of correlation between PLR and CRP. As PLR is an easily available, simple and cheap indirect indicator of inflammation, it can be used in clinical practice as a predictor of MetS.

P4534 | BEDSIDE
Increased serum YKL-40 is a novel marker of metabolic syndrome in adult patients
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Background: Metabolic syndrome (MS) is defined by a cluster of interdependent physiological, biochemical and clinical risk factors and linked to a state of chronic low grade inflammation. YKL-40 is known as an inflammatory glycoprotein which is secreted by various cell lines during inflammation. Thus, we aimed to assess the association of serum YKL-40 levels with the presence and severity of MS.

Methods: In this cross-sectional study, a total 190 consecutive patients [n=124 MS present and n=66 MS absent] were enrolled. MS was defined according to NCEP-ATP III criteria. Serum YKL-40 and hs-CRP levels were measured for all participants. Independent predictors of MS were determined by logistic regression analysis.

Results: Serum YKL-40, hs-CRP and white blood cell count were significantly higher in the MS present group (p < 0.05). There was a graded relationship between increasing number of MS components and serum YKL-40 level (p < 0.05). Also, serum YKL-40 level was positively correlated with hs-CRP level (r = 0.431, p < 0.001) and white blood cell count (r = 0.240, p = 0.001). In multivariable regression analysis, serum YKL-40 level [1.033 (1.020–1.047), p < 0.001] and age [1.030 (1.017–1.043), p < 0.001] were remained as independent predictors for the presence of MS.

Conclusion: In this study, we demonstrated that serum YKL-40 level was significantly associated with the presence of MS. Those findings may implicate that, serum YKL-40 may be a novel and useful indicator for MS.

P4535 | BENCH
Factor Xa inhibits brown adipose tissue function and induces systemic metabolic dysfunction in obesity
Y. Hayashi1, I. Shimizu2, Y. Yoshida2, M. Suda1, R. Ikegami1, G. Katsumi1, H. Kayamori1, S. Jiao1, T. Minamino1, H. Pasaoglu3, D. Aras1, Y. Tayfı2, A. Abacı1, H. Yuksel1, I. Tavıl1, A. Aras1, Y. Tavıl2, A. Abaci2, I. Tavıl1, A. Aras1

Background: Metabolic syndrome (MS) is defined by a cluster of interdependent physiological, biochemical and clinical risk factors and linked to a state of chronic low grade inflammation. YKL-40 is known as an inflammatory glycoprotein which is secreted by various cell lines during inflammation. Thus, we aimed to assess the association of serum YKL-40 levels with the presence and severity of MS.

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Results: Serum YKL-40, hs-CRP and white blood cell count were significantly higher in the MS present group (p < 0.05). There was a graded relationship between increasing number of MS components and serum YKL-40 level (p < 0.05). Also, serum YKL-40 level was positively correlated with hs-CRP level (r = 0.431, p < 0.001) and white blood cell count (r = 0.240, p = 0.001). In multivariable regression analysis, serum YKL-40 level [1.033 (1.020–1.047), p < 0.001] and age [1.030 (1.017–1.043), p < 0.001] were remained as independent predictors for the presence of MS.

Conclusion: In this study, we demonstrated that serum YKL-40 level was significantly associated with the presence of MS. Those findings may implicate that, serum YKL-40 may be a novel and useful indicator for MS.

P4536 | BENCH
The phosphodiesterase-5 inhibitor vardenafil protects against diabetic cardiomyopathy in type-2 diabetes mellitus
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Purpose: Diabetes mellitus (DM) is associated with a special heart disease, termed diabetic cardiomyopathy. The pathological role of cyclic guanosine monophosphate (cGMP) signalling has been intensively investigated in DM. Tardanallin induced the phosphodiesterase-5 (PDE5) inhibition, which is known to decrease the breakdown of cGMP. Vardenafil, an orally availableselective PDE5 inhibitor, has recently been shown to exert cytoprotective effects. We investigated the effect of chronic inhibition of PDE5 by vardenafil in type-2 DM related cardiomyopathy.

Methods: For type-2 DM Zucker Diabetic Fatty (ZDF; homozygous recessive diabetes [fa/fa]) rats were used. Heterozygous (fa/+) or homozygous dominant (+/+) ZDF rats served as controls. Animals received either vehicle (ZDF, ZDF) or 10mg/kg BW vardenafil per os (ZDFVard, ZDFVard) from 7 to 32 weeks of age. Cardiac morphology was followed by echocardiography. Left ventricular (LV) function was assessed using a pressure-volume (PV) conductance microcatheter system. Gene expression analysis of atrial natriuretic factor (ANF; qRT-PCR), cardiomycyte diameter/ribia length (CD/TL) and Masson’s staining (fibrosis score (FS)) were used to probe pathological myocardial hypertrophy.

Results: Cardiac hypertrophy (echocardiography: LV anterior wall thickness in systole (LV/PAW): 2.81±0.1 mm; relative wall thickness (RWT): 0.49±0.02; LV mass/TL: 0.30±0.01 g/cm; CD/TL: 3.53±0.02 μm; ANF: 3.04±0.26 vs ZDF (LV/PAW): 2.53±0.04 mm; RWT: 0.43±0.02; LV mass/TL: 0.23±0.004 g/cm; CD/TL: 3.93±0.02 μm; ANF: 0.92±0.17); p < 0.001, and fibrosis score (FS): 1.05±0.09 vs ZDF (0.57±0.13); p < 0.05) have been observed in ZDF. Drug treatment significantly decreased myocardial hypertrophy and fibrosis (LV/PAW: 2.47±0.05 mm; CD/TL: 3.15±0.02; ANF: 1.39±0.21; FS: 0.59±0.08 vs ZDF; p < 0.05) in DM. PV analysis showed impaired diastolic function and increased cardiac stiffness (time constant of LV pressure decay (τl): 8.18±0.13 ms; EDPVR: 0.045±0.003 mmHg/ml; p < 0.05) while contractility parameters and blood pressure remained unchanged in ZDF. Vardenafil improved diastolic parameters (τl: 8.62±0.34 ms; EDPVR: 0.062±0.006 mmHg/ml vs ZDF; p < 0.05). Vardenafil did not have effect in ZDFL.

Conclusions: We reported that chronic administration of vardenafil prevents DM associated myocardial complications. PDE5 inhibition might be an important target to improve the cardiovascular outcome in diabetic patients in the future.
Peripheral gamma-aminobutyric acid (GABA) signaling in brown adipose tissue induces metabolic dysfunction in obesity

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Accumulating evidence suggests that adult humans possess active brown adipose tissue (BAT) that may contribute significantly to systemic metabolism because of its high energy consumption capacity. Recently, we demonstrated that metabolic stress induces BAT hypoxia, inhibits mitochondrial function and is causal for the development of BAT “whitening” and systemic metabolic dysfunc-

tion in murine obese models. Various neurotransmitters are known to be involved in the maintenance of BAT homeostasis. Among them, the gamma-aminobutyric acid (GABA) signaling in the central nervous system is well accepted to have anti-

obesity effects through the activation of the sympathetic nervous system. Here we show the previously unknown role of peripheral GABA signaling in the develop-

ment of systemic metabolic dysfunction in obesity.

We generated an obese model by imposing a high fat/high sucrose (HFHS) diet on C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant in-
crease in the BAT GABA level in the dietary obese model. Addition of GABA into drinking water led to a marked increase of body weight, induced BAT whitening, and mitochondrial dysfunction in the obese mice. Mitochondrial calcium is impor-
tant for the maintenance of mitochondrial homeostasis, however calcium overload is reported to inhibit mitochondrial function. Treatment of BAT cells with GABA markedly increased mitochondrial calcium level, promoted the production of re-
active oxygen species (ROS) and inhibited mitochondrial respiration. These results indicate that peripheral GABA contributes to the development of systemic metabolic dysfunction by inhibiting BAT function in obesity. The inhibition of pe-

ripheral GABA signaling would become a new therapeutic target for obesity and diabetes.

Purpose: We hypothesized that chronic VNS provides beneficial effects not only on glycemic control, but also on cardioprotection by exerting anti-apoptosis, anti-

oxidative effect and cardiac mitochondrial protection.

Methods: Thirty-six rats were fed with high-fat diet for 12 weeks. Then, all rats were divided into Sham and VNS groups (n=18/group). VNS (20 Hz, 500–0.5 mA pulse width, 0.5–0.75 mA, 14-s ON time and 48-s OFF time) was applied for 12 weeks. Blood samplings were collected for determining metabolic parameters. At the end, the heart was removed for deter-

mination of apoptosis and cardiac mitochondrial function.

Results: Chronic VNS for 12 weeks improved insulin sensitivity, increased %farc-
tion of glucose-stimulated 2-deoxy-D-1H [F] glucose uptake. VNS significantly reduced cardiac ROS production, mitochondrial depolarization and swelling, compared with sham group.

Conclusion: Chronic VNS therapy exerts effective glycemic control and improves left ventricular contractile function via its ability to normalize blood glucose and insulin levels, and cardiac mitochondrial dysfunction.

Acknowledgement/Funding: A NIDDK Research Chair Grant (NC), the Thai-
land Research Fund RTA5850006 (NC), BRG5780016 (SC), TRG5780002 (SK), CMU Center of Excellence Award (NC)

Intercellular communication between chondromodifying enzymes SUV39H1, SRC-1 and JMDJ2C triggers redox signalling and vascular dysfunction in obesity

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Background: Oxidative stress is a prominent feature of cardiometabolic distur-

bances leading to endothelial dysfunction and atherosclerosis. Understanding re-

dox signalling in the context of metabolic disease is of paramount importance for the development of mechanisms-based therapeutic strategies. Adverse chro-

matin remodelling is emerging as a key driver of vascular damage and may play a role in this setting.

Purpose: In the present study we investigate whether epigenetic cues are in-

volved in obesity-related vascular disease phenotype.

Methods: Small visceral fat arteries (SVFA) were isolated from 20 obese and 20 age-matched healthy subjects (age 48.5±9.6 years, p=NS, respectively). Expression profile of chondromodifying enzymes was performed by real-time PCR array in SVFA, and expressed as fold change (FC) vs. controls. Mitochondrial calcium was measured upon 0.5-uM (FC) and endothelial calcium-dependent relaxations to acetylcholine (Ach, 10–9 to 10–4 mol/L) were determined by ESR spectroscopy and organ chamber experiments, respectively. Chondrom immunoprecipitation (ChIP) was employed to study histone modifications. Mechanistic studies were performed in genetically obese mice (Lept/Ob/Ob) and in mice infected with suicide vector (SUV39H1−/−), according to the principles of laboratory animal care.

Results: Mitochondrial oxidative stress and endothelial dysfunction were ob-

served in SVFA from obese as compared to controls. Vascular gene profiling of chondromodifying enzymes revealed a significant dysregulation of methyltrans-

ferase SUV39H1 (FC=6.7, p<0.01), acetyltransferase SRC-1 (FC=3.0, p<0.01) and demethylase JMDJ2C (FC=2.7, p<0.01) in SVFA from obese as compared to controls. These changes favoured demethylation as well as increased acetylation at lysine 9 of histone 3 (H3K9), leading to chromatin accessibility and enhanced transcription of the mitochondrial adaptor p66Shc, a key driver of vascular oxida-

tive stress. Interestingly, reprogramming of SUV39H1, SRC-1 and JMDJ2C in endothelial cells isolated from Lept/Ob/Ob mice suppressed p66Shc upregulation and endothelial superoxide generation. By contrast, genetic deletion of SUV39H1 in non-obese animals was associated with disturbed SRC-1/JMDJ2C signalling, p66Shc overexpression and vascular oxidative burst.

Conclusions: We have identified a complex epigenetic machinery responsible for altered redox signalling in the vasculature of obese subjects. Our findings suggest that targeting chondromodifying enzymes may represent a new strategy to reduce vascular disease burden in the setting of cardiometabolic disorders.

Acknowledgement/Funding: European Foundation for the Study of Diabetes (EFSDF)

The incretin hormone GIP is modulated by inflammatory stimuli and downregulated in critically ill ICU patients: central relevance of interleukin 1 beta

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Purpose: The incretin hormone GLP-1 is recently found to be increased in response to inflammatory stimuli leading to insulin secretion and prevention of hyperglycemia in context of critical illness. We here study the relevance of the other main incretin hormone glucose-dependent insulinotropic peptide (GIP) as a regulatory player of glucose metabolism under inflammatory conditions. GIP is known to be released in response to food intake from endocrine intestinal cells leading to glucose-dependent insulin secretion.

Methods and results: Low dose lipopolysaccharide (LPS) injection (100 μg/kg) - used as an inflammatory stimulus - time dependently increased GIP secretion in C57BL/6J mice. Interestingly, this was only apparently at a low LPS dose (4.1 fold increase with 10 μg/kg; p=0.05) and lost with median LPS dosage (1.1 fold increase with 1 mg/kg; p=0.72) while high LPS concentrations led to a trend to-

wards decreased GIP levels (0.6 fold decrease with 2 mg/kg; p=0.2). To elucidate the relevant mechanisms we injected mice with inflammatory cytokines known to be released in response to endotoxin. GIP levels significantly increased in re-

sponse to IL-1β (1.9 fold; p<0.01) and showed a trend for IL-6 (1.6 fold; p=0.16)
but not for TGF-β (all 4 μg/kg) administration. Using IL-1-Receptor- and IL-6 KO mice we found LPS-mediated GIP secretion to selectively depend on IL-1 but not on IL-6 signaling.

To evaluate the functional relevance of inflammatory GIP secretion we pretreated mice with the GIP-receptor antagonist (Pro3)GIP (25 nmol/kg). This however did not affect LPS-induced inflammatory GIP secretion (Fig. 1). Next, we tested whether a similar inflammatory GIP regulation is present in humans. We thereby found circulating GIP levels to decline in response to an inflammatory stimulus (cardiac surgery with extracorporeal circulatory support; n=18; baseline 44.4±5.7 pmol/l to 29.3±4.9 pmol/l after 24 hours; p<0.05). Furthermore GIP secretion significantly decreased (5.8 fold) in critically ill ICU patients (n=68) in comparison to healthy controls (p<0.001).

Conclusion: GIP provides a novel link between the immune system and the gut. Although GIP seems to hold minor relevance for the regulation of glucose metabolism under inflammatory conditions it acts as an inflammatory-immune modulator. This requires further characterization.

P4541 | BENCH
The absence of Two-pore channels induce metabolic alterations at cardiac level
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Introduction: Two pore channels (TPCs) are potential calcium voltage ion channels, which are related with cardiac pathologies. However, little is known about the role of these new channels in the heart. In previous results we showed that fatty acid transport was altered in cardiac left ventricle of TPC1KO vs. wt mice.

Purpose: To maintain a proper cardiac function a continuous production of energy is critical. Our aim is to go further into cardiac metabolic alterations in TPC1KO vs. wt mice.

Methods: To identify the proteins deregulated by the lack of TPC1 and TPC1/2 we performed an LC-MALDI-MS in cardiac left ventricles of TPC1 and TPC1/2 KO vs. wt mice.

Results: A LC-MALDI-MS was carried out in cardiac left ventricles of TPC1 and TPC1/2 KO vs. wt. A total of 108 proteins were found in TPC1 wt and KO mice; 22 unique were found in TPC1 KO mice, 15 unique in TPC1 wt and 71 in both conditions. In TPC1/2 KO vs. wt mice, 149 proteins were identified; 43 unique proteins were found in TPC1/2 KO; 98 common proteins between both conditions and 8 found only in TPC1/2 KO mice. The 2-DE western blot of FABP3 in wt mice revealed a regulation of 2-deoxy-D-[3H]-glucose uptake by primary cultured neonatal rat cardiomyocytes, which was attenuated by TEN. Elevated lung weight and BW ratio and circulating BNP level of SHIR were ameliorated by TEN. Cardiac and circulating DPP4 activities of SHIR were elevated, which was suppressed by TEN. AngiotensinII (AT-II) (100nM) was upregulated in SHIR, but not in wt.

Conclusions: TPCs are potential calcium voltage ion channels, which are related with cardiac pathologies. However, little is known about the role of these new channels in the heart. Previous results we showed that fatty acid transport was altered in cardiac left ventricle of TPC1KO vs. wt mice. To identify the proteins deregulated by the lack of TPC1 and TPC1/2 we performed an LC-MALDI-MS in cardiac left ventricles of TPC1 and TPC1/2 KO vs. wt mice. We thereby found circulating GIP levels to decline in response to an inflammatory stimulus (cardiac surgery with extracorporeal circulatory support; n=18; baseline 44.4±5.7 pmol/l to 29.3±4.9 pmol/l after 24 hours; p<0.05). Furthermore GIP secretion significantly decreased (5.8 fold) in critically ill ICU patients (n=68) in comparison to healthy controls (p<0.001).

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CULTURED CARDIOMYOCYTES

P4542 | BENCH
Teneligliptin ameliorates hypertensive cardiac remodeling via angiotensin-II-mediated pathological uptake of sodium into intracellular space of cardiomycytes
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Purpose: Hypertension is primary cause of heart failure (HF). Several reports demonstrated the blood-pressure (BP)-lowering property of dipeptidyl peptidase 4 (DPP4) inhibitors. We tested the effect of a new DPP4 inhibitor teneligliptin (TEN) on BP and HF using preclinical hypertensive HF models.

Methods: Sprague-Dawley rats (SHR, 8-week-old male) and age-matched normotensive counterpart (WKY) were treated with TEN (10mg/kg/day) for 4 weeks. Hypertensive HF was evaluated in terms of BP, cardiac function, histological remodeling, and pulmonary congestion. Intracellular pH changes of cultured cardiomycytes were monitored by its specific fluorescence indicator (pHrodo, Life Technologies) and live cell imaging using Confocal Scanner Unit (CU X-1 Yokogawa Electric Corporation) and fluorescence microplate reader (Infinite, TECAN).

Results: Cardiac catheterization revealed that TEN ameliorated hypertension of SHIR (Fig. 1). The maximum dP/dt of SHIR was elevated (10452±539 for SHIR-CON and 5739±599 for WKY-CON), which was reduced by TEN (8033±656 in SHIR-TEN) without affecting heart rate. Diastolic indices (minimum dP/dt and tau) were ameliorated by TEN. SHIR-CON exhibited increased in heart and body weight (BW) ratio, left ventricular (LV) wall thickness, cardiac hypertrophy and fibrosis, which were attenuated by TEN. Elevated lung weight and BW ratio and circulating BNP level of SHIR were ameliorated by TEN. Cardiac and circulating DPP4 activities of SHIR were elevated, which was ameliorated by TEN. Angiotensin II (AT-II) (100nM) was upregulated in SHIR, but not in wt.

Conclusions: Angiotensin II (AT-II) is an important regulator of cardiac remodeling. However, little is known about the role of these new channels in the heart. Previous results we showed that fatty acid transport was altered in cardiac left ventricle of TPC1KO vs. wt mice. To identify the proteins deregulated by the lack of TPC1 and TPC1/2 we performed an LC-MALDI-MS in cardiac left ventricles of TPC1 and TPC1/2 KO vs. wt mice. We thereby found circulating GIP levels to decline in response to an inflammatory stimulus (cardiac surgery with extracorporeal circulatory support; n=18; baseline 44.4±5.7 pmol/l to 29.3±4.9 pmol/l after 24 hours; p<0.05). Furthermore GIP secretion significantly decreased (5.8 fold) in critically ill ICU patients (n=68) in comparison to healthy controls (p<0.001).

Conclusion: GIP provides a novel link between the immune system and the gut. Although GIP seems to hold minor relevance for the regulation of glucose metabolism under inflammatory conditions it acts as an inflammatory-immune modulator. This requires further characterization.

CULTURED CARDIOMYOCYTES
vasculopulmonary axis has not been evaluated before. We aimed to investigate the link between inflammation and fibrosis, in the context of a vasculosplenic axis in an experimental type II diabetes model, the ob/ob mouse, and evaluated whether an

Conclusion: TnC a extracellular matrix glycoprotein prominent during tissue remodelling and wound healing may play a pivotal role in the early pathogenesis of pulmonary hypertension.

Results: 

Table 1. Difference between basal and FCT

<table>
<thead>
<tr>
<th>Normal</th>
<th>Post-PH</th>
<th>Pre-PH</th>
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<th>p</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>Norm vs Post-PH</td>
<td>Norm vs Pre-PH</td>
<td>Post vs Pre-PH</td>
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</tr>
<tr>
<td>ΔRAP (mmHg)</td>
<td>3.2</td>
<td>5.2</td>
<td>5</td>
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<tr>
<td>ΔPAP (mmHg)</td>
<td>4.3</td>
<td>3.1</td>
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<td>-0.01</td>
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<tr>
<td>ΔMPAP (mmHg)</td>
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<td>5.1</td>
<td>4.5</td>
<td>-0.05</td>
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<tr>
<td>ΔCI (l/m²/min)</td>
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<td>0.3</td>
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<tr>
<td>ΔPVR (mmHg)</td>
<td>-12</td>
<td>-21</td>
<td>15</td>
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</table>

Conclusions: Pulmonary pressures rise significantly with volume loading, even in healthy volunteers. The response in acute volume loading is different in pre- and post-capillary PH than other groups and CI increased more in control subjects.

P4547 | BESIDE

The trigger of pulmonary injury after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension

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Purpose: We have been refining the procedure of balloon pulmonary angioplasty (BPA) for patients with chronic thromboembolic pulmonary hypertension (CTEPH) and thus, the incidences of complications were diminished. However, the mechanism of pulmonary injury after BPA is controversial; there are residual risks for complications related BPA.

Methods: We conducted a retrospective cohort study of patients with CTEPH undergoing BPA who were admitted to a high volume center of pulmonary hypertension in Japan between November 2012 and December 2013. Pulmonary injuries after BPA was defined by newly appeared CT Findings (GGO, consolidation and pleural effusion). We analyzed correlations between incidence of PI and procedural characteristics, pretreatment patient’s characteristics, and BPA related vascular injury (BR-VI): the angiographic findings of extravasation with substantial clinical signs of pulmonary bleeding, and significant hypoxia.

Results: We operated 297 procedures in 76 patients. The incidence of PI was 138 procedures (46.5%) and BR-VI appeared 51 procedures (17.2%). To compare procedures with PI and without PI, there was no significant difference in

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procedural characteristics between them. However, the incidence of BR VI was significantly higher in the procedures with PI than without PI (33.3% vs. 3.1%, respectively; p < 0.00001). BR VI was independently associated with a higher risk for the incidence of PI (adjusted risk ratio 13.94, 4.43 to 43.92).

**Conclusions:** Procedural characteristics and Pretreatment patient's conditions did not relate to the incidence of PI after BPA, while BR VI was the only risk factor for PI. These results suggested the trigger of PI would be vascular injury.

**P4549 | BEDSIDE**

**Clinical and echocardiographic characteristics of patients with pulmonary hypertension associated with heart failure with preserved ejection fraction or with pre-capillary pulmonary hypertension**

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**Background:** Heart failure with preserved ejection fraction (HFpEF) is a frequent cause of pulmonary hypertension (PH) that may be difficult to differentiate from precapillary pulmonary hypertension (PrePH), particularly in elderly.

**Conclusions:** To explore clinical and echocardiographic characteristics that could help to differentiate PH-HFpEF from PrePH in current practice.

**Methods:** We reviewed data from 138 stable patients referred to the French PH referral center. PH-HFpEF was defined as mean pulmonary artery pressure (mPAP) ≥25 mmHg, compared to mPAP ≤15 mmHg and mean pulmonary vascular resistance (PVR) ≤3 WU. Clinical and echocardiographic characteristics of 68 PH-HFpEF patients and 70 PrePH patients (group 1 and 4 of PH classification) were compared.

**Results:** Compared with PrePH, PH-HFpEF patients were older (67±2 vs 61±17 years, p<0.01), had more frequent systemic hypertension (53% vs 20%, p<0.001) and diabetes mellitus (37% vs 13%, p<0.001), and higher BMI (32.7±25.6, p<0.001) and higher prevalence of atrial fibrillation (16% vs 3%, p<0.001). No differences were observed in 6-minute walk distance and BNP levels. On RHC, PH-HFpEF had similar mPAP and cardiac output than PrePH, but PH-HFpEF presented higher right atrial pressure (15±8 vs 7±4 mmHg, p<0.001) and lower PVR (4±3 vs 7±3 WU). On echocardiography, PH-HFpEF patients had higher left ventricle (LV) mass index (89±3 vs 53±20 cm²/m², p<0.001), left atrial (LA) area (24±7 vs 17±5 cm², p<0.001) and E/e' ratio (10±4 vs 8±5, p<0.05), and smaller right ventricle (RV) end-diastolic area (21±7 vs 24±8 cm², p<0.001) and RV end-systolic area (14±6 vs 18±28 cm², p<0.001). There was no difference in right ventricle functional parameters (tricuspid annular plane systolic excursion, tricuspid S' velocity and RV fractional area change).

**Baseline characteristics in Chart 1.

**P4550 | BEDSIDE**

**Genetics of pulmonary arterial hypertension in a Spanish cohort.**

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**Background:** Highly concentrated carbon dioxide (CO2) is useful for treating ischemic diseases. We have reported that treatment with a few micrometers of CO2 molecules, atomized by two fluid nozzles (CO2 mist), offers a therapeutic benefit in a rat model with heart failure due to myocardial infarction, as well as in a mouse model with peripheral arterial disease. In this study, we investigated whether CO2 mist treatment could ameliorate the development of right ventricular (RV) dysfunction in pulmonary hypertensive rat models.

**Methods:** Six-week-old male Wistar rats were divided into three groups: one that received injected saline as control; a second that received subcutaneous monocrotaline (MCT; 60 mg/kg) without treatment (PH-UT) group; and a third that received MCT with CO2 mist treatment (PH-CM) after MCT administration. The lower body of each rat was encased in a polyethylene bag, filled with the designated gaseous agent via a gas mist generator, for 30 minutes daily. First, survival rate and body weight were compared among the control, PH-UT, and PH-CM groups. Next, we investigated the effect of CO2 mist on their 1-month survival. At 28 days after initiating treatment, the heart rate and blood pressure of each conscious rat was measured by the tail-cuff method. Subsequently, transthoracic echocardiographic study was performed, and rats were sacrificed. RV protein levels were analyzed by Western blotting.

**Results:** After 2 weeks of either MCT or saline injection, we measured no significant difference in body weight among the groups. However, rats that received MCT without treatment began to die within 3–4 weeks of the initial administration. In contrast, daily treatment with CO2 mist extended the survival period of rats in that group. After 28 days after MCT administration, the hemodynamic status, such as the blood pressure and heart rate, involved with left ventricular function, of rats in the PH-UT group were similar to those of rats in the PH-CM group. However, treatment with CO2 mist was observed to significantly attenuate MCT-induced RV hypotrophy of PIB impaired RV fractional area change. Additionally, the PAA/PAET ratio, which is often used as an index of pulmonary hypertension, was significantly decreased by MCT administration. Western blotting revealed that both RV phosphorylated endothelial nitric oxide synthase and heat shock protein 72 levels increased significantly in the PH-CM group, compared to the PH-UT group.

**Conclusions:** Percutaneous CO2 mist therapy may alleviate RV dysfunction in patients with pulmonary hypertension.

**P4551 | BEDSIDE**

**Assessment of exercise tolerance and oxygenation after balloon pulmonary angioplasty for patients with inoperable chronic thromboembolic pulmonary hypertension**

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**Background:** Chronic pulmonary hypertension (PH) is a frequent cause of morbidity and mortality. Inoperable chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by persistent obstruction of the pulmonary arteries. Balloon pulmonary angioplasty (BPA) could be effective for inoperable CTEPH. However, the assessment of exercise tolerance and oxygenation of CTEPH patients who underwent BPA was limited. The aim of this study was to evaluate the efficacy of BPA in exercise tolerance, oxygenation and respiratory function after BPA procedure.

**Methods:** Consecutive 41 patients (12 male, 66.6±11.6 years old) who underwent BPA were enrolled. We evaluated hemodynamics, arterial blood and mixed venous gases after analysis with Swan-Ganz catheter, and respiratory function test before and after BPA, and 1 year follow-up of 28 patients. Exercise tolerance of 6 minute-walk-distance (6MWD) and oxygen desaturation during 6MWD test were also evaluated.
Results: Although BPA dramatically improved hemodynamics (mean pulmonary artery pressure: 38±4.8 vs 20.8±5.3 mmHg, p<0.001, pulmonary vascular resistance: 727±3 dynes/sec/cm-5 to 270±120 dynes/sec/cm-5, p<0.001), arterial blood and mixed venous O2 pressure at rest after BPA were almost unchanged (66.5±19.8 mmHg to 69.4±13.2 mmHg, p=0.34, and 34.6±4.8 mmHg to 35.7±5.3 mmHg, p=0.87, respectively). BPA also greatly improved exercise tolerance of 6MWD (288±97m to 397±117m, p<0.001), however, oxygen desaturation during 6MWD test was unchanged (−9.5±4.5% to −8.8±5.1%, p=0.64). Percent of lung diffusing capacity for CO (%DLCO) was also unchanged (66.0±17.4% to 69.5±12.2%, p=0.63). Arterial oxygenation, oxygen desaturation during 6MWD test and %DLCO were almost equivalent at 1 year-follow-up. 

Conclusion: BPA could dramatically improve hemodynamics and exercise tolerance. However, arterial oxygenation, oxygen desaturation in exercise, and lung diffusing capacity were almost unchanged. These results would suggest the presence of micro vasculopathy in pulmonary capillary level of CTEPH patients or ventilation-perfusion imbalance post BPA. For these cases, it should be decided carefully to discontinue home oxygen therapy and medical vasodilators even after hemodynamics dramatically improved.

**P4545 | BEDSIDE**

**Pulmonary hypertension in patients with dialysis: epidemiology and clinical impact**

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**Background:** Previous papers reported that pulmonary hypertension (PH) was common and a predictor of mortality in patients with dialysis. However, there was no large-scale study evaluating by using right heart catheterization (RHC).

**Methods:** We enrolled patients with dialysis who underwent elective RHC retrospectively. PH was defined as mean pulmonary arterial pressure ≥25 mmHg; Pre-capillary PH (group 5) and postcapillary PH (group 2) were defined as pulmonary arterial wedge pressure <15 mmHg and >15 mmHg, respectively. Patients who suspected of secondary PH were excluded. We assessed the prevalence and the prognostic impact of each PH in patients with dialysis.

**Results:** Eight hundred ninety patients were examined. Two hundred twenty eight patients (25%) had PH. The prevalence of group 5 was 48% (5) and group 2 was 180 patients (20%). Left ventricular ejection fraction (LVEF) was significant differences among the group (non-PH: 48±12%, group 5: 41±14%, and group 2: 40±14%, p for trend<0.001, respectively). During averaged 3.6 years follow-up, 179 patients died. Survival rate was significantly lower in patients with PH than those without (HR 2.98, 95% CI: 1.66–3.06, p<0.001). On multivariate analysis, both group 2 and group 5 were significant factors on mortality post following confounding factors such as LVEF and age (HR 2.18, 95% CI: 1.08–3.98, p=0.004 and HR 1.83, 95% CI: 1.22–2.71, p=0.030).

**Conclusions:** Present study suggested that PH was common, and both group 2 and group 5 PH were independent predictors of mortality in dialysis patients. PH patient with dialysis requires further intensive care and treatment.

**P4543 | BEDSIDE**

**Echocardiography of right ventricular reserve in healthy subjects**

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**Background:** Right ventricular (RV) contractile reserve measured as exercise-induced increase in the pulmonary artery systolic pressure (PASP) has been shown to predict survival in severe pulmonary hypertension. However, RV contractile reserve can also be measured by changes in stroke volume (SV), tricuspid annular plane excursion (TAPSE) or tricuspid annulus systolic velocity (S).

**Aim:** To explore the limits of normal and functional significance of these changes in healthy subjects, that is not exactly known so far.

**Methods and results:** We measured PASP, TAPSE, SV, and S in 90 subjects aged 39±13 yrs, 50% female, at rest and at maximum exercise, and estimated limits of normal as mean ± 2SD to mean ± 2SD. Normal values of exercise-induced changes (A) were 4 to 10 mm for TAPSE, 6 to 14 cm/s for SV, 0 to 96 ml for SV, 12 to 57 mmHg for PASP and −1.2 to 0 mm/mmHg for TAPSE/PASP. Limits of normal (shaded) and exercise-induced changes as a function of workload in TAPSE and SV are shown in Figure 1. As compared to men (n=45), women had decreased A, ΔTAPSE/PASP, ΔPASP and ΔSV, but increased TAPSE/PASP at peak exercise. Aging was associated with decreased A, ΔTAPSE, ΔPASP, ΔSV and TAPSE/PASP Changes in S, TAPSE, PASP and SV were directly correlated to workload.

**P4554 | BEDSIDE**

**Common pitfalls in pulmonary hypertension diagnosis: the real-world application of ESC guidelines algorithm**

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**Background:** Pulmonary hypertension (PH) diagnosis requires a demonstration of increase in mean pulmonary arterial pressure (PAP) >25 mmHg at rest, assessed by right heart catheterization. To date, comparative epidemiologic data regarding different PH groups are not available and real prevalence of PH in the general population is still unknown. Moreover, trans-thoracic echocardiography, despite being at the center of the diagnostic algorithm suggested by the ESC guidelines, still suffers from numerous issues in clinical practice.

**Purpose:** Our registry aimed to provide data regarding incidence and etiology of PH in a “real-world” unselected population referred to our Hospital. Moreover, we evaluated the implementation of echocardiographic screening for PH and the resulting diagnostic work-up in the everyday clinical practice of a regional hub centre.

**Methods:** Using our institutional database we evaluated retrospectively 13689 consecutive echocardiographic exams performed for any indication in our echo-lab between February 1st, 2013 and January 31st, 2014. For each exam we collected data regarding systolic PAP (PAPs) estimation (numeric, semi-quantitative or no estimation), and presence and severity of tricuspid regurgitation (TR). Subsequently, we analysed how many patients with high suspect of PH (PAPs >50 mmHg or TR velocity >3.4 m/s) reached a final diagnosis during a 12-month follow-up.

**Results:** Among all collected exams, only 7059 (52%) reported a quantitative PAPs estimate. In 2903 (21%) exams we found a semi-quantitative PAPs estimation, 900 (7%) exams reported no PAPs estimation due to technical difficulties in founding TR, and 2827 (20%) mentioned no PAPs at all. In the group of patients with high echocardiographic likelyhood of PH (n=517) only 346 (67%) were subsequently evaluated with pulmonary angio-CT. In the same subgroup, specific laboratory screening tests were suggested as indicated: D-Dimers (67%), liver function (58%), thyroid function (13%), HIV (2%), connective tissue disorder (1%). Finally, only 63 (12%) patients reached a final diagnosis of PH: 5 (8%) in group 1, 37 (59%) in group 2, 13 (21%) in group 3, and 8 (13%) in group 4.

**Conclusions:** Despite PH is related to low survival rates and an overall bad prognosis, its incidence remains highly underestimated because PAPs estimation is far from optimal in everyday routine echocardiography. Moreover, only a minority of patients with likely PH follow an evidence-based diagnostic work-up, and even fewer reach a definitive etiologic diagnosis, and are thus treated accordingly.

**AORTIC VALVE DISEASE I**

**P4555 | BEDSIDE**

**Comparing bone turnover biomarkers levels in aortic stenosis of bicuspid and tricuspid valve**

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**Background:** Aortic stenosis (AS) remains the most frequent acquired heart valve disease. It is proposed that calcification of valve leaflets might have sim-
ilar pathways to skeletal bone formation. The aim of the study was to compare levels of bone turnover biomarkers in pts with bicuspis (BAV) and tricuspid (TAV) calcific AS and estimate their associations with bone mineral density (BMD).

Materials and methods: 129 pts with AS and peak aortic jet velocity more than 4.0 m/s; 78 pts with BAV (56.1±10.1 yrs; m:1.2:1) and 51 pts with TAV (62.17±9.9 yrs; m:1.1:1) were included. 31 healthy people as a control (57.63±8.8 yrs; m:1.1:1) were examined. Serum osteoporogenin (OPG), sRANKL, vitamin D, osteopontin (OPN), C-terminal telopeptide of collagen I (CTX), C-terminal propeptide of procollagen type I (PICP) levels were estimated in all pts by ELISA. BMD of femur was investigated with dual energy X-ray absorptiometry.

Results: Pts with BAV and TAV were comparable for gender and ECHO parameters, but pts with TAV were older (p<0.001). Increased circulating OPN and sRANKL levels were revealed in pts with AS compared to healthy controls (Tab.1). Demographic including of heart failure was common (40% vs. 27, p=0.01), it was similar in BAV and TAV groups. There weren’t correlation between OPG/sRANKL and BMD because BMD wasn’t decreased. Vitamin D level was normal in all groups, but it was negatively correlated with OPN (r=-0.4, p<0.002). We revealed also association between BMD, T-criterion and aortic valve pressure gradient (r=-0.28, p=0.04; r=-0.3, p=0.02 respectively). CTX level was positively correlated with aortic valve pressure gradient (r=0.56, p<0.001).

Table 1. Concentrations of biomarkers

<table>
<thead>
<tr>
<th></th>
<th>BAV</th>
<th>TAV</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>sRANKL, pmol/l</td>
<td>0.43±0.10</td>
<td>0.45±0.05</td>
<td>0.36±0.02</td>
</tr>
<tr>
<td>OPN, pmol/l</td>
<td>6.64±0.4**</td>
<td>6.59±0.7**</td>
<td>4.84±0.32</td>
</tr>
<tr>
<td>CTX, ng/ml</td>
<td>46.67±3.86</td>
<td>45.82±1.48</td>
<td>35.69±1.85</td>
</tr>
<tr>
<td>Vitamin D, ng/ml</td>
<td>34.67±2.72</td>
<td>40.62±1.63</td>
<td>43.01±1.23</td>
</tr>
<tr>
<td>rOPN/OPG</td>
<td>0.36±0.03</td>
<td>0.28±0.10</td>
<td>0.36±0.05</td>
</tr>
</tbody>
</table>

*p<0.05 vs control, *p<0.01 vs control

Conclusion: Increased levels of bone turnover biomarkers were found in AS pts with BAV and TAV that confirms common pathway of the heart valve calcification. Association of aortic valve calcification with bone resorption balance might be a potential target for therapeutic actions.

P4556 | BEDSIDE
Causes of death, mortality and evaluation of prognostic factors in patients with severe aortic stenosis in an aging society
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Background: Severe aortic stenosis (AS) is now predominantly a disease of the elderly, with significant mortality and morbidity. In order to investigate the burden of severe AS in the elderly population, we assessed mortality, causes of death, clinical event rates and prognostic factors of patients diagnosed of severe AS.

Methods: A total of 519 consecutive patients (mean age, 78±9 years) with severe AS (aortic valve area –<1.0cm2) were retrospectively analyzed. All-cause mortality and clinical events including aortic valve replacement, heart failure requiring admission, acute coronary syndrome and syncope, were measured as main outcomes.

Results: During a median follow-up of 3.5 years, 167 patients (32%) died: Over-1 and 3 years were 86% and 70%, respectively. Of all deaths, 61% were cardiovascular-related. Cardiovascular death may be the leading, is interestingly not as high as anything previously proposed.

Survival and Causes of Death

Conclusions: Among the one-third of severe AS patients who died during follow-up, 61% were cardiovascular-related. Cardiovascular death may be the leading, but not the only, cause of death for contemporary severe AS patients. Heart failure is common presentation in severe AS patients, although the incidence of syncope is interestingly not as high as anything previously proposed.

P4557 | BEDSIDE
What is the prognostic significance of tricuspid regurgitation in moderate aortic stenosis?
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Background: We tested the hypothesis that tricuspid regurgitation (TR) is a surrogate marker of aortic stenosis (AS) severity, and specifically that TR severity correlated with established hemodynamic and exercise capacity variables, previously validated as reliable prognostic indicators of survival in moderate AS patients.

Purpose: To validate TR severity as a marker of medium term prognosis in patients with moderate AS, being evaluated for aortic valve replacement (AVR).

Methods: All patients with moderate AS with a valve area –<1.5 cm2 seen over a five-year period, who did not establish aortic cross-established criteria for aortic valve replacement (AVR) and who underwent symptom limited exercise testing (CPX) to assess exercise capacity were included in this study. Patients with structural mitral or tricuspid valve disease were excluded.

Results: We included 152 patients with TR severity in 2 groups - trivial to mild TR versus moderate to severe TR. Differences in clinical variables, exercise capacity, echo parameters and outcomes by TR group were determined using t-tests and chi square tests as appropriate. Survival on medical therapy prior to AVR by TR grade was determined by Cox regression adjusted for age, sex and AVR.

Results: This study included 152 eligible patients. Patients with higher TR grade had worse exercise capacity (lower peak VO2 with a higher prevalence of VE/VCO2 >35). Aortic valve area did not differ significantly between patient groups based on TR grade, but echo indices of LV performance were worse and pulmonary pressures were higher in patients with higher TR grades. There were 22 deaths (14%) over median follow-up – 3.3 years (IQR 2.3–4.0). The hazard ratio for death with higher TR grades was 3.0 with 95% confidence limits (CL) of 1.2–7.6, P=0.0196 adjusted for age, sex and censured at the time, if AVR was performed. TR grade was also a significant predictor of death on medical therapy, prior to AVR if performed with a hazard ratio of 2.7 with 95% CL 1.2–2.7, P=0.0324.

Conclusion: In patients with moderate AS by established valve hemodynamic criteria, the presence of moderate to severe TR was associated with poorer functional capacity, worse left ventricular function, higher pulmonary pressures and more functional mitral regurgitation than patients with mild or no TR. Patients with higher grade of TR has worse survival on medical therapy that patients with mild or no TR.

In patients with moderate AS, TR severity has survival significance and can be used, along with other established clinical and cardiac imaging criteria as a prognostic indicator to assist in patient selection for AVR.

P4558 | BEDSIDE
Impact of pulmonary arterial pressure on long-term survival in patients with aortic stenosis and preserved left ventricular ejection fraction
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Background: The prognostic impact of pulmonary arterial pressure (PAP) remains controversial in aortic stenosis (AS) and few studies focused only on patients with preserved left ventricular ejection fraction (LVEF). We therefore aimed to investigate the impact of PAP, derived from catheterization, on survival in severe AS pts with preserved LVEF.

Methods and results: Between 2000 and 2010, 749 patients (74±8 years, 57% of males) with preserved LVEF (LVEF >50%) and severe AS (valve area <1cm2) without other valvular heart disease underwent cardiac catheterization, including right heart hemodynamic assessment. Pulmonary hypertension (PH) was defined as mean PAP >25mmHg. Systolic and mean PAP were 34.5±12 and 21.9±9mmHg, respectively. Overall, lower LVEF and higher heart rate (all p<0.016) than those without PH. In addition, they more frequently had hypertension, diabetes, coronary artery disease (CAD) and chronic pulmonary disease (all p<0.043). Aortic valve replacement (AVR) was performed in 91% of patients and 30-day mortality was 4.3%, significantly higher in patients with PH (7.7 vs. 3.4%, p=0.014). In logistic regression analysis, PH was an independent predictor of both 30-day and long-term mortality. Nevertheless, only severely elevated PAP seemed associated with reduced survival. In order to improve the
prognosis of these patients, AVR could be considered before the occurrence of severely elevated PAP.

P4559 | BEDSIDE
Assessment of myocardial deformation: predicting left ventricular dysfunction after surgery in patients with chronic mitral regurgitation

Background: The development of postoperative left ventricular (LV) dysfunction is a frequent complication in patients with chronic severe mitral regurgitation (MR) and implies a poor prognosis. Assessment of myocardial deformation enables myocardial contractility to be accurately estimated. The aim of this study was to evaluate the predictive value of preoperative regional LV contractile function assessment using two-dimensional echocardiography–based multilayer speckle-tracking analysis in patients with chronic severe MR.

Methods: Forty-three consecutive patients with chronic severe MR scheduled for mitral valve replacement or repair were prospectively enrolled. Serial echocardiographic studies were performed before surgery, at 7 days follow-up and at least 3 months follow-up postoperatively. The conventional echocardiographic parameters were calculated. Global and regional LV systolic function was estimated by 2D speckle tracking and automated functioned image (AIF) technique.

Results: The patients’ mean age was 51.7±14.3 years and 25 (58.1%) were male. In ROC curve analysis, the most useful cutoff value for discriminating between patients with LV remodeling and patients with LV no-remodeling in severe MR with normal LVEF was approximately 20.5% of 2D mid-layer GLS (sensitivity 0.70, specificity 0.75). Patients were divided into two groups by the baseline global LS –20.5%. Preoperative speckle tracking–derived longitudinal strain values strongly predicted a postoperative LV remodeling or LV dysfunction. And, postoperative degree reduction of LVEDD might be additive predictive factor.

Conclusions: Speckle-tracking echocardiography can be used to predict a decrease in LV dysfunction after mitral valve replacement in patients with chronic severe mitral regurgitation. Postoperative degree reduction of LVEDD might be additive predictive factor for postoperative LV dysfunction or remodeling. These might help prevent irreversible systolic dysfunction in the long term.

P4560 | BEDSIDE
Asymptomatic, severe degenerative mitral regurgitation: a step towards earlier detection of myocardial dysfunction
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Background: 2D speckle tracking echocardiography (2D-STE) has been used to appreciate left atrial mechanics in patients (pts) with severe mitral regurgitation (MR), while left ventricular (LV) deformation properties have not been studied extensively.

Purpose: The aim of the present study was to assess LV global longitudinal strain (LVGLS) in pts with normal ejection fraction (EF) and severe MR.

Methods: We studied 46 consecutive pts (52% men, with mean age 64±15 years) with asymptomatic, severe degenerative MR and normal EF and 30 healthy controls (53% men, with mean age 61±14 years). In addition to conventional echocardiographic measurements, global longitudinal strain of the LV (LVGLS) was estimated off-line from the three apical views by 2D-STE using EchoPac 110 workstation (GE Vivid 9 Ultrasound).

Results: The main results of our study are presented in Table 1. While pts with MR had increased EF compared to controls, they had impaired LVGLS, confirming the outstanding role of strain in the pathophysiological interpretation of cardiovascular diseases. It is impressive that although the increase of EF is a compensatory mechanism to MR, LVGLS unveils the indeed impaired systolic function of the LV, doubling actually the presence of the stage of compensated MR. Consequently, the impairment of the deformation mechanics of the LV in MR can possibly be used to detect latent myocardial dysfunction and to better define the perfect time to intervene, improving prognosis.

Conclusion: 2D-STE can detect impairment of the systolic function of the left ventricle in organic mitral regurgitation before it is apparent from the ejection fraction.

Table 1. Multivariable logistic regression analysis for determinants of postoperative LV remodeling

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>β Coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post OP LVEDD, mm</td>
<td>0.837 (0.647–1.083)</td>
<td>−0.178</td>
<td>0.175</td>
</tr>
<tr>
<td>Post OP EF (%)</td>
<td>1.055 (0.935–1.191)</td>
<td>0.054</td>
<td>0.385</td>
</tr>
<tr>
<td>Baseline mid-layer GLS</td>
<td>2.440 (1.259–4.729)</td>
<td>0.892</td>
<td>0.008</td>
</tr>
</tbody>
</table>

P4561 | BEDSIDE
Whole blood viscosity as an overlooked predictor of spontaneous echo contrast in patients with mitral stenosis
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Introduction: Spontaneous echo contrast (SEC) is specified with dynamic smoke-like appearance in transesophageal echocardiography (TEE) as a source of cardioembolism with prognostic importance. This entity arises from an interaction between red cells and plasma proteins, especially at low shear rates. Mitral stenosis (MS) serves as a low velocity bloodstream milieu, facilitating SEC formation. Whole blood viscosity (WBV) can be calculated with confirmed equations from hematocrit and total plasma protein. We aimed to assess the relationship between WBV and SEC formation in MS.

Methods: 250 patients with MS who were performed TEE before mitral balloon valvuloplasty procedure between 2010 and 2015 were enrolled. SEC(+) group consisted of 152 patients (mean age 56.9±12.9 and 44.7% male) and SEC(−) group consisted of 98 patients (mean age 55.5±13.2 and 42% male). WBV was derived from hematocrit and plasma protein concentration at low shear rate (LSR) (0.5 sec−1) and high shear rate (HSR) (208 sec−1) by validated formulas.

Results: SEC(+) patients had significantly higher WBV for both LSR (80.0±18.7 vs 62.8±19.1, p<0.001) and HSR (17.9±1.7 vs 16.7±1.3, p<0.001). Correlation analysis demonstrated a significant relationship between the grade of SEC and WBV for LSR (r=0.484, p<0.001) and HSR (r=0.463, p<0.001). A cut-off value of 72.3 for WBV at LSR has 73.5% sensitivity and 67.3% specificity for prediction of SEC (AUC: 0.748, p<0.001). A cut-off value of 17.0 for WBV at LSR has 72.5% sensitivity and 60.7% specificity for prediction of SEC (AUC: 0.699, p<0.001).

Discussion: WBV is a simple way of blood viscosity assessment. We have delineated a noteworthy relationship between SEC formation and WBV. Evaluation of WBV with this formula may guide us to risk stratification in patients with MS.
Methods: A total of 184 patients with MAC and 133 patients without MAC were enrolled in this study. WBV was calculated with a confirmed formulation by using hematocrit and total plasma protein at low shear rate (LSR) and high shear rate (HSR).

Results: In patients with MAC, WBV values were significantly higher for HSR (18.0±4.0 vs. 17.2±5.8, p<0.001) and for LSR (78.0±14.2 vs. 61.9±17.1, p<0.001). At multivariate analysis, WBV for both shear rate was an independent predictor of MAC. In ROC curve, a cut-off value 70.1 of WBV at LSR has 83.7% sensitivity and 73.7% specificity (AUC: 0.785, p<0.001) and a cut-off value 17.5 of WBV at HSR has 85.6% sensitivity and 71.4% specificity (AUC: 0.761, p<0.001) for prediction of MAC.

Conclusion: As a major component of shear stress, WBV can be a useful and costless predictor of MAC. Further prospective studies are needed to prove the prognostic value of WBV in cardiovascular pathological conditions.

AORTIC VALVE DISEASE II

P4556 | BEDSIDE

Impact of leaflet tear/partial clip detachment on outcomes of repeat MitraClip therapy in high surgical-risk patients

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Background and introduction: MitraClip (MC) implantation is a safe and efficacious percutaneous approach to treat significant mitral regurgitation (MR) in inoperable and high surgical-risk patients (pts). Failure of the index procedure or occurrence of high-grade MR after a successful intervention may encourage investigators to attempt a repeat MC procedure.

Purpose: We sought to assess procedural details and outcomes of repeat MC therapy.

Methods: Of 410 high surgical risk pts initially treated with the MC at our institution, 17 in-house pts (4.1%) and 4 additional pts transferred from external institutions underwent repeat MC procedures. Mean age of the 21 pts (14 men [67%]) was 77 years; 15 pts (71%) had functional MR (FMR).

Results: Repeat procedures were performed 6.3 (median; range 0.7–34) months after the index intervention. At the time of the repeat procedure, leaflet tear along the edge of the clip (n=5) or partial clip detachment (PCD; n=3) was present in 8 patients (38%). Thirteen (62%) of the 21 repeat interventions were successful (discharge MR grade 2+). After the index procedure, median follow-up was 77 months; 13 patients (62%) – 8 with intact leaflets and 5 with leaflet tear/PCD – died during follow-up. Leaflet tear/PCD did not impact mortality. A trend toward improved survival was observed in FMR patients with a successful repeat procedure.

Conclusions: Repeat MC intervention for significant MR in elderly patients deemed inoperable or at high surgical risk appears to be a viable therapeutic approach after occurrence of high-grade MR after a successful intervention may encourage investigators to attempt a repeat MC procedure. The current findings confirm that repeat MC intervention is strongly associated with procedural failure, whereas survival, at least in patients with FMR, is primarily affected by repeat procedural outcome.

Acknowledgement/Funding: Karl-Heinz Kuck and Ulrich Schaefer have received research grants from Abbott Vascular, Inc.

P4564 | BEDSIDE

The prognostic significance of post-MitraClip vena contracta area in heart failure patients with functional mitral regurjitation

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Background and introduction: In Europe, MitraClip (MC) implantation is predominantly performed in elderly surgical high-risk patients (pts) with functional mitral regurgitation (MR). Success rates in such pts, based on discharge MR severity, are on the order of 90%, with longer-term outcomes affected by discharge MR grade.

Purpose: Since vena contracta area (VCA) reflects MR severity, we sought to assess the prognostic value of VCA measured immediately post-MC.

Patients: We studied 100 consecutive pts (73±10 years, median log. EuroSCORE 18%, 68 men) with functional MR in whom VCA could be measured pre- and post-MC. Baseline left ventricular ejection fraction (LVEF) was 31±13%; 56 pts presented with LVEF ≤30%, 31 with LVEF between 30% and 45%, and only 13 pts had LVEF >45%. Median NT-proBNP concentration was 5520 pg/ml; 28 pts carried a CRT-D device, an additional 23 pts had an ICD. NYHA functional class was III or IV in 96 patients, with no apparent impact of LVEF category on NYHA class noted.

Results: MC therapy was successful (discharge MR severity ≤2+) in 93 pts (54 pts MR 1+, 39 pts MR 2+). Overall, median VCA was significantly reduced from 84 (IQR 60–103) mm² before MC implantation to 15 (IQR 7–30) mm² at the end of the procedure (p<0.0001). Post-MC VCA did not distinguish between discharge MR 1+ and 2+ nor between discharge MR 3+ and 4+, but pooled post-MC values were significantly lower in pts with discharge MR 1+<2+ than in pts with discharge MR 3+<4+ (median 14 mm² vs. 68 mm², respectively; p=0.0011). Out of 98 pts followed for 13.6 (median, IQR 4.8–23.4) months, 33 pts died. ROC analysis identified a post-MC VCA of 17 mm² as the optimal cut-off to discriminate between patients who were alive at 1 year and patients who had died by then. Highly distinct survival curves according to the 17-mm² cut-off indicate a significant survival benefit out to at least 3 years for patients with a post-MC VCA ≤17 mm² (2-year survival 80.2% vs. 40.4% in pts with post-MC VCA >17 mm²; p=0.0001).

Conclusions: In heart failure patients undergoing MC therapy for significant functional MR, post-MC VCA proved to be an intraprocedurally assessable parameter to guide interventional decision-making with respect to the patient’s long-term outcome. MC therapy should aim for a post-MC VCA ≤17 mm².

Acknowledgement/Funding: Ulrich Schaefer and Karl-Heinz Kuck have received research grants from Abbott Vascular, Inc.

P4565 | BEDSIDE

Impact of computed tomography aortic annulus measurements during systole and diastole on prosthesis choice in patients undergoing transcatheter aortic valve implantation

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Background: Measurement of the aortic annulus diameter in patients before transcatheter aortic valve implantation (TAVI) is crucial for the selection of the correct prosthesis size and interventional success rate. Cyclic changes during systole and diastole can result in significant differences in the annulus diameter size.

Purpose: We aimed to analyse the impact of annulus measurements during systole or diastole on the choice of prosthesis size in a virtual model, assuming the Sapien3, ACURATE TA, and CoreValve as prosthesis.

Methods: We determined the effective annulus diameter size of patients with severe aortic valve stenosis scheduled for TAVI by computed tomography during systole (AnnSys) and diastole (AnnDia), as described previously. Patients were then virtually assigned to receive a prosthesis of specific size due to the manufacturer’s specifications. We analysed differences in the strategy to allocate the correct prosthesis size.

Results: In this single-centre registry, 696 patients were included. Although absolute differences between mean AnnSys (24.2±2.1 mm) and AnnDia (23.4±2.1 mm, p<0.0001) were small, these differences would have influenced the choice of prosthesis size. Considering AnnSys as the valid annulus diameter compared with AnnDia resulted in the strategy decisions shown (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Strategy decision</th>
<th>Sapien3</th>
<th>ACURATE TA</th>
<th>CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change [%]</td>
<td>75.4</td>
<td>59.2</td>
<td>70.0</td>
</tr>
<tr>
<td>Choice of larger size [%]</td>
<td>21.8</td>
<td>28.4</td>
<td>28.6</td>
</tr>
<tr>
<td>TAVI feasible [%] (AnnDia: annulus too small)</td>
<td>0.1</td>
<td>8.0</td>
<td>0.1</td>
</tr>
<tr>
<td>TAVI not feasible [%] (AnnDia: TAVI feasible due to smaller annulus)</td>
<td>2.6</td>
<td>4.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Conclusions: In our model in which patients referred for TAVI procedures were allocated to receive a transcatheter aortic valve prosthesis of a specific size, the decision to measure aortic annulus size during systole or during diastole would not only have had an impact on the choice of prosthesis size in more than 20% of patients but also on the judgement of whether TAVI would have been feasible. These results need to be verified in studies of on-going TAVI registries.

P4566 | BEDSIDE

Change in frailty status in octogenarians with severe symptomatic aortic stenosis after aortic valve replacement

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Background: Frailty has emerged as a measure of physiological reserves and as a predictor of mortality, prolonged hospitalization and readmissions after cardiac intervention.

Purpose: The aim of the study was therefore to observe change in frailty status six months after aortic valve replacement (AVR).

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Methods: In this observational prospective cohort study including patients at 80+ with severe symptomatic aortic stenosis (AS) accepted for transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR), frailty status was assessed one day prior to and six months after AVR using the Study of Osteoporotic Fracture (SOF) Frailty Index. Patients were categorized as robust, pre-frail or frail according. EuroScore was used to determine operative risk and Charlson Comorbidity Index to measure comorbidity. The McNemar-Bowker Test of Symmetry was used to investigate whether AVR could change frailty status in the total study population.

Results: In all, 143 patients were included, mean age 83 years (SD 2.7). Thirty-four percent were robust, 27% pre-frail and 39% frail. There was no significant difference in frailty status between treatment groups (p = 0.11) or between sexes (p = 0.98). Frail patients were in a higher New York Heart Association (NYHA) function class (p = 0.03) and had higher S-ProBNP (p = 0.04). No significant differences were detected in EuroScore (p = 0.07), Charlson Comorbidity Index (p = 0.12) or in aortic valve area (p = 0.78). The proportion of patients who improved their frailty status was 34% whereas 18% changed for the worse. However, no significant overall change was observed (p = 0.16).

Conclusion: No significant change was observed in overall frailty status after six months, but our findings show that frailty is a dynamic syndrom; an important finding from a clinical perspective which must be further studied.

P4567 | BEDSIDE
The opening of aortic valve during exercise is a key to prevent development of aortic insufficiency among those with closed aortic valve at rest during ventricular assist device support
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Background: We previously demonstrated that the opening of native aortic valve (AV) at rest was a sufficient condition to prevent development of aortic insufficiency (AI) during left ventricular assist device (LVAD) support. However, clinical impact of native AV opening during exercise in patients with closed native AV at rest remained unknown.

Methods: We enrolled 37 patients whose native AV remained closed at rest at 3 months after CF LVAD implantation, and followed them at our institute between 2006 and 2014.

Results: Of them, 7 patients (19%) who had achieved the opening of native AV during cardiopulmonary exercise testing at the 3rd months (the opening group, Fig A), had no AI during follow-up. Of those, who did not achieved AV opening (the closed group) (p < 0.05 for all). The opening group suffered no AI at the 6th months (Fig B), and had higher readmission-free ratio due to cardiovascular events over the closed group during 2-year study period (100% vs. 56%, p = 0.005).

A. Typical Case (A) and Time Course (B)

Conclusion: The opening of native AV during exercise was sufficient condition to prevent development of AI in patients with closed native AV at rest. Aggressive cardiac rehabilitation to improve exercise tolerability may have a prophylactic impact on development of AI accompanied by better quality of life during CF LVAD treatment.

P4569 | BEDSIDE
Exercise hemodynamics in symptomatic patients with low gradient aortic stenosis with normal ejection fraction. A simultaneous right-heart catheterization and Doppler-echocardiographic study
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Background: Clinical decision making of symptomatic patients with low gradient aortic stenosis (LGAS) and normal EF is controversial. In this population, the severity of AS is not clear and symptoms may be conditioned by abnormal vascular hemodynamics during exercise. Patients with high-gradient severe symptomatic AS show a typical hemodynamic pattern of blunted blood pressure (BP) and fixed stroke volume (SV) response to exercise.

Objectives: To analyze whether the behavior of valvular and vascular load during exercise conditions the physiology of LGAS and normal EF.

Methods: Twenty symptomatic patients (77±6 years old; 17 female) with LGAS (mean pressure gradient 28±6 mmHg; valve area 0.8±0.1 cm²) and normal EF (66±7%) underwent simultaneous right-heart catheterization (continuous mixed venous blood saturation and pulmonary pressure), invasive arterial pressure monitoring, Doppler-echocardiography and gas exchange measurements during cycloergometric exercise. Cardiac output (CO) and SV was continuously monitored using the Fick method. Using a temporal synchronization algorithm, we built a multidimensional temporal data matrix including all the hemodynamic and functional invasive and noninvasive data for each patient.

Results: Valve area (AVA) systematically increased during exercise in the overall population, up to 1.2±0.3 cm² at peak exercise (p < 0.001 vs. baseline; slope: Δ 0.07 cm² per ml/kg/min of VO2). Importantly, mean and systolic BP increased during exercise due to a significant increase in CO and SV, despite systemic vascular resistance (SVR) decreased (~227 dynes/s cm⁻³ per ml/kg/min of VO2). Multivari-ate analysis demonstrated that the SV response for a given patient was independently determined by the amount of change in SVRI and AVA (p < 0.001 for both). In addition, the amount of exercise-induced increase in mean pulmonary artery pressure (from 21±9 at baseline to 41±14 mmHg at peak exercise, p < 0.001) was determined by the change in SVRI and arterial compliance (p < 0.001 for both) and not by baseline values of AS severity.

Conclusions: In patients with LGAS and normal EF, AVA is highly dynamic and flow-dependent. Patients with LGAS and normal EF typically increase BP and SV during exercise despite a fall in vascular resistance. Their capacity to dynamically reduce the vascular and valvular load during exercise are the main determinants of functional status of these patients. As opposed to classical patients with high gradient AS, baseline indices of AS do not account for functional hemodynamics in patients with LGAS and normal EF.

Acknowledgement/Funding: This study was supported by grants PS09/02602, RD12/0042 and CM12/00273 from the Instituto de Salud Carlos III, Spain.
and mean gradients (MG) of 35 ml/b/m² and 40 mm Hg, respectively. One-way dynamic subgroups were analyzed using cut points of stroke volume index (SVI) dynamic profile. Systemic vascular resistance (SVR), systemic arterial compliance (C), age 68±8.24 years, 75% male, mean AVA 3.49±0.86 cm²) were included. There were no significant differences in PSS between the two techniques, but with poor agreement. There was a significant positive bias for FT strain rates which was partially masked by peak early diastolic strain rate with poor agreement between techniques. This finding likely results from poor speckle tracking during diastole.

**Results:** 72 AS patients (age 65±12.98 years, 72% male, aortic valve area AVA = 0.35±0.09 cm², EF = 56±12%, AV weight = 2.46±1g) had complete hemodynamic data. Asymptomatic moderate-severe AS and 23 controls underwent STE/MRI on the same day. Only patients with full STE and MRI datasets were included. Measurements included global longitudinal peak systolic strain (PSS), peak systolic strain rate (PSSR) and peak early diastolic strain rate (PEDSR). Agreement was assessed with t-tests, correlation and intra-class correlation coefficients.

**Conclusions:** Myocardial strain and strain rates measured with FT and STE in asymptomatic patients with AS have poor agreement even in patients with good echocardiographic images. Further work is required to determine whether MRI measured strain/stRAIN can be used in the management of asymptomatic patients with AS.

**Acknowledgement/Funding:** National Institute Health Research, Universities Hospitals of Rochester, Cardiovascular Biomedical Research Unit GlensfIeld Hospital, St. Francis Hospital/SUNY at Stony Brook, Roslyn, United States of America

**Background:** Aortic valve calcification (AVC), and the hydraulic vascular load both play important roles in defining global LV afterload in aortic stenosis (AS). We sought to determine the magnitude of vascular load and its relationship with AVC in severe AS.

**Methods:** Of 719 pts with isolated severe AS who underwent surgical AVR between 2010–2014 and had AV weight, 672 (age = 76±9 yrs, 59% men, mean AVA = 0.35±0.09 cm², EF = 56±12%, AV weight = 2.46±1g) had complete hemodynamic profile. Systemic vascular resistance (SVR), systemic arterial compliance (SAC), and global LV afterload (Zva) could be measured in 276 pts. 4 hemodynamic subgroups were analyzed using cut points of stroke volume index (SAC) and mean gradients (MG) of 35 ml/b/m² and 40 mm Hg, respectively. One-way ANCOVA, comparison of least-squares pair-wise means and Pearson correlations were performed.

**Results:** No correlations were found between AVW and SVR or ZVA. AVW was modestly associated with SAC in unadjusted models and models adjusted for demographics, EF, AVA, vasodilators and diuretics (r=0.14, p=0.02 and r=0.18, p=0.005, respectively). Normal flow/high gradient (NF-HG) and low flow (LF) HF groups had the heaviest valves, whereas the LF/HG group had the worst vascular indices in both unadjusted (table) and adjusted models.

**Conclusions:** 1. AVC was modestly associated only with SAC. 2. Pts with LF/HG have the worst vascular profile which may contribute to a decline in stroke volume and adverse postoperative outcomes.

**P4572 | BEDSIDE**

Pre-procedural dual antiplatelet therapy and bleeding events following transcatheter aortic valve implantation (TAVI)

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**Introduction:** TAVI is associated with bleeding that increases mortality. Little is known about pre-procedural dual antiplatelet therapy (DAPT) use and its impact on hemostasis.

**Purpose:** We sought to determine the frequency, predictors and bleeding risk in patients receiving DAPT before TAVI.

**Methods:** Three-hundred-and-three (n=303, 78.6±7.6 years, 49% female, EuroScore 23.1±16.9) consecutive patients were prospectively analyzed and followed for in-hospital events. According to pre-procedural anti platelet status population was divided into 2 groups: patients receiving aspirin and clopidogrel (DAPT) and those on aspirin only or no antiplatelet therapy (noDAPT).

**Results:** Pre-procedural DAPT was used in 139 cases (46%). Previous PCI (OR 4.8 [2.8–8.3], p<0.0001), implantation of self-expandable prostheses (OR 2.2 [1.2–4.3], p=0.007) femoral access (OR 2.2 [1.1–4.5], p=0.029) and platelet count (OR 1.006,[1.002–1.01],p<0.002) were independent predictors of pre-procedural DAPT. No difference was observed in the rates of any bleeding (23% in DAPT vs. 24.4% in noDAPT, p=0.930) or major/life-threatening bleeding (12.2% in DAPT vs. 14.7% in noDAPT, p=0.715). Propensity-score matching analysis did not alter the results. GFR <30 ml/min was the strongest predictor of bleeding (OR 4.3 [1.9–9.9], p<0.0005). There was a trend towards lower frequency of MI and stroke/TIA in DAPT as compared with noDAPT (3.6% vs.9.8%, p=0.082).

**Conclusions:** Pre-procedural DAPT is frequent and does not increase short-term bleeding complications following TAVI. Possible impact of DAPT use before TAVI on ischemic complications needs to be investigated in larger populations.

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**P4573 | BEDSIDE**

Aortic valve disease II

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**Objectives:** The aim of our study was to assess whether anatomical parameters predict procedural success in patients undergoing transcatheter aortic valve implantation.

**Methods:** 296 consecutive patients suffered from severe symptomatic aortic stenosis underwent multilobe transcatheter aortic valve replacement (MSCT) before TAVI. Anatomical parameters were assessed qualitatively and quantitatively: annulus dimensions (maximum and minimum diameter, perimeter, area, ellipticity index), aortic annulus angulation, calcification of the left ventricular outflow tract (LVOT), aortic annulus (AA), and aortic valve (AV) were measured by two blinded investigators.

The primary endpoint of our study was device success in accordance with the VARC-2 criteria defined as absence of procedural mortality, correct positioning of the prosthesis itself (no prosthesis-patient mismatch, mean pressure gradient <20mmHg, peak velocity <3m/s, no moderate or severe paravalvular aortic regurgitation (AR)) plus the absence of stroke.

**Results:** 296 patients (age 81±16.3 years, 54% male, left ventricular ejection fraction 51.7± 14.4%, EuroSCORE II 5.5 (3.4–11.2%), underwent transcatheter TAVI at our institution.

Device success was achieved in 253 patients (85.5%); 4 peri-procedural deaths, 5
strokes, 13 valve-in-valve procedures due to misplacement of the first prosthesis, and 21 patients with moderate paravalvular AR.

The Rosenhek score and semi-quantitative assessment of LVOT and AA calcifications did not show any relationship to the occurrence of more than mild paravalvular AR or procedural success. Mass and volume of LVOT and AV calcifications were associated with the occurrence of paravalvular AR immediately after deployment of the transcatheter heart valve but not with the final result after corrective measures such as postdilation. However, this did not show any relationship to procedural success.

The annulus dimensions and consequently the cover index (but not the AA annulus [P = 0.27]) were the only parameters that were associated with more than mild paravalvular AR: perimeter (79.2±8.4 vs. 73.6±6.4 mm; P = 0.005), area (480.5±99.0 vs. 421.7±73.4 mm²; P < 0.01), ellipticity index (1.32±0.10 vs. 1.28±0.11; P = 0.006), and the cover index (9.1±1.0 vs. 7.7±5.9%; P = 0.001).

Conclusions: Anatomical parameters except for the dimension of the aortic annulus and the degree of oversizing reflected by the cover index do not predict the occurrence of paravalvular AR or procedural success in patients undergoing transcatheter aortic valve implantation.

P4574 | BEDSIDE Additional value of exercise-stress echocardiography in asymptomatic patients with aortic valve stenosis


Aims: Usefulness of exercise-stress echocardiography for risk stratification of asymptomatic patients with aortic stenosis (AS) is still debated (Class llb recommendation). The exercise-induced increase in transvalvular gradient has been proposed as a risk factor but data are scarce. We sought to evaluate the additional prognostic value of echocardiographic parameters during exercise-stress echocardiography.

Methods: In this observational prospective study, we enrolled all consecutive asymptomatic patients with moderate/severe AS and normal ejection fraction who underwent an exercise-stress echocardiography at our institution. Clinical and echocardiographic data at rest and at peak exercise were collected. The composite primary outcome variable was the occurrence of AS related events (symptoms or heart failure related to the AS or cardiovascular death during follow-up).

Results: Among the 121 patients enrolled, 35 (29%) had an abnormal exercise test (occurrence of symptoms or abnormal blood pressure profile during exercise) and were operated on within the following weeks. Eighty-six (mean [quartiles]; age 67 [57–75] years, 68 male, mean gradient 46 [35–52] mmHg, aortic valve area 0.97 [0.82–1.11] mm²) had a normal exercise test and 34 (48%) reached the clinical endpoint during follow-up (17.5 [10.9–36.4] months). The proposed threshold of 18 mm Hg mean gradient increase had no prognostic value.

In multivariate analysis, rest mean gradient (p = 0.001; HR 1.07 [1.03–1.11]) but not exercise induced mean gradient increase (p = 0.4; HR 0.69 [0.29–1.63]) were predictive of outcome.

Conclusion: Exercise induced increase in mean gradient was not predictive of outcome in patients with normal exercise test. Our results raise questions regarding the added value and therefore the use of exercise-stress echocardiography for risk stratification of asymptomatic patients with AS.

AORTIC VALVE INTERVENTIONS

P4575 | BEDSIDE Changes in clinical, epidemiological and prognostic profiles in native left-sided infective endocarditis without underlying heart disease

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Introduction: Native left-sided infective endocarditis (NSLIE) in patients without underlying heart disease has increased in the last decades, and their clinical, epidemiological and early prognostic profile can be changed.

Methods: Our aim is to compare NSLIE profile between patients with UHD and without (NUHD) undergoing heart disease and 2) to describe changes in this profile in NUHD patients.

Results: From 1987 to 2014 a consecutive series of 254 patients diagnosed with NSLIE was analyzed. The anatomic and clinical severity because of their age and the high prevalence of comorbidities, and the crude in-hospital mortality rate of NSLIE significantly increased from 2001 to 2014 (n = 83).

Discussion: The proportion of NSLIE was significantly higher in the 2001–2014 period (54.2% vs 25.7%, p < 0.001). The mean age was 53.5±18 years in the UHD group and 56.1±4 years in NUHD, p = 0.2. There was no significant difference in the valve affected, but the size of endocardial vegetations was greater in the NUHD group (13±4mm vs 11.6±4mm, p = 0.01). NSLIE caused by Streptococcus viridans was more frequent in the UHD group (34% vs 17.6%, p = 0.004), but Enterococcus spp and Staphylococcus aureus were responsible for 23.1% and 20.4% in the NUHD group, respectively. The NUHD group had a more frequent history of intravascular catheter (12% vs 3%, p = 0.009), liver disease (15% vs 3%, p = 0.001), immunosuppressive condition (8% vs 0.6%, p = 0.002), nephropathy (9% vs 2%, p = 0.018) and diabetes mellitus (7% vs 1.3%, p = 0.021). There were no differences in the development of complications or early surgery rate. Early mortality rate was similar (29% in the NUHD group and 21% in the UHD group, p = 0.452).

Conclusion: NSLIE in patients without underlying heart disease has great clinical severity because of their age and the high prevalence of comorbidities, and it has a similar short-term prognosis for those patients with previous valvular disease.

P4576 | BEDSIDE A new gatekeeper for prevention of in-hospital mortality in infective endocarditis: platelet to lymphocyte ratio

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Background: Risk stratification constitutes for an important step in management of patients with infective endocarditis (IE) due to significant morbidity and mortality despite diagnostic and therapeutic improvements. Recently, platelet to lymphocyte ratio (PLR) has been defined as a novel indirect marker of inflammation and was significantly associated with 30% mortality. We hypothesized that an increased PLR on admission would predict in-hospital mortality in patients with IE.

Methods: In this prospective study, a total of 120 consecutive patients with definite IE were enrolled. Clinical, echocardiographic and laboratory parameters were recorded. The outcome measure was in-hospital death from any cause. Independent predictors of in-hospital mortality were determined by Cox regression analysis.

Results: In-hospital mortality was observed in 28 (23.3%) patients. Patients in in-hospital mortality revealed a higher PLR (414.2±40.3 vs 208.3±33.1), CRP and white blood cell counts as compared with those survived (p < 0.05). In ROC curve analysis, using a cut-off level of 0.75, on admission PLR level predicted
in-hospital mortality with a sensitivity of 78% and specificity of 61%. In multivari-
able Cox regression analyses, S. aureus infection, LVEF < 50%, end-stage renal disease, perivalvular abscess, CRP and on-admission PLR (HR: 1.24, 95% CI: 1.11–1.37, p = 0.014) were found as the independent predictors of in-hospital mor-
disease, perivalvular abscess, CRP and on-admission PLR (HR: 1.24, 95% CI: 1.11–1.37, p = 0.014) were found as the independent predictors of in-hospital mor-

P4579 | BEDSIDE
The impact of a second mitral valve surgery after repairing a rheumatic mitral valve
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Background: The repair of rheumatic mitral valves (MV) is not consensual, based on the less favourable reports concerning the immediate rate and shorter durabili-
ty of mitral repair (MVR).

Methods: From January 1992 to December 2012, 1491 patients with isolated rheumatic MV disease (tricuspid regurgitation admitted) and without previous MV intervention, were submitted to MV surgery, of which 1201 had MVR (80.5%). There were 136 reoperations during follow-up (124 had MVR and 8 replacement in the first surgery). The causes of reoperation were ascertained and survival (Kaplan-Meier) was further analysed to compare the patients who needed a sec-

Purpose: We purposed to analyse MV reoperations in this setting and the impact of a second mitral valve intervention after repairing a rheumatic MV.

Results: The mean age was 60.6±10.5 years, female gender prevailed (73%), the mean time from MVR to reoperation was 10±5.3 years. In 20 patients (16.1%) it was still possible to re-repair the MV. During MV reoperation, an important number of additional procedures (58.8%) was required: tricuspid re-

Conclusions: Despite a degree of subjectivity in reading RHD screening echocardiograms, concordance was in line with reporting of other screening tools. Inter-rater variability did not alter study outcomes suggesting that reporting of screening echocardiograms has clinical utility in those at increased risk of RHD.

Acknowledgement/Funding: Supported by the National Health and Medical Re-
search Council (Australian Government)

P4580 | BEDSIDE
How accurate are cardiologists at detecting aortic and mitral murmurs? a reality check on auscultation skills in the era of transcatheter interventions
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Background: Recent dramatic breakthroughs in the transcatheter treatment of aortic and mitral valve disorders have offered amazing new therapies to patients. However to fully benefit from these procedures, patients need their cardiologist to detect their valve problem in a timely manner. We wanted to test cardiologists’ auscultation skills at detecting common aortic and mitral murmurs.

Purpose: To assess the skill of cardiologists in detecting basic and advanced aortic and mitral murmurs.

Methods: A total of 1098 cardiologists volunteered to undergo a test of their aus-
cultation skills at an annual cardiology meeting (American College of Cardiology) during a 2 year period (2013 to 2014). Cardiologists chose to be tested on a set of basic murmurs including Aortic Stenosis, Aortic Regurgitation, Mitral Steno-

Results: On the advanced murmurs, 932 cardiologists scored 65.8±13% on a pretest which increased to 88.4±15% on the posttest (p < 0.001 by paired t-test).

Conclusions: Cardiologists’ auscultation skills on both basic and advanced murmurs are alarmingly low. These skills are crucial for patients to fully benefit from the amazing advances in transcatheter treatments for valvular heart disease. However, these auscultation skills improve dramatically following intensive rep-

P4579 | BEDSIDE
Inter-rater variability in reporting screening echocardiograms for rheumatic heart disease in high risk populations

Background: By the end of 2012, 75% of the world’s aortic valve disease sufferers were living in the Asia Pacific region. Despite the amazing advances in transcatheter treatments for valvular heart disease.

Purpose: To determine the impact of inter-rater variability in reading RHD screen-
ing echocardiograms with Borderline RHD and NSVAs on identifying those at in-

Results: On the advanced murmurs, 932 cardiologists scored 65.8±13% on a pretest which increased to 88.4±15% on the posttest (p < 0.001 by paired t-test).

Conclusions: Cardiologists’ auscultation skills on both basic and advanced murmurs are alarmingly low. These skills are crucial for patients to fully benefit from the amazing advances in transcatheter treatments for valvular heart disease. However, these auscultation skills improve dramatically following intensive rep-

P4581 | BEDSIDE
Aortic valve replacement with or without concurrent coronary artery bypass grafting in octogenarians: a 8-year cohort study

Background: Given the introduction of transcatheter aortic valve implantation
(TAVI) as well as increasing demand for intervening severe aortic valve and coronary artery diseases, there is significant interest in evaluating outcomes of aortic valve replacement (AVR) with or without (+/-) concurrent coronary artery bypass grafting (CABG). In particular, it has been reported that high-risk patients tolerate decision-making for modality of intervention.

Purpose: We reviewed the characteristics and outcomes of octogenarians undergoing isolated AVR and AVR+CABG at our centre.

Methods: All patients 80 years of age or older undergoing AVR +/- CABG at our City Hospital during 2005-2012 were included, and their characteristics and outcomes collected for analysis.

Results: There were 93 and 104 octogenarians respectively undergoing isolated AVR and AVR+CABG with mean follow-up of 4.4±2.2 years and 4.1±2.3 years. On average 10 more cases of AVR +/− CABG per year were performed from 2010 onwards than before (2010 onwards median=3 per year and before release median=2 per year). We started at our centre. AVR+CABG patients have significantly higher proportion with history of myocardial infarction, left main and three vessel disease (all P<0.005), higher average CCS and NYHA class (both P<0.001), impaired renal function (P<0.019), higher STS score (6.9% vs 4.9%, <0.001) and longer cardiopulmonary bypass and cross-clamp time (both P<0.001) compared to AVR. They also had significantly higher rate of operative mortality (6.7% vs 0.0%, P=0.015) and prolonged ventilation 24 hours (23.1% vs 10.7%, P<0.001), but similar late mortality (P=0.195), Survival at 1, 3 and 5 years were 94.6%, 82.6% and 73.0% for AVR and 91.3%, 86.1% and 67.6% for AVR+CABG.

Conclusion: AVR+CABG had significantly higher but acceptable operative mortality in octogenarians similar to other studies and age-groups. These factors are important for the consideration of patients undergoing AVR +/- CABG or TAVI +/- percutaneous coronary intervention, where age alone should not exclude one from undergoing cardiac surgery.

P4582 | BEDSIDE
Impact of direct transcatheter aortic valve implantation on final device position and paravalvular leak. Is it beneficial?

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Background: Transcatheter aortic valve implantation (TAVI) may be limited by paravalvular leak (PVL) related to malpositioning of the bioprosthesis. Balloon aortic valvuloplasty (BAV) prior device implantation is often used. The potential effect of BAV in the implantation depth (ID) and consequently in post-TAVI PVL is not known.

Purpose: We compared patients in whom BAV was performed prior to device implantation in the same session during TAVI, with those that BAV was not used. ID and PVL was evaluated.

Methods: We studied 191 consecutive patients who underwent TAVI by two interventionalists. The one is using direct TAVI while the other is using BAV prior to implantation, as default strategies. There were 147 patients (78 males; 81±5 years) with native and inoperable severe aortic regurgitation. The aim this study was to evaluate the use of TAVI in patients with pure native aortic valve regurgitation and comparing them with patients with aortic stenosis.

Results: Baseline clinical characteristics were comparable between the BAV and no-BAV group. ID at NC increased from stage 1 to stage 2 to stage 3 (4.5mm±1.8SD to 7.4mm±2.7SD to 8.2mm±5.2SD, respectively), (repeated measures ANOVA, p<0.001). Thus, when we compared the difference of the ID (stage 3-stage 2) between group 1 and group 2, we found significant increase in depth in group 1 (+0.77mm±4.2SD) vs significant decrease of the ID in group 1 (−0.56mm±4.2SD), (p=0.033). These differences were not detected at LC. In a linear regression the absence of BAV prior to device implantation was the only predictor for greater ID after device release. In addition, PVL of grade II immediately post implantation was less in group 2 vs group 1 (6.8% vs 20.4%, p<0.036, respectively), probably as a result of close contact and the absence of tears in the aortic cusps.

Conclusions: The absence of BAV prior to device implantation, lead to a deeper position, probably by restricting the corrective manipulations. However PVL is less. The exact mechanism is not known and further studies are needed to explore these findings.

P4583 | BEDSIDE
Treatment of post procedural aortic regurgitation in transcatheter aortic valve replacement patients


Background: Post procedural aortic regurgitation (AR) is a prevalent adverse outcome of transcatheter aortic valve replacement (TAVR), which has significant impact on mortality.

Purpose: Our goal was to evaluate methods of treatment of post-procedural AR in TAVR patients.

Methods: We categorized patients with AR—mild following valve deployment to 3 groups consisting of balloon post-dilation only, second valve deployment and medical therapy only.

Results: Among 649 patients undergoing TAVR, we identified 96 (15%) patients with AR—mild following deployment, of whom 69 (72%) were treated with balloon expandable device. Treatment groups were balloon post-dilation in 40 (42%), second valve implantation in 9 (9%) among which 5 patients were treated with balloon post-dilation prior to the second valve deployment, and medical therapy in 47 patients (49%). Reduction of AR to mild and below was noted in 59% and 89% of the re-ballooning group and second valve group, respectively, while no reduction was noted in the medical therapy group. Mortality rates at 1-year tended to be lower in patients with re-intervention compared with medical therapy (25% vs. 43%, p<0.08), and lower in patients with low AR severity compared with moderate and above (28% vs. 39%, p=0.1).

Conclusions: Re-ballooning or second valve implantation successfully reduces severity of AR in TAVR patients and should be sought diligently in order to improve survival rates.

P4584 | BEDSIDE
Safety of transcatheter aortic valve implantation in patients with pure native aortic valve regurgitation

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Transcatheter Aortic Valve Implantation (TAVI) has become an alternative to surgical treatment in patients with severe aortic stenosis and high surgical risk, however, in patients with native and inoperable severe aortic regurgitation remains limited. The aim this study was to evaluate the use of TAVI in patients with pure native aortic valve regurgitation and comparing them with patients with aortic stenosis.

Methods: From April 2008 to December 2014, the CoreValve prosthesis (Medtronic, USA) was implanted in 10 consecutive high-risk surgical patients with symptomatic severe aortic regurgitation (AR) and in 431 patients with aortic stenosis (AS).

Results: The mean age and logistic EuroSCORE were similar in both groups (AR vs. AS) 79.2±4.9 vs 79.2±6.8 years, p=0.993 and 15.3±8% vs. 17.7±12, p=0.552 respectively. There were significant differences in measurement of anulus and ascending aortic size (24.5±1.7 vs 22.1±1.8 mm, p<0.001 and 34.1±2.8 vs 31.6±4.1 mm, p=0.005, respectively). Implantation of a TAVI was performed successfully in all patients with AR and the post-procedure aortic regurgitation grade was: absent in 5 patients, moderate-moderate in 4 patients, and moderate-severe in one patient. The NYHA functional class improved from 3±0.6 to 1±0.5 and remained stable at one year. The mortality at 30 days was 10% in patients with AR compared to 3.7% in patients with AS, p=0.307 and there was no significant differences with late mortality (11.2% vs. 15.2%, p=0.736) after a mean follow-up of 30.5±20 months. The patients with AR had more acute kidney injury after procedure and a lower occurrence of new onset left bundle branch block than patients with AS. 40% vs. 15.3% [OR=3.68 (95% CI 1.01-13.4), p=0.037] and 11.1% vs. 47.8%, [OR=0.96 (95% CI 0.92-0.99) p=0.030], respectively.

Conclusions: TAVI with the CoreValve prosthesis for patients with aortic regurgitation and a high surgical risk is a safe and efficient option resulting in a medium-term clinical improvement.
PERICARDIAL AND MYOCARDIAL DISEASE, TUMOURS, OTHER

P4585 | BEDSIDE
Layer-specific strain in diabetic patients with normal ejection fraction using speckle tracking imaging

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Objectives: Preclinical left ventricular systolic dysfunction was documented in diabetes mellitus (DM) patients with normal ejection fraction (EF). The aim of this study is to quantitatively assess whether there is any difference in GLS and GCS of three-layers of cardium between DM patients and normal subjects using speckle-tracking imaging.

Methods: Fifty-seven DM patients and 60 matched controls were studied. All subjects have normal EF (<55%), GLS and GCS of three-layer cardium were assessed using layer-specific speckle-tracking echocardiography.

Results: GLS of three-layer cardium in DM patients are lower than the normal level of control (DM vs normal, endo-GLS: -23.62±3.16 vs -25.06±2.85, P<0.05; mid-GLS: -20.80±2.86 vs -22.15±2.59, P<0.05; epi-GLS: -18.37±2.69 vs -19.63±2.40, P<0.05). GCS of endo- and mid-cardium in DM patients are lower than those of normal controls (DM vs normal, endo-GCS: -29.31±5.31 vs -34.61±4.78, P<0.05; mid-GCS: -17.59±3.57 vs -20.70±3.03, P<0.05). GCS of three-layer cardium is the highest at the apex and the lowest at the base.

Conclusion: GLS of three-layer cardium may be a sensitive indicator of early left ventricular systolic dysfunction in DM patients with normal EF. GLS decreases in the infero-apical cardium, while GCS decreases only in endo-cardium and mid-cardium in DM patients.

P4586 | BEDSIDE
Anakinra: an emerging option for refractory idiopathic recurrent pericarditis: a systematic review of published evidence

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Purpose: Accumulating evidence suggests idiopathic recurrent pericarditis as a disease of probable autoinflammatory origin, and thus anakinra, an interleukin-1 inhibitor, could be of benefit.

The goal of this systematic review was to assess the efficacy and safety of anakinra in this context.

Methods: Among 12 citations retrieved, nine reports (four case series and five single case reports, with an overall population of 30 patients with 20 males and mean age 27 years) were included. The mean disease duration was 14 months and the mean number of recurrences before IVIG was 3. IVIG were prescribed after failure of other therapeutic attempts including at least NSAID, colchicine and corticosteroids. Approximately 47% of patients had idiopathic recurrent pericarditis, 10% had an infective cause, and the remainder a systemic inflammatory disease. Nineteen out of the 30 patients (63.3%) were on corticosteroids at IVIG commencement. IVIGs were generally administered at a dose of 400–500 mg/kg/day for 5 consecutive days for one cycle and with possible repeated cycles according to the clinical response. Complications were uncommon (headache in approximately 3% of cases) and not severe or life-threatening. After a mean follow-up of approximately 33 months, no cases occurred of pericardial effusion after the first IVIG cycle, and 6.6% after subsequent cycles. At the end of follow-up, 22 of the 30 patients (73.3%) were recurrence-free and five patients (16.6%) were on corticosteroids.

Conclusions: IVIG are rapidly acting, well tolerated, and efficacious steroid-sparing agents in refractory recurrent pericarditis after failure of conventional therapies.

P4587 | BEDSIDE
Lipoprotein-associated phospholipase A2 (Lp-PLA2), a vascular inflammation marker, is frequently increased in patients presenting with acute pericarditis

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Introduction: Lp-PLA2 plays a causal role in the development of atherosclerosis and contributes to plaque instability through pathways related to non-systemic inflammation. Lp-PLA2 concentration in healthy controls is 163±43 ng/ml and 235 ng/ml is used as a cutoff value for clinical decision. So far, Lp-PLA2 levels were not reported among acute pericarditis (AP) patients.

Hypothesis: Levels of Lp-PLA2 in AP, a nonvascular inflammation, should be “normal” ~235 ng/ml.

Population and methods: Lp-PLA2 mass (Piac test) was measured in 39 patients with AP presenting with chest pain, ST elevation and increased Troponin I (Tnl).

Results: Patients aged (mean±SD, median): 37.6±14.2, 32, respectively, 90% were males. Mean (SD), median and range of Lp-PLA2 were 247 (66), 237, 139–408 ng/ml, respectively. Abnormal Lp-PLA2 level (greater than 235ng/ml) was present in 51% of cases.

Table 1 depicts Lp-PLA2 associations with markers of inflammation and necrosis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Pearson correlation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-RP</td>
<td>8.4 (7.3) mg%</td>
<td>0.441</td>
<td>0.011</td>
</tr>
<tr>
<td>Trl</td>
<td>3.4 (3.2) ng/ml</td>
<td>0.339</td>
<td>0.037</td>
</tr>
<tr>
<td>CPK</td>
<td>324 (287) units</td>
<td>0.329</td>
<td>0.044</td>
</tr>
<tr>
<td>WBC</td>
<td>10.6 (4.5)10^3 cells/L</td>
<td>0.02</td>
<td>0.905</td>
</tr>
</tbody>
</table>

AP, a nonvascular inflammation, was associated with increased levels of Lp-PLA2 a vascular specific marker.

Conclusions: We demonstrated that Lp-PLA2 is increased in AP patients and its level correlates with systemic markers of inflammation and necrosis suggesting that this enzyme is not exclusively associated with vascular/unstable plaque inflammation.

P4588 | BEDSIDE
Intravenous human immunoglobulins for refractory recurrent pericarditis: a systematic review of all published cases

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Purpose: Refractory recurrent pericarditis is a major clinical challenge after colchicine failure, especially in corticosteroid-dependent patients. Human intravenous immunoglobulins (IVIG) have been proposed as possible therapeutic options for these cases. The goal of this systematic review is to assess the efficacy and safety of IVIG in this context according to published studies.

Methods: Studies reporting the use of IVIG for the treatment of recurrent pericarditis and published up to December 2014 were searched in several databases. All references found, upon initial assessment at title and abstract level for suitability, were consequently retrieved as full reports for further appraisal.

Results: Among the 18 citations retrieved, 17 reports (4 case series and 13 single case reports, with an overall population of 30 patients with 20 males and mean age 27 years) were included. The mean disease duration was 14 months and the mean number of recurrences before IVIG was 3. IVIG were prescribed after failure of other therapeutic attempts including at least NSAID, colchicine and corticosteroids. Approximately 47% of patients had idiopathic recurrent pericarditis, 10% had an infective cause, and the remainder a systemic inflammatory disease. Nineteen out of the 30 patients (63.3%) were on corticosteroids at IVIG commencement. IVIGs were generally administered at a dose of 400–500 mg/kg/day for 5 consecutive days for one cycle and with possible repeated cycles according to the clinical response. Complications were uncommon (headache in approximately 3% of cases) and not severe or life-threatening. After a mean follow-up of approximately 33 months, no cases occurred of pericardial effusion after the first IVIG cycle, and 6.6% after subsequent cycles. At the end of follow-up, 22 of the 30 patients (73.3%) were recurrence-free and five patients (16.6%) were on corticosteroids.

Conclusions: IVIG are rapidly acting, well tolerated, and efficacious steroid-sparing agents in refractory recurrent pericarditis after failure of conventional therapies.

P4589 | BEDSIDE
Cardiac assessment of patients with familial amyloid polyneuropathy

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Background: Familial amyloid polyneuropathy (FAP) is an autosomal dominant disease, caused by a mutation in the transthyretin gene. It is characterized by a wide heterogeneity of genotypes and predominantly neurological and cardiac phenotypes.

Purpose: The purpose of this study was to assess cardiac involvement in a group of patients with FAP.

Material and methods: Forty five consecutive patients with genetically verified FAP were prospectively included in the study. All patients were referred to our center because of signs and symptoms of peripheral neuropathy. Cardiac assessment included a clinical examination, electrocardiography (ECG), echocardiography (Echo). The mean age (range) of the patients was 58.6±6.8 years (42–72 years), 26 of them were male. The following mutations were isolated - Glu89Gln in 35 patients, Val30Met in 5, Ser77Phe in 4 and Ser23Pro in one patient.

Results: Cardiac involvement was evident on echocardiography in all patients. There was a significant increase in left and right ventricular wall thickness
and the late gadolinium enhancement (LGE) on CMR in patients with HCM.

**Purpose:**
Sign of myocardial fibrosis/scarring and subsequent depolarization abnormality

**Background:**
Medicine III, Heidelberg, Germany

**Warrant genetic analysis and lead to diagnosis.**

**Expected FAP and the presence of some typical features on Echo and ECG may**

**Cardiac involvement was found in all evaluated patients at the time of**

diagnosis, but peripheral neuropathy was more common presenting condition.

**Cardiac assessment is an important part of the evaluation of patients with**
suspected FAP and the presence of some typical features on Echo and ECG may warrant genetic analysis and lead to diagnosis.

**P4590 | BEDSIDE**
Comparative assessment of right ventricular outflow tract (RVOT) dimensions by echocardiography and magnetic resonance tomography in arrhythmogenic right ventricular cardiomyopathy (ARVC)

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ARVC is an inherited disease that accounts for up to 25% of sudden cardiac deaths in young individuals. Hence, an early diagnosis is essential to prevent fatal outcome. According to the 2010 Task Force criteria (TFC), in transthoracic echocardiography (TEE), a diagnostic criterion is met if RVOT dilation in addition to RV wall abnormalities is present. Recent studies questioned the diagnostic performance of TEE in comparison to cardiac magnetic resonance (CMR). Therefore, we investigated the reproducibility of TEE and CMR RVOT measures in patients with ARVC.

**Methods:**
Besides the TTE RVOT measurements of the TFC (RVOT-PLAX-RVOT1, Fig. 1a; and RVOT-PSAX-RVOT2, Fig. 1b), we assessed 3 additional end-diastolic RVOT measures. These included the RVOT diameter in prolongation of M-Mode for the aorta and LA in PLAX (RVOT3, Fig. 1a), the RVOT diameter in prolongation of M-Mode for the Teichholz calculation of LVEF (RVOT4, Fig. 1a), and the distal RVOT diameter right below the pulmonary valve (RVOT5, Fig. 1c).

**Results:**
These are preliminary results from an ongoing study. Up to now, in 24 patients with a definite, borderline or possible ARVC diagnosis, CMR and TTE were performed. Significant differences between CMR and TTE were found for RVOT2 (p=0.011) and RVOT5 (p=0.002). RVOT1 and RVOT4 exhibited the highest correlation (r=0.88 each), compared to RVOT3 (r=0.80). The best agreement between TTE and CMR was found for RVOT4.

**Conclusions:**
Meaning the RVOT in the Teichholz projection provides the highest reproducibility between TTE and CMR, implying a high robustness. TFC defined RVOT1 also provides a good correlation, whereas RVOT2 differs significantly between both methods. If our results can be validated in a larger cohort, the novel RVOT4 measurement has the potential for an improved diagnosis of ARVC.

**P4591 | BEDSIDE**
Fragmented QRS complexes in patients with hypertrophic cardiomyopathy: a marker of myocardial fibrosis detected by cardiac magnetic resonance imaging with gadolinium enhancement

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Background: Fragmented QRS complexes (fQRS) have been shown to be a sign of myocardial fibrosis/scarring and subsequent depolarization abnormality in patients with dilated cardiomyopathy, cardiac sarcoidosis and repaired cardiac tetralogy.

**Purpose:**
The aim of this study was to evaluate the association between the fQRS and the late gadolinium enhancement (LGE) on CMR in patients with HCM.

**Methods:**
The 12-lead ECGs of 191 patients with HCM who underwent CMR with gadolinium were analysed for the presence of fQRS. fQRS was defined as an additional deflections on the beginning or top of R wave (R'), or notchting/fragmentation in the nadir of the R or S wave in 2 contiguous leads. Patients with typical bundle branch block pattern and with QRS $>$ 120 ms (n=31) were excluded from analysis.

**Results:**
Of the remaining 160 patients, 64 (40%) had fQRS on 12-lead ECG and 102 (63.8%) had LGE on CMR. Patients with and without fQRS were of similar gender (69% vs. 73% male respectively, p=0.52) and age (56±16 vs. 57±14 years respectively, p=0.78). LGE was significantly more prevalent in patients with fQRS complexes than patients without fQRS complexes (n=47, 73% vs. n=55, 57%, p=0.037). The positive predictive value of fQRS for LGE on CMR was 73.4%, with a specificity of 70.6%, sensitivity of 46% and negative predictive value of 42.7%.

Patients with fQRS had also longer QRS duration (101ms±16ms vs. 92ms±13ms, p=0.001) indicating depolarization abnormality/delay in these patients.

**Conclusions:**
The presence of fQRS on 12-lead ECG is associated with LGE on CMR and may warrant further evaluation for better risk stratification in patients with HCM.

**P4592 | BEDSIDE**
Prognostic significance of non-dilated left ventricular size and mitral regurgitation in patients with end-stage phase of hypertrophic cardiomyopathy

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Background:
Although a subtype of hypertrophic cardiomyopathy (HCM), end-stage phase of HCM characterized by left ventricular (LV) systolic dysfunction, has been reported to have a poor prognosis, some patients with end-stage HCM survive for a relatively long period. In patients with LV systolic dysfunction, degree of LV dilatation and functional mitral regurgitation (MR) are generally thought to be important predictors of poor prognosis. However, there has been little information on the relations among LV size, presence of MR and prognosis in end-stage HCM patients.

**Purpose:**
The aim was to determine whether echocardiographic assessment of LV size and MR provides incremental prognostic information for those patients.

**Methods:**
We studied 31 consecutive patients with end-stage HCM.

**Results:**
During a follow-up period of 5.6±2.4 years, there were 13 HCM related deaths (cardiovascular survival rate of 64% at 5 years from diagnosis of end-stage phase). When the patients were divided into two groups by LV size at diagnosis of end-stage HCM: a non-dilated LV group (LV end-diastolic diameter (LVEDD) $<$50 mm, n=9) and a dilated LV group (LVEDD $>$50 mm, n=22), clinical course in the non-dilated LV group was significantly worse. As for the clinical impact of MR, no patient in the non-dilated LV group showed significant MR and 7 of the patients with dilated LV size showed significant MR during follow-up. Once significant MR was reached, HCM related deaths were significantly more frequent in patients with MR (Figure: HCM related deaths according to LV size and presence of significant MR).

**Conclusions:**
Patients with end-stage HCM, particularly those with less LV dilatation at diagnosis of end-stage phase and with significant MR during follow-up, had a poor prognosis.
Results: 172 mutation carriers had sufficient functional MRI studies and 160 for additional LGE analysis (mean age at MRI 42±15 years; 43% males). Mean LVEF was 57±10% (range 11–75%) and RVEF 55±9% (range 13–71%). There was a significant correlation between LVEF and RVEF (r=0.83; p<0.001). LV-LGE was present in almost all mutation-carriers with reduced LVEF but, interestingly, also in 30% (44/148) of mutation carriers with preserved LVEF (Fig. 1). On average, 7% of LV myocardium was affected, particularly in the interventricular septum (segments 5 and 11).

Conclusions: In PLN R14del mutation carriers, both reduced LV and RV function can be observed, attesting to the biventricular nature of the disease. LV myocardial fibrosis appears to often be an early manifestation, seen even in the presence of preserved LVEF. We are currently investigating the correlation between myocardial fibrosis, electrocardiographic features and arrhythmia occurrence.

PAEDIATRIC CARDIOLOGY, OTHER

P4595 | BENCH

HsTNFα/Bench activity and the severity of inflammation, hypertrophy and fibrosis in pts with inflammatory cardiomyopathy
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Objective: To evaluate the role of hsTNFα in the verification of the inflammatory cardiomyopathy (ICM).

Methods: 35 patients mean age 40.8±11.3 (21 male, 14 female), I-II class NYHA, mean LVEF 33.8±6.36%, with symptomatic heart failure median 2.0 [1.0; 3.0] years and suspected inflammatory cardiomyopathy underwent endomyocardial biopsy (EMB). EMB specimens were investigated with histological and molecular-genetic methods with PCR detection of cardiotropic viruses. Diagnosis was based on World Health Organization criteria. Leucocytes and macrophages criteria amount was ≥14. Sera were taken for testing hsTNFα.

Results: The total number of EMB patients was 35 (100%). ICM was diagnosed in 15 cases (42.8%) [9 cases (25.7%) were virus-positive and 6 cases (17.1%) were virus-negative]. DCMP without signs of active inflammation was revealed in 20 pts (57.1%). [12 cases (34.2%) were virus positive and 8 cases (22.8%) were virus negative]. Mean NYHA FC was 2.06±0.77 in ICM pts group and 2.17±0.57 in DCMP pts group (p=0.6). According to EMB results, the myocardiun median of lymphocytes, expressing CD4+, CD8+ and CD68+ were 13.5 [10.0; 20.0], 10.0 [6.0; 11.7] and 3.5 [0.0; 15.5] relatively in pts with ICM, that was significantly higher compared with DCMP group without active inflammation: relatively 1.8 [0.0; 3.2] for CD4+, 3.1 [1.5; 4.2] for CD8+ (p<0.0001) and 0 [0.0; 0.6] for CD68+ (p=0.009). Between the whole groups of ICM and DCMP without active inflammation there was no significant difference in the level of hsTNFα 3.1 [1.3; 9.7] versus 1.9 [0.8; 3.9] (p=0.47) relatively. According to the quantiles of infiltrating cells/mm² of myocardium, the patients were divided into four groups: 1 group (0–4 cells), 2 group (5–10 cells), 3 group (11–17 cells), 4 group (>17 cells). Pts with more than 17 cells/mm² had the maximum level of hsTNFα 5.1 [3.2; 10.3] versus 1.3 [0.4; 3.1] in other groups (p=0.03). ICM group pts also have had positive correlation of hsTNFα with the total number of myocardiun infiltrating cells/mm² r=0.5,p=0.02 [especially with CD68+cells/mm² r=0.88,p=0.01]; CD4+ (r=0.57,p=0.008), degree of hypertrophy (r=0.7,p=0.002) and fibrosis (r=0.6,p=0.024).

Conclusions: The level of hsTNFα was significantly higher in the pts with the most pronounced inflammatory process and associated with the severity of myocardial inflammation, degree of hypertrophy and fibrosis.

PAEDIATRIC CARDIOLOGY

P4594 | BENCH

Cardiac MRI characterization of phospholamban R14del-related cardiomyopathy
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Background: The Dutch R14del founder mutation in the gene encoding for phospholamban (PLN) causes dilated and/or arrhythmogenic cardiomyopathy and is associated with increased risk of malignant ventricular arrhythmias and heart failure.

Purpose: To study ventricular function, and extent and localization of fibrosis using cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE) in PLN R14del mutation carriers.

Methods: Contrast CMR studies of a representative sample of 196 mutation carriers were retrospectively analyzed. All imaging was performed in our University Medical Center, Academic Medical Center and Hospital. Left ventricular (LV) and right ventricular (RV) volumes, mass and ejection fraction (EF) were measured. The amount of LGE was quantified and expressed as percentage of myocardiun mass.

Results: 172 mutation carriers had sufficient functional MRI studies and 160 for additional LGE analysis (mean age at MRI 42±15 years; 43% males). Mean LVEF was 57±10% (range 11–75%) and RVEF 55±9% (range 13–71%). There was a significant correlation between LVEF and RVEF (r=0.83; p<0.001). LV-LGE was present in almost all mutation-carriers with reduced LVEF but, interestingly, also in 30% (44/148) of mutation carriers with preserved LVEF (Fig. 1). On average, 7% of LV myocardium was affected, particularly in the interventricular septum (segments 5 and 11).

Conclusions: In PLN R14del mutation carriers, both reduced LV and RV function can be observed, attesting to the biventricular nature of the disease. LV myocardial fibrosis appears to often be an early manifestation, seen even in the presence of preserved LVEF. We are currently investigating the correlation between myocardial fibrosis, electrocardiographic features and arrhythmia occurrence.
P4597 | BEDSIDE
Clinical and echocardiographic predictors for the recurrence of subaortic stenosis
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Introduction: Obstruction of the left ventricular outflow tract (LVOT) and resultant sub-aortic stenosis (SAS) may represent an acquired condition since it is rarely recognized during the newborn period, but is common in later life. Recurrence of SAS after corrective surgery, requiring reoperation, occurs in up to 55% of patients. Conflicting data exist regarding the predictors of recurrence of SAS after surgical resection.

Purpose: This study aimed to determine predictors for the recurrence of SAS requiring repeat surgery after initial surgical resection.

Methods: Demographic, clinical, anatomical pre- and post-operative echocardiographic characteristics of 93 consecutive paediatric and adult patients with SAS were recorded. Parameters were compared between two groups, those who underwent repeat surgery and those who did not. Multivariate regression analysis was used to determine the predictors of the recurrence of SAS requiring reoperation. Receiver operator curve analysis was utilized to determine the sensitivity and specificity of prediction of the need for re-operation.

Results: Thirty seven patients (39.8%) required reoperation for recurrent SAS. These patients underwent initial operation at a younger age (5.3±10.0 vs 11.6±15.7, p=0.001) than those without reoperation. Preoperatively they had lower left ventricular ejection fraction (67.6±9.5% vs 73.6%±7.5%, p=0.007) and fractional shortening (FS) (43.5±9.0 vs 39.0±9.4, p=0.027) and the narrowest angle (130.5±8.5° vs 136.1±8.3°, p=0.006) and smaller mitral valve annulus diameter (15.6±5.9 mm vs 20.2±6.4 mm, p=0.003). They had a shorter distance between the point of obstruction of the LVOT and the aortic valve annulus both in systole and diastole (4.9±2.3 mm vs 6.9±4.1 mm, p=0.008 and 4.5±2.8 mm vs 6.7±4.2 mm, p=0.006). Post-operative residual SAS with high peak and mean trans-aortic gradients (28.7±15.1mmHg vs 20.4±10.5mmHg, p=0.003 and 15.5±3.8mmHg vs 10.2±2.5mmHg, p=0.002) was more common in patients with recurrence compared to those without recurrence (80% vs 21.5%, p<0.001). The aortic angle beta (<–0.436, p=0.001) at baseline and the presence of residual SAS post-operatively (beta=4.900, p=0.001) predicted the recurrence of SAS with 94.4% sensitivity and 88.9% specificity (AUC: 0.970, 95% CI: 0.893–0.997, p=0.0001).

Conclusions: Requirement for reoperation in patients with SAS may be predicted by pre-operative echocardiographic factors which include LV function and geometry, and post-operative residual obstruction.

P4598 | BEDSIDE
Relation between soluble suppression of tumorigenicity 2 (sST2) and brain natriuretic peptide (BNP) in healthy pediatric subjects: from birth through adulthood

The aim of this study was to measure circulating levels of sST2 and BNP in 131 healthy subjects as a function of age, from birth up to adulthood. Moreover, brain natriuretic peptide (BNP) measurement in parallel with sST2 could offer further insight into its role in cardiac physiology.

Methods: Plasma sST2 and BNP were measured in 131 healthy subjects (% males) divided according to age into 5 groups: 28 newborns (0–3 days), 22 neonates (3–30 days), 24 infants (1–12 months), 31 toddlers (1–2 years), 30 adolescents (13–18 years), and 25 adults (>18 years).

Results: sST2 was present in peripheral circulation of all age-groups (Fig A). Newborns showed higher sST2 compared to the other groups (p<0.0001, Fig A).

No sST2 variation was observed throughout the puberty up to adulthood. BNP exhibited the same trend during growth, showing a significant relation with sST2 (r=0.614, p<0.0001) (Fig B).

P4599 | BEDSIDE
It is the time to reconsider the evolution of preexcitation syndrome in children?

Background: With the development of ablation techniques, the natural follow-up of preexcitation syndrome (PS) became difficult to assess. Several years ago studies reported a spontaneous disappearance of PS in children <12 years (y) with a long accessory pathway (AP) effective refractory period (ERP), but stability in children >12 y or with inducible PS and short AP-ERP. The purpose of the present study was to collect the data of untreated children with PS, studied 2 times at least one year of interval and assess the evolution.

Methods: 2 baseline electrophysiological studies (EPS) were performed within 1 to 25 years of one another (mean 7±5 y) in 41 children/teenagers, 19 boys, 22 girls, aged initially from 2 to 19 years (12±4), with overt PS. First EPS (EPS1) was indicated for syncope (n=4), atrioventricular reentrant tachycardias (AVRT) (n=18) or for asymptomatic PS (n=19). The protocol was similar, performed in control state (CS) and after isoproterenol.

Results: At EPS2, among the 41 patients studied for syncope at EPS1, 1 has still syncope, 2 have AVRT, 1 is asymptomatic. Among children with AVRT at EPS1, 15 (84%) have still AVRT, 2 are asymptomatic and 1 presented with rapid AF (malignant form). Among asymptomatic children, 14 (74%) remain asymptomatic, 2 have AVRT, 3 have syncope. AVRT occurring in initially asymptomatic children or children with initially syncope occurred in 2/4 with inducible AVRT at EPS1. The fastest rate conducted by AP tended to be less rapid at EPS2 in CS and after isoproterenol than at EPS1 but differences were not significant (181±75 bpm vs 190±63 in CS) (0.6) (198±82 bpm vs 239±82 after isoproterenol) (0.88). AP-ERP was similar in CS at EPS2 (280±67 ms) and tended to increase from 201±51.5 at ESP1 to 248±73ms at EPS2 (p<0.07) after isoproterenol. AP has lost antegrade conduction in 6 children with initially long AP-ERP but all 5 children with initially inducible AVRT had still inducible AVRT. Two children with initially inducible AVRT at EPS1 had inducible AVRT at EPS2 in asymptomatic PS with initially negative EPS in 4 children.

Conclusions: Unlike previous studies, we found no improvement of clinical and electrophysiological data in children with a PS, even those with an initially long AP-ERP after a mean follow-up of 7±5 y. Most children with spontaneous or inducible AVRT’s at the first evaluation still have inducible AVRT’s at the second evaluation. AP-ERP did not increase significantly. Therefore, long-term follow-up is required in the paediatric population with a PS.

P4600 | BEDSIDE
Follow-up of children and teenagers with paroxysmal supraventricular tachycardia but without preexcitation syndrome
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1 University Hospital of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France; 2 Hospital Brabois of Nancy, INSERM, Centre d’Investigations Cliniques 9501, Université de Lorraine, Vandoeuvre les Nancy, France

Background: Paroxysmal supraventricular tachycardia (SVT) is considered as benign if ECG in sinus rhythm (SR) is normal, but its occurrence in children/teenagers is always associated with an anxiousness of parents, child and doctors. The purpose of the study was to report the clinical and electrophysiological data of children with SVT, their follow-up and management.

Methods: 162 children and teenagers aged from 5 to 19 years (mean 15±3) with normal ECG in SR were studied for spontaneous SVT. Transcatheter electrophysiological study was systematic. Children were followed from 1 month to 13 years (mean 2.15±2.6 years).

Results: SVT was poorly tolerated in 27 patients (17%). SVT was related to atr-
VAD utilization is increasing in children with heart failure (HF) un-

**Background:**

Pisana, Pisa, Italy

Pre-implant values in 3 days (Fig B).

**Purpose:**

With early indications for their use in pediatric population. Soluble suppression of tumorigenicity 2 (sST2) time-course in pediatric patients with heart failure supported by ventricular assist device implant

C. Caselli¹, A. Di Molletta², R. Ragusa³, A. D’Amico⁴, M. Cabiatì⁵, M. Cantinotti⁶, O. G. Ferdinando⁷, S. Del Ry², A. Amodeo², M.G. Trivella¹.

**Methods:**

In 61 untreated patients one death occurred after AAD infusion used to stop SVT, but other patients (37%) remained asymptomatic or had short and well-tolerated SVT.

**Conclusions:**

Management of SVT in children remains difficult despite the development of RF ablation of SVT. Indications of ablation tended to be more frequent in AVNRT than in AVRT. Failure of ablation remains higher than in adults, mainly high in AVRT. Child remains symptomatic in 24% of cases after successful ablation but false recurrences are frequent (18%). In absence of ablation, one third of children had a spontaneous favourable evolution. However in symptomatic children with frequent SVT’s despite antiarrhythmic drugs or beta-blockers, ablation should be indicated to avoid drugs-related adverse effects.

**P4602 | BEDSIDE**

Soluble suppression of tumorigenicity 2 (sST2) time-course in pediatric patients with heart failure supported by ventricular assist device implant

C. Caselli¹, A. Di Molletta², R. Ragusa³, A. D’Amico⁴, M. Cabiatì⁵, M. Cantinotti⁶, O. G. Ferdinando⁷, S. Del Ry², A. Amodeo², M.G. Trivella¹.

**Methods:**

A group of 9 pediatric patients submitted to VAD implant [56±27.6 (mean±SD) months, 5 males, 14±7 LVEF%, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles 1/2] were studied. Indications for support was idiopathic dilated (7 patients) and non compaction cardiomyopathy (2 patients). A group of 90 healthy age- and sex-matched children were used as controls (73±7.7 months, 56% males). sST2 plasma levels were measured by a dedicated ELISA before (day 0) and at 4 hrs, 1.7, 3.14, and 30 days after LVAD implant.

**Results:**

Before VAD implant, sST2 levels are highest in HF compared with healthy children (p<0.0001 newborns vs. children, Fig A). After device implantation sST2 plasma levels significantly increased during first day and returned to pre-implant values in 3 days (Fig B).

sST2 in HF pediatric patients

**Conclusion:**

In pediatric population, circulating levels of sST2 were associated with presence of HF and if its plasma levels are modified after VAD implantation is an active, regulated process similar to osteogenesis, relating to the chronic inflammatory signals.

**P4603 | BEDSIDE**

Risk stratification and outcome in patients with coronary artery lesions caused by kawasaki disease

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Outcome in patients with coronary artery lesions (CAL) caused by Kawasaki disease (KD) depends on coronary artery aneurysm (CAA) characteristics in the acute phase. (Aim) Risk stratification (RS) and prediction of outcomes in patients with CIF. In the patients with CAL, AVSD and/or isolated mitral cleft was the only risk factors for mortality and reper-

**Methods:**

We reviewed the outcome and incidence of cardiac events in 214 patients (159 male 55 female) who had CIA an initial coronary angiogram within 100 days of the acute onset between 1978 and 2011. We divided the patients into three groups determined by the maximum CAA diameter (L<8mm; M 8±0.5 or S <6mm). Further, we classified between either bilateral group or unilateral group, adopting the laterality of the maximum CAA to decide the respective group, and between either body surface area <0.5 or >0.5. Cardiac events (CE) included death, acute myocardial infarction (MI) and coronary artery revascularization. CE free rates were analyzed by Kaplan-Meier method.

**Results:**

The follow-up period in respective groups were 182±10, 162±8 and 11±17 years (mean±SD). Cardiac events occurred in 43 pts as shown here by groups. About half of which related to MI. Coronary artery revascularization was undertaken in about 70%. The 25-year CE free rate in respective groups based on the diameter and the laterality of the maximum CAA is shown in Table. The 25-year cardiac events free rate

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BSA, body surface area.

**Conclusion:**

CE in patients with CAL caused by KD can occur, in the case with "the maximum CAA diameter ≥6.0 mm when BSA ≥0.50" and "the maximum CAA diameter <6.0 mm when BSA = 0.50" in the acute phase. In the patients with bilateral large CAA, incidence of cardiac events was more frequent than in pts with unilateral large CAA. At least one optimal coronary revascularization would improve the outcome for such patients.

**P4604 | BEDSIDE**

Possible mechanism of coronary calcification in chronic-phase Kawasaki disease

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**Background:**

Kawasaki disease (KD) is a systemic vasculitis prevalent in infants and sometimes complicates coronary artery lesions (CALs). It has been well known that coronary calcification is common in chronic patients with CALs but, nevertheless there are still many unclear points regarding the mechanism and clinical significance of it. Recently, it has been reported that vascular calcification is an active, regulated process similar to osteogenesis, relating to the chronic

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**Conclusion:**

CE in patients with CAL caused by KD can occur, in the case with "the maximum CAA diameter ≥6.0 mm when BSA ≥0.50" and "the maximum CAA diameter <6.0 mm when BSA = 0.50" in the acute phase. In the patients with bilateral large CAA, incidence of cardiac events was more frequent than in pts with unilateral large CAA. At least one optimal coronary revascularization would improve the outcome for such patients.
inflammation and oxidative stress. Therefore, vascular calcification also promote bone resorption and decrease bone mineral density (BMD). In this study, in KD, we evaluated the possible implication of significant calcification prevalent in CALs to the long-term prognosis.

Methods: We included 48 patients with a history of KD (age: 16.9±6.2 year-old). The breakpoint was 19 patients without CALs and 29 with CALs; 16 without calcification and 13 with calcification on multi-detector computed tomography. We measured %FMD as an endothelial function marker and hs-CRP as an inflammatory marker, serum hydroxproside and urinary 8-OHdG as oxidative stress markers. Patients in CAL(−) group took no medicine and those in CAL(+) group were under antiplatelet and/or anticoagulant therapy, particularly, those with calcification were additionally administrated statin or ARB.

Results: Values of %FMD in CAL(+) group were significantly lower compared with those in CAL(−) (p<0.05), and values of hs-CRP in patients with calcification were still lower than those without calcification (p<0.05). Values of hs-CRP in CAL(+) group were significantly lower than those in CAL(−) (p<0.05). 8-OHdG values as oxidative stress marker in CAL(+) group were significantly lower than those in CAL(−) (p<0.05). The BMD in CAL(+) group tended to be lower with the age-matched reference values (88.1±7.1% of normal).

Conclusions: In KD chronic stage, the decreased %FMD may be an essential condition to occur coronary calcification. Decreased BMD in patients with coronary calcification suggested the possible relation of vascular calcification and osteo-dysplasia in KD. The findings of similar to the general mechanisms of arterial calcification. The discrepancy in endothelial dysfunction, inflammation and oxidative stress in this study may suggest that it is necessary to consider some novel therapy for improved prognosis of KD patients.

P4605 | BEDSIDE

New concept for left ventricular training in corrected transposition of the great arteries after double switch operation

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Purpose: Patients with corrected transposition of the great arteries (cTGA) beyond the newborn age need a left ventricular (LV) training to undergo a double switch operation (DS) (atrial plus arterial switch operation). A new approach with pulmonary arterial banding (PAB) and atrioseptectomy to increase pre- and afterload is presented in this study. The objective of the study is to evaluate the beneficial effects on LV remodeling and outcome of DS.

Methods: We report on six consecutive patients with cTGA to be trained for DS using this enhanced LV training (eLVT). Five patients had conventional PAB before, but did not reach a sufficient gradient across the banding. All six patients underwent eLVT as the last procedure to reach DS.

Results: Five of six patients underwent successful DS at mean 1.2 years after enhanced LV training (eLVT). The postoperative period was short and uneventful in all patients with a total ventilation time of 24 hours, stay on ICU of 3 days and hospital stay of 11 days (mean ± standard deviation). Overt or asymptomatic follow up period of 1.5 years (7.2 patient years) uneventful cardiac function and biventricular circulation, no additional arrhythmic episodes and regression of tricuspid valve regurgitations were observed.

Conclusion: With the eLVT re-PAB operations can be reduced and DS performed at low risk and short periods on intensive care units. If it is equally efficient in patients older than 12 years, has to remain open. Long term follow-up is still needed and results from other centres are essential to underline the benefit of this procedure.

P4606 | BEDSIDE

Outcome of bilatoc sluss shunt placement without patient ductus arteriosus ligation in neonates with pulmonary atresia

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Background: Modified Blalock Taussig shunt (mBTS) placement has been a life-saving palliative surgical intervention in neonates with congenital heart disease who lack adequate pulmonary blood flow. There is currently no general consensus about the ligature of associated patent ductus arteriosus (PDA) during the procedure.

Purpose: The purpose of the study was to describe the outcome of mBTS without PDA ligation in patients with pulmonary atresia.

Methods: A retrospective chart review was done on all neonates diagnosed with pulmonary atresia who underwent a mBTS during the last 4 year period. Inclusion criteria included: all newborn infants with age of 26 days or less diagnosed with pulmonary atresia who underwent a mBTS placement without PDA ligation. Infants with pulmonary atresia but without associated PDA and those with associated major aortopulmonary collateral arteries (MAPCAs) were excluded from the study. Outcomes of this study included infant mortality and recurrence of pulmonary overcirculation, low diastolic blood pressure, shunt occlusion and death in the early post-operative period.

Results: A total of 29 charts were reviewed and 3 were excluded. 2 were excluded due to the presence of MAPCAs and 1 due to absence of PDA. 26 patients met the study criteria. The age of the patients ranged from 2 to 20 days with gestational age of 32 to 39 weeks. Their birth weights ranged from 1.8 kg to 3.8 kg. Shunt size ranged from 3 mm to 4 mm. 2 (7%) patients developed persistent low diastolic blood pressure (less than 25 mmHg) post operatively that required subsequent PDA ligation. Both patients were delivered at the gestational age of 32 weeks with birth weights of 1.8 kg and 1.9 kg. 3 (11%) patients developed shunt occlusion within the first week of surgery. All 3 were placed on Prostaglandin E1 to keep their ductus arteriosus patent before undergoing stent angioplasty. There were 2 (7%) deaths as a result of shunt occlusion 6 weeks after surgery.

Conclusion: Modified BTS without PDA ligation in neonates who have pulmonary atresia and birth weight less than 2 kg is associated with increased incidence of low diastolic pressure. Failure to ligate PDA during mBTS placement is not associated with increased incidence of early shunt occlusion and is beneficial in the long-term management of patients with early ductus arteriosus closure. We recommend to ligate PDA with Prostaglandin E1 to maintain the ductus arteriosus patent before further intervention.

P4607 | BEDSIDE

Prognostic value of profound iron deficiency in patients with Coronary Artery Disease - establishment of a new functional definition of iron deficiency in the AtheroGene Study

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Introduction: Iron deficient heart patients see improvement with intravenous supplementation. Traditionally, diagnosis of iron deficiency has been based on the assessment of low transferrin saturation (TSat) and reduced serum ferritin. However, these standard measures of iron status seem unreliable, especially in acute clinical settings. There are pathophysiological premises that soluble transferrin receptor (sTfR) and, in particular, circulating hepcidin, which orchestrates systemic iron metabolism, could be more sensitive alternatives for iron deficiency diagnosis. In this study, we aimed to evaluate the prognostic value of a new hepcidin-based definition of iron deficiency in cardiovascular disease.

Methods: Levels of hepaticin, ferritin, sTfR, iron and transferrin were measured at baseline –in 1,303 patients with acute coronary syndrome (ACS) and 2,022 patients with stable angina pectoris (SAP). Iron deficiency diagnosis was defined as a concomitance of depleted body iron stores (demonstrated as low serum hepcidin) and insufficient iron levels in metabolizing cells (demonstrated as high-srum sTfR). Serum hepcidin was measured using a newly available ELISA (DRG). Serum sTfR was measured using an immunobassay (Roche Cobas). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction (MI).

Results: During a median follow-up of 4.6 years, 5.5% of all subjects died. Both, low hepaticin and high sTfR predicted higher mortality rates, even after adjustment for all significant predictors in univariate models. When the traditional definition of iron deficiency and the new functional definition were included in one Cox proportional hazard model, only iron deficiency defined based on serum hepcidin and sTfR remained a significant predictor of 30-day and long-term mortality in patients without coronary artery disease in particular in patients with ACS (Hazard ratio [HR] 2.48, 95% CI 1.2–5.3, in a multivariate model, when preserved iron status was set as standard). In addition, the new definition was a powerful predictor of the combined endpoint cardiovascular death and MI (HR 1.68, 95% CI 1.1–2.6; p<0.019 in CAD, and HR 1.85, 95% CI 1.0–2.3; p=0.039 in ACS). Finally, addition of functional iron deficiency clearly improved various model performance measures, including c-statistics (AUC: 0.778).

Conclusions: A functional definition of iron deficiency based on a concomitance of low-serum hepcidin and high-serum sTfR more accurately allows identifying patients with a particularly poor outcome. These results will impact the paradigm of iron supplementation in cardiovascular disease.

P4608 | BEDSIDE

Association between plaque vulnerability and omega-3 polyunsaturated fatty acids in normal low-density- lipoprotein cholesterol patients with coronary artery disease

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Objective: The aim of this study was to evaluate the relationship between omega-3 polyunsaturated fatty acids (n3PUFAs) and coronary artery vulnerability in normal low-density-lipoprotein (LDL) cholesterol patients with coronary artery disease.

Background: Recent reports suggest that lower serum n3PUFAs is a new risk marker for coronary artery disease.

Methods: Consecutive normal LDL cholesterol patients with stable angina pectoris (n=100) without any lipid lowering therapies were divided into two groups based on the presence of in vivo thin cap fibroatheroma (TCFA) in the de novo target
vessels assessed by the combined use of virtual histology intravascular ultrasound and optical coherence tomography.

**Results:** Eicosapentaenoic acid (EPA)/arachidonic acid (AA), docosahexaenoic acid (DHA)/AA and EPA+DHA/AA ratio were significantly lower in patients with in vivo TCFa than patients without in vivo TCFa (0.30 [0.26–0.37] vs 0.48 [0.33–0.58], 0.86 [0.73–0.94] vs 0.98 [0.82–1.16] and 1.16 [0.95–1.24] vs 1.46 [1.13–1.64], p < 0.05). Although percent necrotic core volume was significantly higher in the definite TCFa group (23.5% [21.7 to 25.1] vs 20.3% [16.2 to 22.8], p < 0.01), there was no significant correlation with laboratory data. On the other hand, EPA/AA, DHA/AA and EPA-DHA/AA ratio were positively correlated with thinnest fibrous cap thickness (r=0.75, p < 0.01; r=0.43, p < 0.01; and r=0.66, p < 0.01).

**Conclusion:** Low EPA/AA, DHA/AA and EPA-DHA/AA ratio might be associated with coronary plaque vulnerability even in patients with a normal LDL cholesterol level.

### P4610 | BEDSIDE

**Relations of estradiol, total testosterone and sex-hormone binding globulin to 11-year cardiac metabolic risk factors changes in postmenopausal women: the Rotterdam Study**

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**Background:** Information is sparse on the role of sex-hormones in the change of long-term individual cardio-metabolic risk factors in postmenopausal women. Objective: We investigated relations between estradiol, total testosterone (TT) and sex-hormone binding globulin (SHBG), and changes in blood lipids, glucose levels, blood pressure and anthropometric measures over time.

**Methods:** Data of 2,827 postmenopausal women (>55 years), participating in the prospective population-based Rotterdam Study, were available. Sex-hormones (estradiol, TT and SHBG) were measured at baseline whereas cardio-metabolic risk factors (fasting total serum cholesterol, fasting high density lipoprotein (HDL)-cholesterol, fasting glucose, systolic (SBP) blood pressure, body mass index (BMI) and waist circumference (WC)) were assessed at baseline as well as 5 and 10 years later. Generalized estimating equations were used to analyze relations between sex-hormones (as continuous) and average annual individual cardio-metabolic risk factor changes. Bonferroni correction for multiple testing was applied (P < 0.004 was considered as significant).

**Results:** One unit increase in estradiol level was associated with an annual rise of 0.02 mg/dl in serum total cholesterol and with a corresponding annual decrease of 0.03% in HDL-cholesterol, glucose or WC (P < 0.004). One unit increase in estradiol level was associated with an annual rise of 0.03 kg/m2 in BMI (P < 0.003). There was no association between sex-hormones (as continuous) and average annual individual cardio-metabolic risk factor changes. Bonferroni correction for multiple testing was applied (P < 0.004 was considered as significant).

**Conclusion:** This is one of the first studies that simultaneously examine the associations of change in levels of individual cardiac metabolic risk factor over time with regard to sex-hormones levels. Levels of estradiol, TT and SHBG were associated with diverse changes in individual cardiac metabolic risk factors, suggesting that various levels of sex-hormones may be associated with different levels of cardiac metabolic risk in postmenopausal women.
nificantly correlated with Ln-SAA-LDL (P=0.005), but not with other biomarkers. Furthermore, stepwise multivariate regression analysis, including possible confounders and these biomarkers, revealed that Ln-SAA-LDL, but not other biomarkers, was an independent determinant of Ln-Gensini score (P=0.004).

**Conclusions:** Serum levels of SAA-LDL, but not VEGF-C, VEGF-A, sVEGFR-2, or AT-LDL, were independently associated with the presence and severity of CAD. The follow-up data of the ANOX study will provide evidence for the predictive values of these biomarkers independent of known risk factors and the severity of CAD at the baseline.

**Acknowledgement/Funding:** Grant-in-Aid for Clinical Research from the National Hospital Organization

### P4612 | BEDSIDE

**Combining B-type natriuretic peptide and high-sensitivity cardiac troponin I in the evaluation of patients with suspected inducible myocardial ischemia**


**Background:** The diagnosis and prognosis of coronary artery disease currently relies on diagnostic imaging procedures, which are facing concerns due to their high costs and potential risks. Considering this, an easy to use, widely available and cost-effective gatekeeper is of great clinical importance. Previous studies showed high-sensitivity cardiac troponin I (hs-cTnI) and B-type natriuretic peptide (BNP) were independently associated with myocardial ischemia. Therefore their combination additionally to clinical judgment might fill this role.

**Methods:** 1421 consecutive patients referred to rest/bicycle myocardial perfusion SPECT were recruited. We included patients who undergoing exercise stress testing or coronary angiography. Blood samples were drawn before, immediately after and two hours after stress testing. Clinical judgment was assessed using a visual analogue scale before and after stress testing. The diagnostic endpoint of myocardial ischemia was evaluated by myocardial perfusion SPECT and coronary angiogram, if available. Areas under the receiver operating characteristic curves (AUC) were constructed and compared. Prognostic endpoints (death, myocardial infarction, revascularization) were determined by 2 year follow up. Cox regression was used to assess for independence of predictors.

**Results:** Diagnostic setting: Myocardial ischemia was found in 605 (42.6%) of all patients. Levels of hs-cTnI and BNP were significantly higher in patients with inducible myocardial ischemia at all time points (p < 0.01 for all). BNP and hs-cTnI were associated highly significant with presence of exercise induced myocardial ischemia in univariate and multivariate regression (BNP p<0.008, hs-cTnI p<0.001). When combining both biomarkers with the clinical judgment, BNP did not provide a significant advantage to the AUC (0.73 without vs 0.74 with BNP). In all analysis addition of biomarkers markedly improved the AUC compared to clinical judgment alone (p<0.05 for all).

**Prognostic setting:** Median duration of follow up was 754 days and at 720 days the combined endpoint was reached in 300 (21.9%) of patients. Cox proportional hazards analysis showed BNP and hs-cTnI were independent relevant predictors of death, myocardial infarction and revascularization. For calculation of the hazard ratios biomarkers were log-transformed and yielded a HR 1.56 for BNP and 2.35 for hs-cTnI.

**Conclusion:** BNP provided additional value to hs-cTnI and clinical judgment for prognosis, but not for diagnosis, in patients referred to evaluation of suspected exercise induced myocardial ischemia.

### P4613 | BENCH

**Lack of efficacy of higher dose vitamin D supplements on systolic blood pressure and arterial stiffness measure in older people after 12 months of treatment. Results of BEST-D trial**

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**Background:** Lack of plasma levels of 25-hydroxy vitamin D (25(OH)D) are associated with higher risks of cardiovascular disease (CVD). Before planning a large trial of vitamin D to assess effects on CVD outcomes, we conducted a pilot study to determine the optimum dose of vitamin D supplement for such a trial and assessment(s) of vitamin D on blood pressure and arterial stiffness in the BEST-D trial (EudraCT: 2011–005763–24).

**Methods:** 305 patients were randomized to daily supplementation with 100μg vitamin D3, 50μg vitamin D3 or placebo. The primary assessment compared plasma 25(OH)D levels at 12 months between the two active doses. Secondary assessments included the effects of any dose of vitamin D versus placebo on systolic blood pressure (SBP), aortic pulse wave velocity (PWVaco) and augmentation index (AIx), assessed using the Arteriograph (Tensiomed), and stiffness index (SI) and acceleration index (RI), assessed using PulseTrace PC2A, at baseline and at 12 months.

**Results:** Mean (SD) baseline age was 72 years (6), 51% were male and the mean systolic blood pressure (SBP) was 131 (SD 19). Treatment with either dose of vitamin D was associated with a doubling in mean (SE) plasma 25(OH)D levels (119 [1.7] vs 53 [2.4] nmol/L, p<0.0001), but had no significant effect on mean levels of SBP or any of the measures of large or small arterial stiffness after 12 months (Table).

**Table:** Effects of vitamin D supplements

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SBP (mmHg)</th>
<th>PWV (m/s)</th>
<th>AI (%)</th>
<th>SI (m/s)</th>
<th>RI (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>132 (1.0)</td>
<td>10.0 (0.1)</td>
<td>37 (0.9)</td>
<td>9.4 (0.2)</td>
<td>67 (1.7)</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>132 (1.0)</td>
<td>10.0 (0.1)</td>
<td>37 (0.9)</td>
<td>9.4 (0.2)</td>
<td>67 (1.7)</td>
</tr>
<tr>
<td>Placebo</td>
<td>132 (1.0)</td>
<td>10.0 (0.1)</td>
<td>37 (0.9)</td>
<td>9.4 (0.2)</td>
<td>67 (1.7)</td>
</tr>
<tr>
<td>Mean (SE)</td>
<td></td>
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</table>

**Conclusion:** Dietary supplementation with vitamin D (average 75 μg/day) was associated with a doubling in plasma 25(OH)D levels, but had no significant effects on SBP or any measure of large or small arterial stiffness after 12 months. Lack of use of adequate doses of vitamin D are required to assess the effects of vitamin D on CVD outcomes, in addition to effects on bone health and cancer.

**Acknowledgement/Funding:** British Heart Foundation

### P4614 | BEDSIDE

**Impact of exercise training on dipeptidyl peptide 4 and its relation to endothelial biomarkers in patients with stable coronary artery disease**

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**Background:** Dipeptidyl peptide 4 (DPP4) is known to be present in many tissues, including endothelium and its effects go beyond metabolic aspects. DPP4 seems to exert many functions on cardiovascular system and it was shown that the inhibition of DPP4 activity may improve cardiovascular profile. This finding suggests new possibilities for treatment of cardiovascular diseases by using thera-pieutic options which may reduce DPP4 activity.

**Purpose:** To investigate the effects of regular exercise training on DPP4 and relationship between changes in DPP4 and circulating blood markers of endothelial dysfunction (nitric oxide (NOx), and Xanthine Oxidase (XOD)), in patients with stable coronary artery disease (CAD).

**Methods:** 42 subjects: 23pts with stable CAD (CAD group; 55±2.6 years, 14men) and 19 healthy controls (C group; 55±1.8 years, 11 men) were studied. At baseline in all pts and controls, levels of DPP4, NOx and XOD by peripheral vein sampling, were evaluated and exercise test was performed. After the initial study, all patients underwent a supervised 3 weeks exercise training at residential center, and after that period values of DPP4, NOX and XOD as well as exercise tolerance were determined again.

**Results:** Baseline value of DPP4 was significantly higher in CAD than in C group (P=0.008). After 3 weeks of exercise training DPP4 decreased significantly in CAD group (from 792.0±260.0±73 to 511.1±173.8±53, P<0.0005), as well as XOD (P<0.0005), while NOx increased (P=0.025). Exercise capacity (METs) at baseline were significantly lower in CAD than in C group (P=0.016), and it significantly increased in CAD group after exercise period (P<0.0005). A positive correlation in difference achieved during exercise period was found between increase in NOx level and decrease in XOD (r=−0.841, p<0.0005), between increase in NOx and decrease in DPP4 (r=0.713, p<0.0005) and between NOx increase and increase in METs (r=0.893, p<0.0005). Also, positive correlation in difference achieved during exercise period was found between decrease in XOD and decrease in DPP4 (r=−0.581, p<0.004), between decrease in XOD and increase in METs (r=0.562, p<0.001) and between decrease in DPP4 and increase in METs (r=−0.719, p<0.005).

**Conclusion:** In pts with stable CAD regular exercise training leads to significant reduction of DPP4 and restoration of endothelial function which is expressed through significant increase of NOx and decrease of XOD. There is a positive correlation between increase in NOx and decrease in DPP4 and decrease in XOD and decrease in DPP4.
Results: A total of 147 (25.9%) patients progressed to persistent AF. Patients with higher RDW quartiles also had more cardiovascular risk factors and co-morbidity. After a median follow-up of 4.8 (3.4–6.9) years, there were more cardiovascular events and deaths in the higher RDW quartiles. Multivariate analysis identified RDW was a significant predictor for the progression (adjusted odds ratio [OR] 1.35, 95% CI 1.04–1.73, p=0.039), the composite clinical outcomes (adjusted OR 1.29, 95% CI 1.04–1.62, p=0.024) and bleeding events (adjusted OR 1.57, 95% CI 1.16–2.12, p=0.004).

Conclusions: RDW can be a new, useful, novel marker for the prediction of AF progression as well as clinical and safety outcomes in patients with paroxysmal AF.

Methods: The healthy reference population for the present study was derived from the first 3,451 participants in The Maastricht Study (TMS), an extensively phenotyped population based cohort. The healthy reference population was defined by excluding individuals with diabetes mellitus, a clinical history for known cardiovascular disease by questionnaire, N-terminal pro-B-type natriuretic peptide >125 ng/l or estimated Glomerular Filtration Rate <60 ml/minute/1.73 m². Non-parametric analysis were performed to determine 99th percentile values of hs-cTn.

Results: From TMS cohort, a total of 1,803 individuals were included in the healthy reference population for hs-cTn. Six-hs-cTn values according to Dixon’s outlier detection method, leaving 1,797 individuals for the analyses. Overall 99th percentile upper reference limit of hs-cTnT and hs-cTnI was 15 (95% CI, 14–16) ng/l and 14 (95% CI, 12–18) ng/l, respectively. The 99th percentile of hs-cTnT was 20 (95% CI, 19–23) ng/l and for women 12 (95% CI, 10–13) ng/l. The 99th percentile of hs-cTnI was 20 (95% CI, 13–23) ng/l and 12 (95% CI, 9–14) ng/l for men and women respectively. The 99th percentile values of hs-cTn increased with age, and most prominent in the stratum ≥65 years.

Conclusion: 99th percentile values for hs-cTn assays are strongly sex- and age-dependent. Side by side comparison reveals remarkably similar 99th percentiles upper reference limits for the high sensitive troponin T and I assay, which is in contrast with current clinical practice. Clinical validation studies are needed to investigate whether the sex- and age-specific cut-off values outperform fixed cut-off values for diagnosing myocardial infarction.

Methods: We aimed to evaluate relationship between RDW values and clinical outcomes in patients with paroxysmal AF. Methods: We analyzed 567 patients who were newly diagnosed as paroxysmal AF. Clinical outcomes were analyzed after median 4.8 (3.4–6.9) year follow-up. Progression of AF was defined as paroxysmal AF at enrollment becoming persistent AF at 1-year follow-up. The composite clinical outcomes were defined as the composite of death, hospitalization due to heart failure, new onset stroke. Bleeding events were composed of major and minor bleeding. The relationship of RDW with clinical outcome or bleeding events was analyzed using continuous or categorical variables as quartiles: <12.8, 12.8–13.2, 13.3–13.8 and ≥13.9.

Results: A total of 147 (25.9%) patients progressed to persistent AF. Patients with highest RDW quartile were oldest and more frequent history of heart failure. Progression into persistent AF was increased in a stepwise manner as an increment of RDW (16.4% vs. 22.2% vs. 32.1% vs. 35.6%, p<0.001), CRP (0.03 vs. 0.05 vs. 0.08 vs. 0.16, p<0.001), and INR (1.2 vs. 1.3 vs. 1.5 vs. 1.7, p<0.001). However, mortality or hospitalization rate was not different among RDW groups. Multivariate analysis identified RDW was a significant predictor for the progression (adjusted odds ratio [OR] 1.35, 95% CI 1.04–1.73, p=0.039), the composite clinical outcomes (adjusted OR 1.29, 95% CI 1.04–1.62, p=0.024) and bleeding events (adjusted OR 1.57, 95% CI 1.16–2.12, p=0.004).

Conclusions: RDW can be a new, useful, novel marker for the prediction of AF progression as well as clinical and safety outcomes in patients with paroxysmal AF.

Conclusions: This study demonstrates that plasma MIF values are elevated in response to myocardial ischaemia and may be a useful diagnostic biomarker.

Acknowledgement/Funding: NH & MRC of Australia

P4616 | BEDSIDE

Long-term mortality in hospitalized patients with cardiac troponin values below the 99th percentile

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Background: An increased cardiac troponin (cTn) concentration is defined as a value exceeding the 99th percentile of a normal reference population. This discriminatory value is designated as the decision limit for the diagnosis of myocardial infarction (MI). The prognostic use of cTn values below the decision limit, however, has not been studied in hospitalized patients (pts).

Purpose: To assess the prognostic usefulness of cTn values below the decision limit in hospitalized pts without acute MI.

Methods: During 2010 a total of 3762 consecutive, hospitalized pts with a suspected acute MI had cTnI measured. The upper reference limit for the assay used was 30 ng/L (CV<10%). A total of 2185 pts had cTnI values ≤30 ng/L, thus fulfilling the inclusion criteria of this study. All pts were followed for up to 4 years with a median follow-up of 2.8 years. The pts were stratified into two different prognostic groups. Also, these data show that age is strongly associated with elevated cTnI values even in pts without acute MI.

Results: The 2185 pts were divided into two groups. Group I: cTnI values <10 ng/L (n=453), and group II: cTnI values ≥10–30 ng/L (n=1732). Group II pts were older with a mean (SD) age of 65 (16) yrs vs 55 (16) yrs in group I (p<0.0001) and also had more cardiovascular risk factors and co-morbidity. After a median follow-up of 3.2 yrs, 507 of the 2185 pts had died. Pts with cTnI values ≤10 ng/L had a significantly better survival than pts with cTnI values of 10–30 ng/L (p<0.0001; Figure). When performing an age-adjusted log-rank test of survival, however, this significance disappeared (p=0.08).

Conclusions: This study demonstrates that plasma MIF values are elevated in response to myocardial ischaemia and may be a useful diagnostic biomarker.

Acknowledgement/Funding: NH & MRC of Australia

P4617 | BEDSIDE

Macrophage migration inhibitory factor (MIF) levels in the blood rise in response to myocardial ischaemia evoked by an exercise stress test


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Background: Recent studies have demonstrated that macrophage migration inhibitory factor (MIF) plasma levels rise early in the course of myocardial infarction. Purpose: To determine whether myocardial ischaemia without infarction is also accompanied by elevation in plasma MIF levels. Methods: The study cohort comprised patients referred for evaluation of possible myocardial ischemia by either stress echocardiography or nuclear perfusion studies. Blood samples were obtained before and at 5 and 15 minutes after exercise. All samples were kept on ice until centrifugation and stored at -80°C prior to analysis for MIF (ELISA, R&D Systems, ng/ml), TroponinT (Tn, electrochemiluminescent immunoassay, Roche, γ/3) and hsCRP (immunoturbidimetric assay, Abbott Architect, mg/l). Subjects with exercise induced regional wall motion abnormality or reversible perfusion defect were classified as positive whilst those without such changes and without ecg changes were classified as negative. Results are mean±sd, unless stated otherwise.

Results: There were 19 positive (63±10.6 years, 5 stress echo) and 64 negative (62±5.10) subjects. There were no differences in baseline CRP (2.7±2.3 vs 4.3±2.7) or MIF (59.9±33.4 and 52.5±21.5) between positive and negative cases. There were no changes with exercise for Tn or CRP in either group. In contrast there was significant rise in plasma MIF following exercise in the positive but not the negative group (Fig). The figure shows mean (sem) change from baseline at 5 and 15 min for positive (black bar) and negative subjects. *, ** signify p<0.05, <0.01 between groups.
**P4619 | BEDSIDE**

**Paroxysmal versus non-paroxysmal atrial fibrillation in Europe: the EORP-AF General Pilot Registry**

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**Background:** Atrial fibrillation (AF) has different presentations (first detected, paroxysmal, persistent, permanent), with uncertain impact on outcome.

**Objective:** To investigate clinical presentation, management and outcome of paroxysmal and non-paroxysmal AF within EORP-AF General Pilot Registry.

**Methods:** Overall 2589 patients with available 1-yr follow up data were evaluated according to AF type.

**Results:** Patients with paroxysmal AF (26.8%) were younger, had lower prevalence of heart disease (particularly valvular) and major co-morbidities, as well as lower CHADS2, CHA2DS2VASc and HAS BLED scores. Patients with first detected AF (29.9%) had characteristics similar to persistent AF patients (25.9%), but lower use of oral anticoagulants, if indicated. Patients with persistent AF represented 17.4% of the cohort. At 1 year, the rate of stroke/TIA and thromboembolism was low (0.6–1.0%) and did not differ between paroxysmal and non-paroxysmal AF. All-cause mortality was higher in non-paroxysmal vs. paroxysmal AF (Log rank test, p=0.0018) (Figure). On multivariable analysis, the OR for all-cause death was 1.864 (95% CI 1.230–2.826, p=0.0029) for non-paroxysmal AF, relative to paroxysmal AF. Among men, the HR for LLT at baseline was 1.26 (95% CI 1.14 to 1.40). Among women, the HR for LLT at baseline was 0.89 (95% CI 0.77 to 1.02), and as an updated covariate was 1.14 (95% CI 1.00 to 1.30).

**Conclusions:** In CV risk estimation, the apparent effect of treatment such as LLT is significantly different when models use treatment at baseline compared to as an updated covariate. A limitation of these models currently is that they are not adjusted for a change in cholesterol ratio during follow-up, which may influence the HR of LLT as an updated covariate. Further research should resolve which methodology will produce valid risk models and hence optimal prescribing decisions.

**Acknowledgement/Funding:** Health Research Council of New Zealand, Heart Foundation of New Zealand

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**P4621 | BEDSIDE**

**The added value of a combined genetic score as cardiovascular risk predictor in a Portuguese population with intermediate risk according to the European score**

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Cardiovascular risk stratification has included traditional cardiovascular risk factors including tobacco, cholesterol and blood pressure adjusted to age and sex. The utility of genetic risk scores (GS) as predictor of cardiovascular risk remains inconclusive.

In the context of trying to evaluate the ability of a multiloci genetic score (GS) within the intermediate risk subgroup, defined by the European score, to add predictive power for the development of coronary arterial disease (CAD)

**Methods:** Study of 609 individuals with 59±4.3 years considered at intermediate risk (European score: 29.2–41.0). The multifactorial and multiloci genetic score was determined in the whole population after genotyping with specific primers. A GS based on 29 genes associated with atherosclerotic disease in general and coronary heart disease was created. Multivariate analysis and respective ROC curves and area under curve (AUC) were performed using the traditional risk factors (TRF). The analysis was repeated, adding the previous GS.

**Results:** By multivariate analysis GS was an independent predictor for DAC (OR=2.19; 1.47 to 3.25, p<0.0001). Diabetes mellitus (OR=3.37; 2.28–4.97; p<0.0001), arterial hypertension (OR=2.08; 1.24–3.5; p<0.0001) and smoking (OR=2.97; 2.06 to 4.28; p<0.0001) were also independent predictors for CAD. AUC increased from 0.70 to 0.72 after adding GS to the AUC obtained for TRF. When discriminated by tertiles of GS the AUC for TRF decreases according to the increase of genetic risk (1st tertile GS AUC [TRF]=0.71; 2nd tertile GS AUC [TRF]=0.72, 3rd tertile GS AUC [TRF]=0.68).

**Conclusion:** In our population the GS increased the predictive value of TRF in the subgroup of patients at intermediate risk by the European Score. The predictive value of TRF is lower in patients with higher GS. In this subgroup the inclusion of genotyping may be considered for better stratification of cardiovascular risk.

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**P4620 | BEDSIDE**

**Beyond Framingham risk equations: how can cardiovascular risk be estimated when treatment changes over time?**

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**Background:** Among people without cardiovascular (CV) disease, prescribing decisions for lipid- and blood pressure-lowering medications often depend on estimates of CV risk from tools such as the Framingham equations or SCORE charts, using risk factors measured at baseline. However, many patients receive new or changing treatments (eg. statins) during follow-up, raising questions about the validity of contemporary data to create risk tools for primary prevention. We evaluated the impact on estimated risk by the European score (score 2.5–7.5) and compared this with a genetic score (score 0–2) to estimate the increase of genetic risk (1st tertile GS AUC [TRF] =0.71; 2nd tertile GS AUC [TRF] =0.72).

**Methods:** To investigate clinical presentation, management and outcome of paroxysmal and non-paroxysmal AF within EORP-AF General Pilot Registry.

**Results:** Patients with paroxysmal AF (26.8%) were younger, had lower prevalence of heart disease (particularly valvular) and major co-morbidities, as well as lower CHADS2, CHA2DS2VASc and HAS BLED scores. Patients with first detected AF (29.9%) had characteristics similar to persistent AF patients (25.9%), but lower use of oral anticoagulants, if indicated. Patients with persistent AF represented 17.4% of the cohort. At 1 year, the rate of stroke/TIA and thromboembolism was low (0.6–1.0%) and did not differ between paroxysmal and non-paroxysmal AF. All-cause mortality was higher in non-paroxysmal vs. paroxysmal AF (Log rank test, p=0.0018) (Figure). On multivariable analysis, the OR for all-cause death was 1.864 (95% CI 1.230–2.826, p=0.0029) for non-paroxysmal AF, relative to paroxysmal AF. Among men, the HR for LLT at baseline was 1.26 (95% CI 1.14 to 1.40). Among women, the HR for LLT at baseline was 0.89 (95% CI 0.77 to 1.02), and as an updated covariate was 1.14 (95% CI 1.00 to 1.30).

**Conclusions:** In CV risk estimation, the apparent effect of treatment such as LLT is significantly different when models use treatment at baseline compared to as an updated covariate. A limitation of these models currently is that they are not adjusted for a change in cholesterol ratio during follow-up, which may influence the HR of LLT as an updated covariate. Further research should resolve which methodology will produce valid risk models and hence optimal prescribing decisions.

**Acknowledgement/Funding:** Health Research Council of New Zealand, Heart Foundation of New Zealand

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**P4622 | BEDSIDE**

**Validation of SAME-TT2R2 score for predicting poor anticoagulation in a prospective real world cohort of atrial fibrillation patients initiating Vitamin K antagonists**

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International guidelines recommend that an average individual time in therapeutic range (TTR) should be ~65–70% for optimal efficacy and safety outcomes whilst on a vitamin K antagonists (VKA). The SAME-TT2R2 score would help decision making by identifying those newly diagnosed atrial fibrillation (AF) patients that could do well on VKA. In a prospective population cohort of AF patients, we validated the predictive value of the SAME-TT2R2 score for discriminating those who would achieve a high TTR following initiation of VKA therapy.

**Methods:** We included consecutive non-valvular AF patients that initiated oral anticoagulation (OAC) in our outpatient anticoagulation clinic. Baseline SAME-TT2R2 score was calculated and at six months we calculated TTR using the Rosendaal method. Patients with valvular AF (prosthetic or not) were excluded. We also excluded those patients that did not receive at least 6 months OAC treatment. Patients that were admitted to hospital, as this would influence achievement of stable anticoagulation.

**Results:** During 2013, 719 patients with non-valvular AF were initiated on OAC.
with acenocoumarol in our out-patient anticoagulation clinic. Based on our study
inclusion/exclusion criteria, only 459 patients (64% of the whole cohort) entered
the final analysis: 222 (47%) male, median age 76 (interquartile range, IQR 70–
82); median (IQR) CHA2DS2-VASC score was 4 (3–5) and median (IQR) HAS-
BLED score was 3 (2–3). Median (IQR) SAME-TT2R2 score was 2 (1–2).
At 6 months, the mean ± standard deviation (SD) TTR at 64±17% overall, and 248
patients (54%) had a TTR value > 65%. Patients with a SAME-TT2R2 score
=0–1 had a median TTR of 67±18% whereas in patients with a SAME-TT2R2 score
≥2, was 61±16%, p<0.001. The odds ratio (OR) for having a low TTR value was
2.73 (95% CI 1.44–5.26, p=0.001) for those patients with a SAME-TT2R2 score
≥2.

Conclusions: In a prospective real world AF cohort of patients initiating oral
antiocoagulation with acenocoumarol, we have validated the clinical value of the
SAME-TT2R2 score, for the identification of which patients would have poor qual-
ity anticoagulation. Thus, rather than imposing a “trial of VKA” for such patients
(and exposing such patients to thromboembolic risks), we can a priori identify
those patients who can (not cannot) do well on a VKA. Such patients would ben-
efit from additional strategies for improving anticoagulation control with VKA or
alternative oral anticoagulant drugs.

Results: The median risk of events was 9.7% according to the AHA/ACC calcula-
tor, and 2.6% according to the European SCORE (total events only). Compared to
SCORE, the AHA/ACC calculator showed greater discriminative power for iden-
tifying patients with CACS > 300 (C-statistic: 0.74 (95% CI 0.67–0.82) vs. 0.69
(95% CI 0.61–0.78), p=0.008). The proportion of patients who would be treated
with statins according to the ESC guidelines was numerically higher than accord-
ing to the AHA/ACC recommendations (69% vs. 61%, p=0.060). For patients with
higher-risk findings on CCTA, the likelihood of receiving statins was similar with
both guidelines (p=NS). Patients with low risk findings (CACS = 0 or no visible
plaque) were more likely to receive statins if managed according to the European
guidelines.

Conclusions: The ESC and AHA/ACC guidelines seem to have similar accuracy
in assigning statins to patients with high-risk features on CCTA. However, patients
with low-risk findings are more likely to receive statins if managed according to
the European guidelines, which may result in lower yield and cost-effectiveness.

P4624 | BEDSIDE
Accuracy of statin assignment according to the European vs. American
guidelines - a coronary CT angiography study
A. Tralhao, A.M. Ferreira, P.A. Goncalves, S. Madeira, R. Rodrigues, M. Castro,
H. Marques. Hospital Luz, Imaging Center, Lisbon, Portugal

Introduction: The American scientific societies (AHA/ACC) have issued new
guidelines on the assessment of cardiovascular (CV) risk and the initiation of
statin therapy. The aim of this study was to compare the accuracy of the ESC and
AHA/ACC guidelines in assigning statins to patients with higher risk features on
coronary CT angiography (CCTA).

Methods: We assessed 327 patients (181 men, age 59±9 years) undergoing
CCTA for the presence of coronary artery disease (CAD). Patients -40 or > 75 years
with diabetes or known CV disease were excluded. The burden of coronary
atherosclerosis was assessed by the coronary artery calcium score (CACS) and
the presence of obstructive CAD (stenosis ≥50%).

Conclusions: This global GRS, mainly in its extreme values, allows the prediction
of the probability of the development, or not, of CAD and also allows that the
genetic risk have similar weight to one of the traditional risk factors.

P4625 | BEDSIDE
Predictors and risk model for stroke and death in non-anticoagulated
patients with atrial fibrillation: The Fushimi AF Registry
Y. Hamamatsu1, Y. Yamashita1, H. Ogawa2, M. Esoato2, Y.H. Chun2, H. Wada1,
K. Hasegawa1, M. Abe1, G.Y. Lip1, M. Akao1 on behalf of The Fushimi AF
Registry investigators.1 Kyoto Medical Center, National Hospital Organization,
Kyoto, Japan; 2 L suffered Takeda General Hospital, Kyoto, Japan; 3 University
of Birmingham, Centre for Cardiovascular Sciences, Birmingham, United Kingdom

Background: Atrial fibrillation (AF) increases the risk of stroke and death. Data
on the predictors for stroke and death in "real-world" AF patients are limited, especially from large prospective Asian population cohorts.

**Purpose:** The aim of this study is to investigate the predictors and risk model for stroke and death in the Fushimi AF Registry.

**Methods:** The Fushimi AF Registry is a community-based prospective survey designed to enroll all patients. The inclusion criterion for the registry is the documentation of AF on a 12-lead electrocardiogram or Holter monitoring at any time, and there are no exclusion criteria. We started to enroll patients from March 2011, and follow-up data were available for 3,304 patients by the end of March 2014 (median follow-up period 741 days). We explored the predictors for composite endpoint of "death, stroke, and systemic embolism (SE)" during follow-up period in 1,553 patients not receiving oral anticoagulants (OAC) at baseline. The risk model for predicting death/stroke/SE was determined by the cumulative numbers of risk factors which were significant on multivariate analysis. The risk model was based on the risk in Thai population.

**Results:** The mean age was 73.2±12.5 years, and 679 (44%) patients were female. The mean CHADS2 and CHA2DS2-VASc score were 1.76 and 3.08, respectively. The mean CHA2DS2-VASc score were 1.76 and 3.08, respectively. Cumulative events during follow-up were as follows: stroke in 60 (4%), death in 231 (15%), respectively. On multivariate analysis, advanced age (<75 years) (hazard ratio (HR): 1.68, 95% confidence interval (CI): 1.24–2.28), underweight (body mass index < 18.5 kg/m²) (HR: 1.69, 95% CI: 1.23–2.29), previous stroke/SE/transient ischemic attack (HR: 1.65, 95% CI: 1.21–2.23), heart failure (HR: 1.61, 95% CI: 1.18–2.17), chronic kidney disease (HR: 1.53, 95% CI: 1.16–2.02), and anemia (HR: 2.36, 95% CI: 1.75–3.21) were independent predictors for death/stroke/SE. A risk model based on these 6 variables could stratify the incidence of death/stroke/SE in patients without OAC, as well as those with OAC in our registry, with a high predictive value (C-indexes 0.76 in patients without OAC, and 0.70 in patients with OAC).

**Conclusion:** Advanced age, underweight, previous stroke/transient ischemic attack, heart failure, chronic kidney disease, and anemia were independently associated with the risk of death/stroke/SE in "real-world" non-anticoagulated Japanese patients. The inclusion criteria for the registry were as follows: 18 to 75 years of age, and at least one of cardiac risk factors (atrial fibrillation, hypertension, diabetes, dyslipidemia, heart failure, and chronic kidney disease). The risk model for predicting death/stroke/SE using these 6 variables in patients without OAC, as well as those with OAC. The World Health Organization (WHO) also issued guidelines for assessment and management of cardiovascular (CVD) risk using risk prediction chart. The authors and the readers should refer to the study by WHO for more information.

**Acknowledgement/Funding:** Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, MSD

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**P4629 | BEDSIDE**

**CAIDE risk score predicts atherosclerosis and vascular events in HIV patients.** Preliminary data from the Italian multicentre cohort of Cardiovascular and late-life Dementia risk in HIV (CARDH) study.

**Purpose:** To evaluate the determinants of accelerated atherosclerosis and cognitive decline risk in a midlife HIV population.

**Methods:** HIV patients from our Infectious Disease Units were consecutively enrolled. Patients were characterized for clinical and viro-immunological parameters, traditional cardiovascular (CV) risk factors, and psychological factors previously associated with CV risk (Type D personality, Alexithymia and depression). The authors and the readers should refer to the study by WHO for more information.

**Results:** A cohort of 198 subjects (75.2% male, age 47.6±6.0 yr, 43.7% with AIDS diagnosis) was recruited. Of them, 85% was on HAART with mean treatment duration 67.2±52 months. The mean CAIDE score was 7.2±5.2% (mean risk 3.7±3.2%), with 20.8% presenting a CAIDE risk >7.4%. At baseline, significant associations between CP and age (p<0.001), lipodystrophy (p=0.02), alexithymia (p<0.001), HeartScore (p=0.0001), CAIDE risk score (p<0.001), and multivariate analysis only increasing age (OR=1.10 [95% CI: 1.0–2.1]; p=0.023), and CAIDE risk score (OR=1.16 [95% CI: 1.0–1.3]; p=0.04) were independently associated with CPs. A higher CAIDE risk score was the only significant predictor of vascular events at 2.5 years, independently of other variables (OR=3.56 [95% CI: 1.1–10.7]; p=0.024), including age, CP, HeartScore and Alexithymia.

**Conclusions:** We conclude that in midlife HIV patients, the CAIDE risk score, predicts atherosclerosis and future vascular events better than a traditional CV risk algorithm. Cognitive decline risk in HIV may be more related to CV risk than viroimmunological factors.

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**Conclusions:** We conclude that in midlife HIV patients, the CAIDE risk score, predicts atherosclerosis and future vascular events better than a traditional CV risk algorithm. Cognitive decline risk in HIV may be more related to CV risk than viroimmunological factors.
associated with variables. External validation was performed on the population of the FAST-MI 2005 (1798 NSTEMI, 51% PCI) and FAST-MI 2010 registries (1928 NSTEMI, 66% PCI). Discrimination was assessed by the C-statistic and calibration by plotting predicted/observed probabilities by deciles of the population.

Results: 19 variables were predictors of Non-PCI and used to build the score: unstable angina (vs NSTEMI), female gender, age > 80, no previous PCI, history of COPD, history of MI, no sinus rhythm, admission with Killip class ≥ 2, heart rate > 110 bpm, heart failure, anemia, troponin rise and creatinine level > 130 μmol/L. Discrimination was acceptable with a C-statistic = 0.69. External validation showed a C-statistic at 0.62 (FAST-MI 2010) and 0.67 (FAST-MI 2005). For an individual patient, according to the quartiles of Non-PCI score, the rates of non-PCI ranged from 78–72% (Q1), 70–59% (Q2), 68–49% (Q3) and 49–35% (Q4).

Conclusion: In patients with acute MI, a score easily available at admission can help to predict the probability of non-PCI during hospitalization and thus help tailor initial antithrombotic treatment.

CLINICAL PARAMETERS TO IMPROVE RISK PREDICTION

P4630 | SPOTLIGHT
Heritability of coronary calcium quantity and total plaque burden: a classical twin study
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Through the comparison of monozygotic (MZ) and dizygotic (DZ) twins phenotypic similarities can be quantified and the weight of genetic and environmental factors can be determined in an unique way. It has been reported that coronary atherosclerosis has a strong genetic determination. However, it is unclear if coronary calcium quantity and total plaque burden are inherited similarly. Our goal was to assess the magnitude of genetic and environmental impact on coronary calcium quantity and total plaque burden. Coronary CT-angiography was performed in 208 twin subjects, of whom 62 were MZ pairs and 42 were DZ pairs (mean age: 58±8.7 vs. 55.8±9.8, p=0.218, respectively). Total Ca-score was independently added by Agatston-score measurement. Total plaque burden, which incorporates non-calcified, calcified and partially calcified plaques was assessed by the segment involvement score (SIS: total number of segments with plaque) and segment stenosis score (SASS: sum of all stenoses, minimal = 1, mild = 2, moderate = 3, severe = 4). SSS index (SSSi) was calculated by SSS/total segment number. Concordance between MZ and DZ pairs was assessed by non-parametric correlations. Rough heritability was calculated according to the Falconer-method. The Agatston-score was > 0 in 38.7% of the MZ twins (median:132.3 [IQR: 27.5–387.4]), and in 40.5% of the DZ twins (median: 107.8 [IQR: 35.9–230.3]), p=0.880. The SISi and SSSIi were positive in 55.6% of MZ and in 55.9% of DZ twins. The median SSSI of MZ versus DZ twins was 0.2 (IQR: 0.1–0.4) versus 0.3 (IQR: 0.1–0.5), respectively, p=0.972. The median SSSI of MZ versus DZ twins was 0.3 (IQR: 0.1–0.5) versus 0.3 (IQR: 0.1–0.7), respectively, p=0.940. Relatively strong heritability was found regarding Ca-score (h2=1.015), while the plaque burden showed a weaker genetic dependency (SASSi: h2=0.632 and SSSI: h2=0.466).

This classical twin study shows that coronary calcium quantity has a relatively strong heritability, whereas plaque burden, which incorporates non-calcified, calcified and partially calcified plaques, is more determined by environmental factors. The latter implies that non-calcified plaque development is predominantly affected by environmental factors, which underscores the importance of preventive measures in cardiovascular risk reduction.

P4632 | BEDSIDE
Cardiac function-specific risk factors for one-year mortality in patients admitted with acute coronary syndromes
O.P. Perelstein, I. Goldenberg, R. Klempnner, R. Kuperstein. Sheba Medical Center, Heart Institute, Ramat Gan, Israel

Introduction: Risk stratification in acute coronary syndromes (ACS) is based on clinical and laboratory values.LVEF is a strong predictor of mortality in coronary disease.

Methods: To evaluate the prognostic implications of LVEF in patients admitted with ACS; to assess whether identification of cardiac function-specific risk factors can be used to improve risk stratification.

Results: Through 2000 to 2010 more patients were admitted with preserved LVEF and less with LV dx. Patients with severe LV dx had high mortality rates at 1-year (36%) as compared with patients with mild/moderate LV dx and preserved LVF (10% and 4%, respectively; Fig). Mortality according to EF at admission did not change over the years (p>NS). Multivariate analysis showed that among patients with preserved LVEF or mild/moderate LV dx the presence of co-morbidities such as hypertension, diabetes, hyperlipidemia and peripheral arterial disease were independently associated with 1-year mortality. In contrast among patients with severe LV dx, clinical features at admission such as syncope, anterior MI location, ST-segment elevation and Killip Class>2 were independently associated with 1-year mortality.

Conclusion: Assessment of admission LVEF has important prognostic implications in patients with ACS and can be used to improve risk stratification through identification of cardiac function-specific risk factors.

P4633 | BEDSIDE
Relative performance of three different estimated glomerular filtration rates on clinical outcomes in patients with acute myocardial infarction undergoing percutaneous coronary intervention

Background: Chronic kidney disease has been associated with poor clinical outcomes in patients with acute myocardial infarction (AMI). Newer methods as the MDRD-4 formula and the new Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation were introduced to enhance estimation of glomerular filtration rate (eGFR) beyond of the classical Cockcroft-Gault (C-G) formula.

Purpose: We aimed to compare the relative predictability for the clinical outcomes in patients with AMI among three different formulas.
Methods: We analyzed consecutive 11,454 AMI patients (66.9±12.5 years old, 8,412 males) undergoing percutaneous coronary intervention (PCI). The relative performance of each formula was assessed in the in-hospital and one-year clinical outcomes using continuous or categorical variables according to eGFR: >90, 60–30, and ≤30 ml/min/1.73m². In-hospital outcome was defined as in-hospital mortality and complications. 1 year clinical outcome was defined as the composite of 1-year major adverse cardiac events (MACE) including death, recurrent MI, and target vessel revascularization (TVR) and CABG.

Results: The mean eGFR-SC was lower than those of eGFR MDRD-4 and eGFR CKD-EPI (66.6±28.6 vs. 72.1±24.7 vs. 72.9±22.4, p<0.001). However, moderate renal dysfunction (eGFR ≤60 ml/min/m²) by all 3 formulas was a significant predictor for in-hospital outcomes as well as one-year mortality and MACEs. Predictability for in-hospital outcomes with eGFR-SC (area under the curve [AUC] 0.688, 95% confidence interval [CI] 0.67–0.71, p<0.001) and eGFR-CKD-EPI (AUC 0.688, 95% CI 0.67–0.71, p<0.001) was higher than that with eGFR-MDRD-4 (AUC 0.684, 95% CI 0.66–0.70, p<0.001). Predictability for one-year mortality and MACEs with eGFR-SC was higher than those with eGFR-MDRD-4 and eGFR-CKD-EPI using categorical variables (AUC for mortality: 0.769 vs. 0.728 vs. 0.747, p<0.001; AUC for MACEs 0.619 vs. 0.602 vs. 0.615, p<0.001). Net reclassification index for improvement in risk prediction using PCE in different Mhnic populations eGFR-SC was 18.6%, 8.0%, respectively compared with eGFR-MDRD-4, whereas 0.9%, 2.1% compared with eGFR-CKD-EPI.

Conclusions: Moderate renal dysfunction by any formulas for eGFR was a significant predictor of in-hospital and one-year adverse clinical outcomes. The application of the eGFR-SC demonstrated better predictability for in-hospital and one-year adverse clinical outcomes compared with eGFR-MDRD-4 and eGFR-CKD-EPI.

P4634 | BEDSIDE
Predictive value of apoB/apoA1 ratio on the risk of myocardial infarction in different ethnic groups
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Background: Previous studies have shown that apoB/apoA1 ratio predicts the risk of acute myocardial infarction independently of risk factors profile and traditional lipid markers. Recently, the 2013 ACC/AHA guidelines on cardiovascular disease prevention introduced a new tool for risk assessment, the Pooled Cohort Equations (PCE).

Purpose: In a multietnic case-control study population, we evaluated whether the predictive value of apoB/apoA1 ratio is independent of the cardiovascular risk assessed using PCE in different ethnic populations.

Methods: The study population was composed by 1478 subjects enrolled in the FAMI Study: 739 patients with documented ST-elevation myocardial infarction as their first manifestation of coronary artery disease and 739 matched control subjects, both from urban areas of Italy, Scotland, and China. For all subjects blood serum samples were centrally analysed for total cholesterol (TC), LDL cholesterol, HDL cholesterol, apoB and apoA1 and cardiovascular risk was estimated using the PCE.

Results: The mean values of traditional lipid markers were significantly lower in the Chinese population than in the European one [TC (mean±SD) 208.6±47.4 vs. 203.0±41.9, p<0.0001; LDL-C 137.0±43.7 mg/dl vs. 157.9±54.2 mg/dl, p<0.0001; HDL-C 41.4±9.7 mg/dl vs. 45.8±12.6 mg/dl, p<0.0001, respectively]. In patients with STEMI, mean PCE cardiovascular risk score was similar between ethnic groups, but significantly higher than in matched controls (European STEMI 19.0%±12.4 vs. European controls 19.7%±12.7; p<0.0001; Chinese STEMI 19.6%±14.1 vs. Chinese controls 16.3%±12.1; p<0.001). The accuracy of PCE risk score was comparable between ethnicities [AUC (95% CI), European 0.63 (0.59–0.67) vs. Chinese 0.57 (0.53–0.61), p<0.001]. In multivariate analysis, the incremental apoB/apoA1 ratio was significantly associated with a progressively increased risk of STEMI independently of the PCE risk score both in the European population (OR [95% CI] II v. I tertile: 1.5 (1.08–2.24); III v. I tertile: 2.63 (1.82–3.84) and in the Chinese one (OR [95% CI] II v. I tertile: 1.92 (1.27–2.91); III v. I tertile: 3.64 (2.33–5.74)).

Conclusions: In different ethnic groups, apoB/apoA1 ratio is associated with the risk of STEMI with an incremental predictive value independently of traditional lipid markers and the new PCE risk estimating model.

P4645 | BEDSIDE
Association of creatinine clearance with clinical outcomes in patients with atrial fibrillation: The Fushimi AF Registry
M. Abe1, H. Ogawa1, T. Unoki1, M. Ishii1, N. Masunaga1, M. Esato2, Y. Chun3, W. Wada1, K. Hasegawa1, M. Aka0 on behalf of the Fushimi AF Registry investigators, 1Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; 2Ginkgo Takeda General Hospital, Kyoto, Japan

Background: The adequate antithrombotic therapy including non-vitamin K antagonist oral anticoagulants was varied by the creatinine clearance (CrCl). However, the relationship between CrCl and clinical outcomes in patients with atrial fibrillation (AF) was not fully evaluated.

Methods: The Fushimi AF Registry is a community-based prospective survey of atrial fibrillation patients who visited the participating medical institutions in Japan. Follow-up data were collected on 3,390 patients from 2010 to 2014. The CrCl was calculated with the Cockcroft-Gault equation, and 2,872 patients with available CrCl data were examined.

Results: Significant differences in baseline characteristics and clinical outcomes were observed vs. 72.1% of patients stratified by CrCl (Table). The incidence of death and major bleeding, but not stroke, were significantly different in each group. Those were the highest in the group of patients with hemodialysis or CrCl <15.

Conclusion: Patients with lower CrCl were highly associated with death and major bleeding.

Acknowledgement/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, and MSD

P4636 | SPOTLIGHT
The relation of ambulatory heart rate with all-cause mortality among middle-aged men: a prospective cohort study
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Background: Current evidence on the predictive role of ambulatory heart rate for mortality is conflicting. This may be due to lacking or insufficient adjustment for potential confounding factors like cardiorespiratory fitness and occupational and leisure time physical activity. Moreover, most of the existing studies are not based on continuous measurements of heart rate throughout a day, but on relatively few measurements over short periods throughout the day.

Purpose: The aim of this study was to investigate the association between average 24-hours continuously measured ambulatory heart rate and all-cause mortality.

Methods: In this study conducted within a group of male workers free of heart disease, a total of 48 events from the national mortality registration with a mean follow-up period of 16.5 years, the relation of ambulatory heart rate with all-cause mortality was found among the tertile of workers with highest average ambulatory heart rate compared to the tertile with lowest ambulatory heart rate (Hazard ratio = 3.21, 95% confidence interval: 1.22–8.44). No significant independent association was found between resting clinical heart rate and all-cause mortality.

Conclusions: In this study conducted within a group of male workers free of coronary heart disease at baseline, continuously ambulatory measured average heart rate was shown to be significantly associated with all-cause mortality while adjusting for resting clinical heart rate, cardiorespiratory fitness, occupational and leisure time physical activity as well as for classical risk factors. These findings support that average heart rate throughout the day, more than resting heart rate, is a strong independent predictor for all-cause mortality in healthy middle-aged working men.

Acknowledgement/Funding: Belgium Ministry of Public Health
P4637  |  BEDSIDE
Combined ECG-based risk stratification for sudden cardiac death in patients after myocardial infarction: 5-year data
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Purpose: To evaluate predictive value of heart rate turbulence (HRT) and microvolt T-wave alternans (mTWA) for risk stratification for sudden cardiac death (SCD) in patients after myocardial infarction (MI).

Methods: Study group: 111 patients after MI occurred more than 60 days before inclusion (77 men; age 64±10.5 years). All subjects had 24-hour ambulatory ECG monitoring with HRT and mTWA evaluation. Follow-up period was 60 months; primary endpoint was SCD, secondary endpoint included all non-sudden deaths from cardiovascular diseases.

Results: During follow-up we registered 19 cases of SCD and 11 cases of non-sudden deaths from cardiovascular diseases (including 7 lethal MI and 3 lethal strokes). HRT2 significantly increased risk of all-cause mortality (odds ratio (OR) 4.7 (95% CI 1.8–12.7), p=0.002) and SCD (OR 4.1 (95% CI 1.4–11.9), p=0.01; during the first 12 months OR for SCD was 20.5). MTWA was > 53 mcV at heart rate 100 bpm increased SCD risk (OR=3.1 (95% CI 1.1–8.8), p=0.03) with no significant increase in risk of all-cause mortality, whereas mTWA at 0.05 AM > 18 mcV, in contrast, significantly increased risk of all-cause mortality (OR=2.3 (95% CI 1.1–5.3), p=0.04) with no significant increase of SCD in the subgroup with LVEF<40%. Combined risk assessment at 12 months revealed that the most significant combination was HRT2 and mTWA100 > 53 mcV, which increased risk both of all-cause mortality (OR=30.7 (95% CI 3.5–271.6), p<0.001) and SCD (OR 65.9 (95% CI 6.5–688.8), p<0.001); However, at 60 months this predictive value for SCD decreased (OR=20.8 (95% CI 2.8–114.0), p<0.001), and completely disappeared for all-cause mortality, and maximum significance was observed for LVEF<40% in combination with ventricular tachycardia.

Conclusion: In post-MI patients, abnormal HRT and mTWA can reliably predict increased risk of all-cause mortality and SCD. Patients with concomitant HRT2 and increased mTWA at heart rate 100 bpm are at the highest risk of SCD in the first year; but after the first year the group of highest risk include patients with low LVEF and VT+.

P4638  |  BEDSIDE
Respiratory sinus arrhythmia: a surrogate of vagal tone independently predicts mortality after myocardial infarction
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Purpose: Respiratory sinus arrhythmia (RSA) is a non-invasive measure of cardiac vagal outflow that has been shown to predict adverse outcome in survivors of acute myocardial infarction (MI). We aimed at investigating whether the predictive power of RSA measured from an individual patient was predictive of malign heart risk predictors.

Methods: 941 survivors of acute MI were prospectively enrolled and followed up for 5-year all-cause mortality. Patients underwent 30-minute recordings of ECG, continuous blood pressure (photoplethysmographic device), and respiratory chest excursions during the peak of exercise using movably placed electrodes. RR intervals lying within the expiration phase were used as anchor points, and RSA was calculated as the average change of RR intervals around these anchor points. The optimum cutoff value (>0.19 ms) was determined by Youden’s index.

Other risk predictors studied were LVEF, GRACE score, post-extrasystolic potentiation (PESP), mean respiratory rate, spontaneous baroreflex sensitivity (BRSPRSA), and the number of ventricular premature complexes (VPCs) per hour. The independent prognostic value of these variables was investigated by multivariable Cox analysis.

Results: 72 patients died during follow-up. Five-year mortality rates in patients with normal and abnormal RSA/PRRSA were 4.2% and 14.4%, respectively. In multivariable Cox analysis, RSA/PRRSA was an independent risk predictor (hazard ratio 3.05, p<0.001, see Table 1).

Table 1

<table>
<thead>
<tr>
<th>Risk predictor</th>
<th>Hazard ratio (95% CI)</th>
<th>z</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>RSA &gt;0.19 ms</td>
<td>3.05 (1.76–5.30)</td>
<td>15.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF &lt;35%</td>
<td>1.93 (1.11–3.35)</td>
<td>5.3</td>
<td>0.021</td>
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<tr>
<td>GRACE score &gt;120</td>
<td>3.15 (1.79–5.55)</td>
<td>15.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PESP present</td>
<td>2.74 (1.47–5.08)</td>
<td>10.1</td>
<td>0.001</td>
</tr>
<tr>
<td>BRSPRSA 1.58 ms/mm Hg</td>
<td>2.19 (1.18–4.05)</td>
<td>6.2</td>
<td>0.013</td>
</tr>
<tr>
<td>Respiratory rate ≥18/min</td>
<td>2.17 (1.25–3.79)</td>
<td>7.5</td>
<td>0.006</td>
</tr>
<tr>
<td>VES ≥10%</td>
<td>1.13 (0.62–2.08)</td>
<td>0.16</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Conclusions: Respiratory sinus arrhythmia (RSA/PRRSA) is a non-invasive measure of vagal tone that is suitable as a mortality predictor in survivors of acute MI. RSA/PRRSA was independent from both well-established and recently-introduced non-invasive risk predictors.

P4639  |  BEDSIDE
Relationship between cardiac autonomic dysfunction measured by heart rate recovery after exercise and coronary artery calcification
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Background: Patients with cardiac autonomic dysfunction have been shown to have increased cardiovascular events including sudden death and most of them are from coronary artery disease. Heart rate recovery (HRR) after exercise is one of the methods measuring cardiac autonomic dysfunction and impaired HRR has been suggested as a predictor of adverse cardiovascular events.

Purpose: We sought to investigate whether HRR is associated with the degree of coronary artery calcification as a marker of atherosclerotic coronary artery disease.

Methods: Patients without known coronary artery disease who underwent both exercise treadmill test and coronary computed tomography angiography as evaluations for chest pain or routine health examinations were analyzed retrospectively. HRR was defined as the difference between the heart rate at peak exercise and the heart rate 1 minute after exercise during a recovery phase. The degree of coronary artery calcification was represented as Agatston calcium score.

Results: Total 457 patients were identified. Median HRR value was 29 beat/min (bpm), and we compared clinical characteristics between the group with below median value and the other. The group with below HRR 29 bpm showed significantly older age, higher BMI, higher hypertension and diabetes prevalence. The severity of coronary artery calcification was also higher in the group with below HRR 29 bpm as compared with the other, but the difference was not statistically significant (112.7±308.8 vs 65.9±205.1, p=0.059). We calculated receiver operating characteristic curve according to the different calcium score level (> 10, > 100, > 400). The area under (AUC) of HRR showed its highest value at predicting calcium score of more than 100 (AUC=0.629, 95% CI 0.560–0.699), whereas the AUC of age was higher (AUC=0.744, CI 0.688–0.801). In the regression analysis using generalized linear model, age, hypertension, diabetes and low HRR was significant predictor for high calcium score, however, multivariate analysis showed age was the only significant parameter for high coronary calcium score (coefficient 5.55, standard error 1.25, p<0.0001).

Conclusion: We did not find a significant correlation between cardiac autonomic dysfunction measured by HRR and the degree of coronary artery calcification. Age was more closely related to the severity of calcification than HRR.

P4640  |  BEDSIDE
New scoring using serum albumin and body mass index can predict driveline infection during long-term left ventricular assist device treatment
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Background: Survival in patients with continuous flow left ventricular assist device (CF LVAD) had been increased owing to improved perioperative management procedures. The second target for successful long-term LVAD treatment is to reduce readmission rate due to device-specific infection, which was one of the major unsolved complications.

Purpose: To construct a scoring system to predict readmission due to driveline infection (DLI).

Methods and results: Among 57 enrolled patients who had received CF LVAD and been followed for 530 days on median at our institute between 2008 and 2014, 21 patients experienced readmission due to driveline infection (DLI) at 190 days after the surgery on median. Considering the result of Uni/Multivariable Cox regression analyses demonstrating lower serum albumin concentration (S-ALB) (hazard ratio 0.144) and body mass index (BMI) (hazard ratio 0.843) both obtained at discharge were independent predictors of readmission due to DLI, we constructed a New Score “7 [S-ALB (g/dL) – BMI]” (Fig. A), which significantly stratified readmission-free rate into 3 groups [low (<50 Pt), intermediate (50–40 Pt), and high group (> 40 Pt)] during 2-year study period (p=0.008) (Fig. B). Survival remained unchanged irrespective of DLI, whereas those with DLI needed longer in-hospital treatment (p<0.05).

Conclusion: A New Score could predict DLI by using two simple nutrition parameters. Early nutrition assessment and intervention may reduce readmission and improve patients’ quality of life during long-term LVAD support.
P4642 | BEDSIDE
Exploration of risk factors for major bleeding in Japanese patients with atrial fibrillation: 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. Although oral anticoagulation greatly reduce the risk of stroke in atrial fibrillation, the risk of bleeding with this therapy remains challenging. The purpose of this study was to validate the anticoagulation therapy among Japanese patients with atrial fibrillation. Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients who visited the participating medical institutions in Fushimi-ku, Kyoto. Fushimi-ku is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. Follow-up data were available for 3,390 patients, and the median follow-up period was 777 days.

Results: Of 3,390 patients, major bleeding occurred in 108 patients (3.2% of total). Patients with major bleeding were more often male (with vs. without major bleeding: 71.3% vs. 59.0%; p <0.01), older (76.2±8.1 vs. 73.6±11.0; p=0.014), had more co-morbidities (heart failure, vascular disease and chronic kidney disease [CKD]), had more history of major bleeding (8.3% vs. 2.4%; p<0.01) and received more antplatelet therapy (40.6% vs. 28.7%; p<0.01). However, body weight, hypertension (HTN), diabetes mellitus (DM), previous stroke, drinking habit and anticoagulation prescription (58.3% vs. 52.8%; p=0.26) were comparable between the two groups. Multiple logistic regression analysis including sex, heart failure, DM, anticoagulation prescription and six components of HAS-BLED score (age ≥65 years, previous stroke, HTN, CKD, history of major bleeding and antplatelet therapy) revealed that male gender, age ≥65 years, history of major bleeding and antplatelet therapy were the independent determinants of major bleeding. (male [odds ratio: 1.78, 95% CI: 1.17–2.63, p<0.01], age [odds ratio: 2.17, 95% CI: 1.13–4.71, p=0.018], previous major bleeding [odds ratio: 4.22, 95% CI: 1.88–8.52, p<0.01], antplatelet therapy [odds ratio: 1.78, 95% CI: 1.17–2.63, p=0.01]).

Conclusion: In addition to three components of HAS-BLED score (bleeding, elderly, antplatelet therapy), male gender was independently associated with the incidence of major bleeding in “real-world” Japanese AF patients.

Acknowledgment/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, MSD

P4643 | BEDSIDE
Multicohort genome-wide study with variants associated with cardiovascular risk factors and coronary artery disease in a Southern European population

Genome wide association studies (GWAS) have indicated multiple risk SNPs for cardiovascular (CV) disease, but data from clinical populations are scarce for South European (SE) populations. We therefore explored the risk of major and minor bleeding across 35,000 SE patients from 4 multicohort studies (23,825 from 3 SE countries and 11,000 from Portugal) using a genome-wide approach. We validated previously reported SNPs in SE populations, and conducted association analyses for new risk SNPs. The studies included 1367 patients with major bleeding and 28,912 controls. The multivariate-adjusted Cox regression analyses were performed to study the association between the SNPs and time to major and minor bleeding. A total of 112 million SNPs were genotyped. At the individual locus level, 13 SNPs were significantly associated with major bleeding (p <0.05) and 45 SNPs with minor bleeding (p <0.05). The most significant association was found with rs2126607 (near ANGPTL3) with a odds ratio (OR) of 2.12 for major bleeding. In contrast, the association of rs1313952 (near INT2) with minor bleeding had an OR of 2.31. The association was confirmed in an independent replication cohort of 4,396 patients. These results suggest that common genetic variants may contribute to the risk of bleeding in SE populations.

Acknowledgment/Funding: This work was supported by the European Union’s Horizon 2020 research and innovation programme (project 667823: BEAT-DIA).
Conclusions: In our population, the multiplicative GRS model was found to be preferably used to determine the coronary risk than using only a particular polymorphism.

P4646 | BEDSIDE
Genetic risk score - multivariate study including traditional risk factors

Several polymorphisms have been linked to coronary artery disease (CAD). However, many of these polymorphisms act in common pathophysiological axes and to have clinical significance as vascular risk markers, in one hand they must withstand the multivariate analysis and, in the other hand, they should have a predictive value independent of the well-known traditional risk factors (TRF).

Aim: Analyze the genetic polymorphisms linked to CAD occurrence, in a multivariate study including the TRF.


10 criteria.

Conclusions: This study clearly demonstrates that the genetic risk factors (OR=2.05, p<0.0001) add risk to traditional risk factors relatively to the CAD development. Knowing the mechanisms involved, it may arise new approaches to prevent the coronary disease in healthy population, but with increased genetic risk.

P4647 | BEDSIDE
Can we characterize the risk of stroke and death in patients with non-valvular atrial fibrillation based on the parameter defining a CHA2DS2-VASc score equal to 1?

P4648 | BEDSIDE
Central obesity modifies the role of triglycerides in the risk of fatal and non-fatal cardiovascular event: 10-year follow-up (2002-12) of the ATTICA study
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Background: Elevated serum triglycerides have been treated as independent cardiovascular disease (CVD) risk factor, but their net effect on 10-year CVD risk is still under research due to the multi-factorial basis of hypertriglycerideremia that combines hormonal, genetic, anthropometric and dietary characteristics. Moreover, central obesity has been linked with increased 10-year CVD risk that has been explained through glucose-metabolism paths, but rarely through triglycerides. The aim of the present study was to investigate the association between central obesity, triglycerides and 10-year CVD risk.

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.

Results: The 10-year incidence was 19.7% in men and 11.7% in women (p<0.001). Unadjusted analysis showed that triglycerides increased 10-year risk (Relative Risk (RR) per 1 mg/ml = 1.005, 95% Confidence Intervals
R. Pracon1, M. Kruck1, J. Pregowski3, M. Demkow1.

Agatston method. Serum Lp-PLA2 mass was assessed by PLAC® test. 

Materials and methods: 

As a highly specific biomarker of plaque vulnerability, it is unknown whether Lp-PLA2 contributes to presence of non-calcified coronary artery plaques in patients with CAC score zero. 

Conclusions: 

The majority of patients with intermediate pretest probability of CAD have coronary artery plaques, and Lp-PLA2 concentration is independently correlated to their presence.

P4650 | BEDSIDE 

Lipoprotein-associated phospholipase A2 as independent predictor of atherosclerosis among patients with zero coronary artery calcium score 

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Objectives: To evaluate the presence central obesity that promotes insulin secretion and thus, subjects with central obesity should be treated as high CVD risk individuals due to impaired glucose metabolism, but also due to increased triglyceride levels.

Conclusions: 

The Kaplan-Meier curves (figure) show that there was a significant difference in the risk of stroke/death when CRP level was considered.

Conclusion: 

Comparison of contemporary risk models for predicting mortality and arterial bypass grafting 


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Background: 

Aortic valve replacement (AVR) and/or coronary artery bypass grafting (CABG) make up the majority of cardiac surgeries with increasing demand as the population ages. Accuracy of risk stratification is important, especially as interventional aortic valve and coronary procedures continue to blossom, but have been rarely studied for the combined AVR+CABG operation.

Purpose: 

We compared the prognostic utility of EuroSCORE, EuroSCORE II and Society of Thoracic Surgeon’s (STS) Score for AVR+CABG.

Methods: 

All patients undergoing AVR+CABG at our City Hospital during 2005–2012 were included, with the three risk scores calculated and their discrimination and calibration for mortality and morbidities assessed.

Results: 

450 patients undergoing AVR+CABG were included, with mean follow-up of 4.7 years. Operative mortality was 6.4% (29), and mean scores were EuroSCORE 12.5±11.1%, EuroSCORE II 6.6±1.6% and STS Score 5.5±4.4%. C-statistics were 0.587, 0.669 and 0.699 respectively for operative mortality. Hosmer-Lemeshow test P-values were 0.064, 0.718 and 0.567, and Brier Score 0.716, 0.585 and 0.588. Independent predictors of operative mortality were history of myocardial infarction and impaired renal function. STS score also was the best score at detecting late mortality (c=0.643), composite morbidity (c=0.627), stroke (c=0.642), prolonged ventilation–24 hours (c=0.642), and return to theatre (c=0.612).

Conclusion: 

The STS score has the best discrimination (albeit moderate) for mortality and most complications after AVR+CABG, while its calibration was similar to EuroSCORE II and better than EuroSCORE I. It should therefore be used in risk stratification and also consideration of surgical or percutaneous approach to patients with concurrent severe aortic valve and coronary artery disease.

P4652 | BENCH 

Sleep duration and risk of incident of ischaemic heart disease: a 7-year prospective study of 0.5 million Chinese adults 

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Purpose: To investigate whether the risk stratification of these patients could be improved by using CRP level at admission as an additional tool to the usual clinical approach.

Methods: 

Between 1998 and 2011, among 1,212 consecutive NVAF patients hospitalised for AF, 246 patients had a CHA2DS2-VASC score = 1, and 198 of them had CRP determination. All patients were followed-up at least 6 months and cardiovascular events recorded. The composite endpoint was defined as the first occurrence of stroke or death.

Results: 

Mean age was 56.6±10.3. At baseline, the CRP was >3 mg/L in 103 (52%). A CHA2DS2-VASC score = 1 is associated with a stroke and death rate of 2.92 per 100 person-years (95% CI: 1.12–5.92) at one year. After a follow-up of one year, no patient presented an event in the group of patient with a CRP level ≤3 mg/L and 6 events occurred in the group of patient with a CRP level ≥3 mg/L.

Conclusion: 

The Kaplan-Meier curves (figure) show that there was a significant difference in the risk of stroke/death when CRP level was considered.
P4653 | BEDSIDE
Elevated brain natriuretic peptide plasma level as a marker of increased maternal complications in pregnant women with preeclampsia/eclampsia syndrome
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Background: Plasma brain natriuretic peptide (BNP) level is known to be elevated during normal pregnancy, as pregnancy is associated with volume expansion. In preeclampsia/eclampsia syndrome, the BNP level is shown to be even higher than maternal morbidty levels. Whether or not elevated BNP level is associated with increased maternal complications, is not clearly defined.
Purpose: To evaluate the role of elevated BNP as a marker of increased maternal complications in pregnant women suffering from preeclampsia/eclampsia syndrome.
Methods: Fifty pregnant ladies were included; all were diagnosed as having preeclampsia/eclampsia syndrome. Basic clinical characteristics and obstetric history and examination were evaluated. An echocardiography was performed, to ensure absence of any structural heart disease and a 24-hour urinary protein test was done. A venous sample was withdrawn from all pregnant ladies, on presentation, and tested for BNP plasma level using a point-of-care test. Ladies were followed up till delivery and maternal complications were reported.
Results: Twenty seven (54%) ladies had preeclampsia and 23 ladies (46%) had eclampsia syndrome. The mean systolic blood pressure was (177.5±21.3 mmHg) and the mean diastolic blood pressure was (110.4±11.2 mmHg). Thirty (60%) ladies developed complications during pregnancy, including HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), renal impairment, vaginal bleeding and cerebral hemorrhage and 2 ladies died before delivery. The median BNP plasma level, for all patients, was 92.6 ng/dl. The median BNP was significantly higher in patients who developed complications (130.2 Vs 52.5 ng/dl; p=0.002). The highest BNP level (1170 ng/dl) was found in a patient who died of pulmonary edema, shortly after presentation. Ladies who developed complications had significantly higher heart rate (mean 109.9 Vs 100.3 bpm; p=0.005), systolic blood pressure (mean 184.1 Vs 165.8 mmHg; p=0.001), diastolic blood pressure (mean 114.1 Vs 103.9 mmHg; p=0.001), 24-hours urinary protein level of 3.1 Vs 2.8 g; p=0.009) and delivered earlier than women without complications (mean pregnancy duration 34 Vs 36 weeks; p=0.04).
Conclusion: Higher BNP plasma level is helpful in defining preeclampsia/eclampsia patients with higher risk of maternal complications. Measuring BNP can help earlier detection and management of complications and it also prompts tighter blood pressure control.

P4654 | BEDSIDE
Lipoprotein-associated phospholipase A2 does not improve mortality prediction
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Background: Lipoprotein associated phospholipase A2 (Lp-PLA2), was linked to cardiovascular events in observational studies. Nevertheless, its direct inhibition did not result in risk reduction. The utility of Lp-PLA2 assessment for prediction of mortality among coronary heart disease (CHD) patients is unclear.
Purpose: To study the long-term association of Lp-PLA2 with mortality among CHD patients, with the aim of gaining insight into its clinical utility in risk prediction beyond traditional risk factors.
Methods: Among 3122 CHD patients included in the Bezafibrate Infarction Prevention (BIP) study, 2538 survived to the 5th follow-up year and had frozen serum samples. Lp-PLA2 activity was measured with colorimetric activity method.
Results: Patients in the 3rd Lp-PLA2 activity tertile (>247.2 mmol/min/ml) had lower systolic blood pressure, and higher prevalence of: men, metabolic syndrome, coronary artery bypass graft and smoking history compared to the 1st and 2nd tertiles (<202.0 mmol/min/ml) respectively. Lp-PLA2 correlated with HDL-C (r=0.44), non HDL-C (r=0.37) and fibrinogen (r=0.12) but was only weakly correlated with C-reactive protein.
Over median follow-up of 7.4 years, 504 deaths were reported. The 3rd Lp-PLA2 activity tertile was associated with greater mortality risk; adjusted Hazard Ratio (HR): 1.35 [95% confidence interval (CI): 1.10–1.66] compared to the 1st tertile. HR decreased to 1.28 (95% CI: 1.01–1.61) following adjustment for traditional non-risk factors. However, inclusion of Lp-PLA2 in the model did not improve model discrimination or calibration. Accounting, in addition, for circulating lipids further attenuated the HR (1.13; 95% CI: 0.88–1.47).
Conclusions: The association between Lp-PLA2 activity and long-term mortality was explained by traditional risk factors, particularly HDL-C and non HDL-C. This suggests that Lp-PLA2 plays a minor role in underlying the mortality. The patients were divided according to tertile of Lp-PLA2 measurement to traditional risk factor for predicting long-term mortality among CHD patients.

P4655 | BEDSIDE
Relation between high-density lipoprotein efflux capacity and coronary plaque progression in type 2 diabetes patients with intensive lipid-lowering therapy
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Background: Despite intensive lipid-lowering therapy using statins, patients with type 2 diabetes mellitus (T2DM) still have a high “residual risk” of future cardiovascular events. High-density lipoprotein (HDL) may provide cardiovascular protection, but its relation to the residual risk is unknown.
Purpose: We assessed the association between the functionality of HDL and serial changes of coronary plaques by intravascular ultrasound (IVUS) in T2DM patients with intensive lipid-lowering therapy.
Methods: Thirty T2DM patients who received intensive statin treatment and percutaneous coronary intervention using IVUS were examined. IVUS analysis on non-culprit coronary lesions was performed at baseline and after follow-up for 8–9 months. Cholesterol efflux capacity of HDL, an index of HDL functionality, was measured with a validated in vitro system.
Results: During the follow-up period, intensive statin treatment reduced low-density lipoprotein cholesterol (LDL-C) level from 96±29 mg/dl to 83±21 in all of the patients. However, unexpectedly, a significant progression of coronary plaque was observed (a 3.4±8.8% increase in percent plaque volume, p=0.038). Patients who had progression of coronary plaque (group P; n=20, male/female: 14/6) and regression of coronary plaque (group R, n=10, male/female: 7/3) were similar in terms of LDL-C levels. But cholesterol efflux capacity of HDL and HDL cholesterol (HDL-C) level at follow-up were significantly lower in the group P than in the group R (16.9±1.6% vs. 18.7±1.4%, p=0.023 and 46±9mg/dl vs. 64±10mg/dl; p=0.001, respectively). Cholesterol efflux capacity and HDL-C were significantly and inversely associated with the progression of coronary plaque (odds ratio [95% confidence interval]: 0.15 [0.02–0.65], p=0.019 and 0.09 [0.01–0.55], p=0.027, respectively) after adjusting for age by multiple logistic regression analysis.
Conclusions: Cholesterol efflux capacity of HDL, in addition to HDL-C level, may be a useful biomarker for predicting coronary plaque progression and a novel therapeutic target to reduce the residual risk in T2DM patients with intensive lipid-lowering therapy.
P4657 | BEDSIDE
Plasma hydroxyxanthranilic acid and incident type 2 diabetes in patients with stable angina pectoris
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Background: The tryptophan metabolite hydroxyxanthranilic acid (HAA) has been related to cardiovascular disease. Moreover, HAA was recently identified as a potent regulator of lipid metabolism and inflammation.

Purpose: We evaluated the associations of plasma HAA levels to incident type 2 diabetes (T2D) in patients with suspected stable angina pectoris (SAP).

Methods: A total of 4122 patients underwent elective coronary angiography at two Norwegian university hospitals in 2000–2004. Patients with self-reported diabetes mellitus and/or glycated haemoglobin >6.5% (n=1603) were excluded leaving 2519 patients eligible for the analyses. The participants were followed for incident T2D throughout 2009. Odds ratios (OR) and 95% confidence intervals (CI) for were calculated using logistic regression and are reported per standard deviation increment of plasma HAA (log-transformed). We assessed risk classification by calculating the continuous net reclassification improvement (NRI) = 0).

Results: Median age at inclusion was 62 years and 73% were males. During follow-up, a new diagnosis of T2D was recorded in 114 (4.5%) of the participants. Median plasma HAA values were substantially higher in those who subsequently developed T2D than in those who did not (40.0 vs. 33.8 mmol/L, P < 0.001). In age and gender adjusted analyses, HAA provided an OR (95% CI) for incident T2D of 1.65 (1.25–2.17), P = 0.001. Adding body mass index, serum creatinine, study centre and fasting status to the multivariable model somewhat attenuated the association, which, however, remained statistically significant (OR [95% CI]: 1.34 [1.08–1.67], P = 0.009). Further adjustment including serum apolipoprotein A1, C-reactive protein, fibrinogen, and D-dimers did not affect the risk estimate of HAA (95% CI): 1.34 [1.07–1.67], P = 0.01). Moreover, HAA significantly improved risk classification for T2D (NRI [95% CI]: 0.19 [0.07–0.38], P = 0.04).

Conclusion: In a large cohort of patients with SAP, we identified plasma HAA as a strong predictor of incident T2D. Underlying pathomechanisms should be further elucidated.

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P4658 | BENCH
The arachidonate 15-lipoxigenase enzyme product present in heart tissue from patients with ischaemic heart disease induces hypercoagulability
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Background and introduction: Platelet activation plays a significant role in haemostasis and thrombosis and also in the pathophysiology of cardiovascular disease. Recent studies suggest a link between atherothrombotic events and the enzyme arachidonate 15-lipoxygenase (ALOX15), which catalyses the formation of 15-hydroxy eicosatetraenoic acid (15-HETE) from arachidonic acid. Recent studies have shown that ALOX15 is highly expressed in human ischaemic heart tissue, and that 15-HETE increases platelet aggregation and thrombin generation. However, little is known about the effects of 15-HETE on clot formation. We hypothesized that increased production of 15-HETE may contribute to atherothrombotic events by increasing clot formation.

Purpose: To determine if the concentration of 15-HETE in heart tissue and serum is increased in patients with ischaemic heart disease and if 15-HETE induces hypercoagulability in human blood.

Methods: We used liquid chromatography - mass spectrometry (LC-MS) to analyse 15-HETE levels in heart tissue and in serum from 5 patients undergoing coronary artery bypass grafting (CABG; ischaemic tissue) and from 5 patients undergoing aortic valve replacement (AVR; non-ischaemic tissue). Whole blood clot formation was assessed with rotational thromboelastometry. Activation of clot formation was assessed using intrinsic (INTEM), extrinsic (EXTEM) and fibrinbased (FIBTEM) systems which are absence or absence of 15-HETE. Clotting time, clot formation time, maximum clot firmness, and α-angle were measured.

Results: LC-MS analysis showed that 15-HETE concentrations were significantly higher in heart biopsy samples and serum from patients undergoing CABG compared with patients undergoing AVR. Addition of 15-HETE to human whole blood reduced the clot formation time in the INTEM assay, increased the maximum clot firmness in the EXTEM assay, and shortened the tissue factor-activated clotting time and increased the α-angle in the FIBTEM assay.

Conclusions: Work identifies increased concentrations of the ALOX15 product 15-HETE in human ischaemic heart biopsy and our data demonstrate that the ALOX15 product secreted from ischaemic heart tissue accelerates clotting time and is thus prothrombotic. We suggest that patients with increased ALOX15 expression and increased 15-HETE levels have an increased risk of thrombotic events.

Acknowledgement/Funding: The Swedish Research Council, The Swedish Heart-Lung Foundation and the Laboratory Medicine Sahlgrenska University Hospital

P4659 | BEDSIDE
Relationship between serum beta-2-microglobulin and cardiovascular risk factors
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Background and purpose: Serum beta-2-microglobulin (B2M) level reflects cellular turnover (especially lymphocytes) and renal tubular function. We previously reported its association with cardiovascular and all-cause mortality. We sought to explain this association in terms of cardiometabolic risk factors.

Methods: Data on 6,474 participants (3114 men, 3360 women; age, mean±SD, 44.7±17.2 yrs) of the Third National Health and Nutrition Examination Survey were analyzed using ANCOVA. The relationship of B2M with age, BMI, blood pressure, glycemia, lipids, inflammation, liver and renal function were studied. Where appropriate, data were log-transformed.

Results: Serum B2M level (mean±SE) was 1.92±0.66 and 1.92±0.77 mg/L in men and women respectively (P < 0.05). It correlated with age (r=0.57), BMI (r=0.15), systolic blood pressure (r=0.38), ALP (r=0.21), triglycerides (r=0.25), HDL (r=0.14), AST (r=0.18), ALP (r=0.29), CRP (r=0.28) and eGFR (r=0.66) (all p-values <0.001). The only fully adjusted model, serum B2M remained positively associated with systolic blood pressure (r=0.11, 95% CI: 0.04 to 0.18); AST (r=0.14, 95% CI: 0.10 to 0.18), ALP (r=0.10, 95% CI: 0.07 to 0.13), and CRP (r=0.05, 95% CI: 0.04 to 0.07), and negatively associated with HDL (r=−0.11, 95% CI: −0.07 to −0.15) and eGFR (r=−0.83, 95% CI: −0.80 to −0.69) (all p-values <0.001).

Conclusions: The association of serum B2M level with Framingham risk fac-
tors as well as other risk factors of cardiovascular disease helps to explain why it is a good predictor of cardiovascular risk and mortality. This readily available blood test may be useful to identify high-risk patients and prompt the search for reversible causes.

P4660 | BEDSIDE
Postoperative myocardial injury assessed by high-sensitivity cardiac troponin T and revised cardiac risk index in patients undergoing non-cardiac surgery
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Introduction: High-sensitivity cardiac troponin T (hs-cTnT) is useful for detecting myocardial injury and is expected to be a prognostic information marker in patients undergoing non-cardiac surgery. Revised cardiac risk index (RCRI) is also useful for risk stratification in patients undergoing non-cardiac surgery. The aim of this study was to evaluate perioperative myocardial injury assessed by hs-cTnT according to RCRI score.

Methods and results: This study was a prospective noninterventional trial, included 171 consecutive patients undergoing non-cardiac surgery. Serum levels of hs-cTnT were measured before and 24 and 72 hours after non-cardiac surgery. Myocardial injury was defined as postoperative hs-cTnT >0.014 ng/mL and a relative hs-cTnT change of ≥20%. Two patients undergoing dialysis patients were excluded (n=169). Postoperative hs-cTnT levels were significantly increased (before: 0.012±0.009 versus after 24 hours: 0.020±0.045 ng/mL, P < 0.001) and 43 patients (25.4%) were diagnosed as myocardial injury. The rates of myocardial injury for patients with high RCRI score, but it was not observed in patients with RCRI 0. Heart failure was an independent predictor for postoperative myocardial injury.

Conclusions: Postoperative myocardial injury was frequently observed in patients with high RCRI score, but it was not observed in patients with RCRI 0. Heart failure was an independent predictor for postoperative myocardial injury.
P4646 | BEDSIDE
Relationships of QTc interval with cardiac biomarkers in young adults
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Background: Prolonged QT interval is a predictor of sudden cardiac death and is currently under debate whether subclinical clinical cardiac alterations are involved in QT interval determination among young and healthy adults.

Methods: Healthy adults aged 25–41 years were enrolled in a prospective population-based cohort study in the Principality of Liechtenstein. Main inclusion criteria were prevalent diabetes, overt cardiovascular disease or a body mass index <35 kg/m2. Corrected QT (QTc) interval was automatically measured from a standard 12-lead electrocardiogram and validated by a trained physician. N-terminal prohormone brain natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin I (hs-cTnI) were measured by a Roche analyzer and a Singulex assay, respectively. NT-proBNP and hs-cTnI were log transformed because of a non-normal distribution pattern. Multivariable regression models adjusting for potential confounders were constructed to assess the relationships of QTc interval with NT-proBNP and hs-cTnI.

Results: Our sample consisted of 2102 participants (53.6% females) with a median age of 36.7 years. The median hs-cTnI and NT-proBNP levels were 0.69 pg/ml and 34 pg/ml, respectively. The median (interquartile range) QTc interval was 429 (414–442) ms. Results of NT-proBNP and hs-cTnI levels across quartiles of QTc interval are shown in the table. In multivariable analyses using NT-proBNP and hs-cTnI as log-transformed continuous parameters, the beta coefficients (95% confidence interval) were 2.48 (1.34, 3.62), p < 0.0001 per log pg/ml increase in NT-proBNP and −0.28 (−1.15; 1.00), p = 0.95 per log pg/ml increase in hs-cTnI.

Conclusion: There is a strong continuous relationship between NT-proBNP and QTc interval in young and healthy adults, an association that was not evident for hs-cTnI levels. These results may suggest that intravascular volume but not subclinical myocardial injury are related to QTc prolongation.

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P4642 | BEDSIDE
Neutrophil/lymphocyte ratio predicts cardiovascular risk. The PREDMED trial
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Background: The pathophysiological background of common atrial fibrillation (AF) is not well established despite its increasing prevalence in the general population and significant public health burden. Pathways of oxidative stress, nitric oxide bioavailability and L-arginine derivatives are hypothesized to be related to AF. Circulating neutrophil/lymphocyte ratio (N/L) and related inflammatory markers can be assessed in the general population and may show an association with AF.

Purpose: This study investigates correlations of methylated L-arginine metabolites and other diagnostic variables in the general population with AF.

Methods: Neutrophil and lymphocyte counts were determined in 10 healthy subjects. The plasma levels of PTX3 in neutrophils pre- and post-ED were measured by ELISA. The values of FMD were low in pre-ED compared to controls (4.7±1.8 vs 7.5±2.1; p = 0.003) and tended to decrease at the end of the treatment itself. The high values of NT-proBNP and hs-cTnI associated with those of the plasma levels of PTX3 were measured by ELISA. The gene and protein expression of PTX3 on neutrophils was analyzed by flow cytometry and Real-Time PCR. The fluid overload was assessed by estimation of pulmonary artery systolic pressure (PAPs) measured during transthoracic echocardiography, impaired blood pressure was assessed by the presence of arterial stiffness (CA-BELES, expression of arterial stiffness) and ankle-brachial index (ABI), endothelial dysfunction through the flow-mediated vasodilation (FMD) of the brachial artery with ultrasound B-mode method.

Results: PTX3 levels observed at the beginning of the dialysis session (pre-ED) were significantly higher than in controls (2.4±3.63 ng/ml vs. 1.05±0.21 ng/ml; p = 0.005) and tended to decrease at the end of the treatment itself. The high values were associated with a significant increase in gene and protein expression of PTX3 in neutrophils in pre-ED. The values of FMD were low in pre-ED compared to controls (4.7±1.8 to 7.5±2.1; p = 0.01), it normalized after 4 hours of ED (7.03±0.7; p = 0.001) and tended to decline after 24 hours (5.9±0.4). The values of FMD pre- and post-ED inversely correlated (p = 0.02) with those of the plasma levels of PTX3 (27±2.2±4.4 mmHg) and post-ED (18±1.8±1.6 mmHg). Furthermore, in the plasma levels of PTX3 in neutrophils, the expression of NT-proBNP and p-sMC expression were reduced, and a significant increase in NT-proBNP was observed with a decrease in NT-proBNP and −0.08 (−1.15; 1.00), p = 0.95 per pg/ml increase in hs-cTnI.
and the increase of PAPS correlated with neutrophil activation and with the increase (p<0.01) of the expression of intracellular and circulating PTX3 and ROS. In multivariate analysis the PAPS pre-ED and the circulating levels of PTX3 were independently associated with the values of FMD and CABLES.

**Conclusions:** The fluid overload can affect endothelial function and arterial stiffness, through an increase of PTX3.

**RISK FACTORS IN CLINICAL PRACTICE**

**P4665 | BEDSIDE**

**Seasonal variation of the critical limb ischemic events in the whole Hungarian population**

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**Background:** Seasonal manifestations of cardiovascular diseases (CVD) are described in case of acute myocardial infarction, sudden cardiac death, atrial fibrillation, aortic rupture/dissection, Stroke, deep venous thrombosis and pulmonary embolism. Paucity of data is available concerning critical limb ischemia (CLI) on this regard.

**Purpose:** To assess the seasonal trend of critical limb ischemia events in the whole Hungarian population.

**Methods:** Based on the health care administrative data (disease classification and procedure codes) of the whole Hungarian population, in a nine years period (2004-2012), all the events were detected which meet the criteria of CLI. Case detection was based on finding the PAD related major limb amputation and lower limb revascularization (surgical/endovascular) accompanied with pain/tissue necrosis. Seasonality was assessed in an Age-period model.

**Results:** In the whole Hungarian population, over a nine year period (2004–2012), in 144,200 subjects, 55,900 events were identified which met the definition of CLI. PAD related major amputations represented 70%, lower limb revascularization with pain/tissue necrosis was detected in 30% of the cases. The incidence rate of CLI events (taken together and separately also) showed significant decline in late summer and autumn. This was consistent over the whole observational time.

**Conclusion:** This analysis, as the most complete report so far showed consistent results with other smaller studies addressing seasonality of CLI. Biological plausibility is supported by other data showing that cardiovascular risk factors are also seasonal, characterized by a decline in summer. A meaningful temporal relationship, in this manner is also presumable.

**P4666 | BEDSIDE**

**Relationship between traditional cardiovascular risk factors and specific coronary angiographic findings: data from a large cohort of catheterized patients**

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**Background:** The exact relationship between cardiovascular risk factors and coronary angiographic findings has been scarcely addressed. We aimed to evaluate the association between coronary artery stenosis status and conventional risk factors in a large population of catheterized patients.

**Methods:** The study included 1228 subjects who consecutively underwent coronary angiography in our Catheter Laboratory. The severity of coronary artery disease was calculated.

**Results:** Smoking proved the most important CAD predictive factor (p<0.01), followed by dyslipidemia, diabetes, family history and hypertension in a descending order of significance. Obesity rates did not differ significantly between the CAD positive and negative groups (p=0.6), nor changed significantly as the number of diseased vessels increased (p=0.39). Smoking, dyslipidemia and diabetes were positively associated with atherosclerotic involvement of all three major coronary arteries, while hypertension related only to LAD and LCX significant stenosis. The only established risk factors that could reliably predict LMCA were diabetes and age (p=0.01).

**Conclusions:** The risk factor profile of catheterized patients is associated with angiographic findings in a selective way. The angiographic extent of CAD was found to have the strongest positive correlation with male gender and the weakest with hypertension. In terms of CAD positivity, the most important predictive factor was smoking obesity. Sex did not prove to be either a significant predictor of CAD at coronary angiography or an important determinant of CAD severity. Only diabetes and age could reliably predict LMCA disease.

**P4667 | BEDSIDE**

**Atrial fibrillation and impaired renal function predict cardiovascular outcome in mostly hypertensive patients with symptomatic peripheral artery disease and preserved ejection fraction**

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**Purpose:** The study investigated the prognostic role of atrial fibrillation (AF) and renal function in patients (pts) with symptomatic peripheral artery disease (PAD) and preserved left ventricular ejection fraction (LVEF).

**Methods:** The occurrence of major adverse cardiovascular events (MACE, composite endpoint of death, myocardial infarction, stroke, percutaneous coronary intervention and coronary bypass surgery) was prospectively assessed in 183 PAD pts, Fontaine stages IIB and III. LVEF <50% (66% males, 86% hypertensive, mean age 69.7 years, mean ABI 0.59). The diagnosis of AF was based on history and electrocardiographic evidence of arrhythmia. Multivariate Cox regression analysis adjusted for age, gender, traditional cardiovascular risk factors, critical limb ischemia (CLI), estimated glomerular filtration rate (eGFR), AF, coronary and cerebrovascular disease and medications used was applied to assess the independent predictors of poor clinical outcome.

**Results:** The prevalence of AF was 15.3% among PAD pts. During the median follow-up period of 24 months, 42 pts (23%) had an event. These pts were older (72 vs 69 years; p=0.03), more likely to have AF (29% vs 11%; p=0.013), CLI (50% vs 28%; p=0.015), history of coronary and cerebrovascular disease (52% vs 37%; p=0.07) and worse renal function (eGFR <60 ml/min, 62% vs 41%; p=0.028). After multivariable adjustment, AF (HR=2.1, 95% CI: 1.07–4.10; p=0.03) and eGFR <60 ml/min (HR=1.9, 95% CI: 1.05–3.68; p=0.035) remained the only independent predictors of unfavorable outcome (Figure). The model that incorporated AF and renal function to ABI tended to improve prediction of MACE (AUC increased from 0.60 to 0.68; p=0.07).

Kaplan-Meier curves for MACE in PAD pts

**Conclusion:** Impaired renal function and AF are strong and independent predictors of MACE in symptomatic PAD pts with preserved LVEF.

**P4668 | BEDSIDE**

**Are intermediate ankle-brachial index values related to circulating inflammatory, thrombotic and lipid markers in hypertension? Insights from a large cohort of never treated hypertensives**

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**Purpose:** Ankle brachial index (ABI) is a diagnostic tool for peripheral arterial disease; moreover it has a prognostic value for future cardiovascular events. However, the role of intermediate ABI values (0.9 to 1.3) is currently underappreciated. We investigated the interplay of intermediate ABI values with levels of circulating inflammatory, thrombotic and lipid markers in a large cohort of newly diagnosed, never treated hypertensives.

**Methods:** 1,204 newly diagnosed, never-treated hypertensives were recruited. ABI was measured with the oscillometric method; subjects with ABI <0.9 or >1.3 were excluded. Levels of CRP, fibrinogen, Lp(a), plasminogen activator inhibitor-1 (PAI-1) and plasma renin activity (PRA) were measured from blood samples. Correlation coefficients and regression after controlling for confounders were calculated.
Results: The age of the cohort was 53±12 years old; mean BP was 150±18/90±11 mm Hg and mean ABI was 1.16±0.09. ABI exhibited a negative correlation with CRP (r = −0.118), fibrinogen (r = −0.058), Lp(a) (r = −0.071) and PAI-1 (r = −0.059); P < 0.05 for all. The correlation of ABI with FPA was not statistically significant. In multiple linear regression analyses, after adjusting for confounders (age, sex, systolic/diastolic BP, total cholesterol, smoking, presence of diabetes mellitus), ABI emerged as an independent predictor only of CRP (B = −0.751, P < 0.05).

Conclusions: Intermediate ABI values confer a pro-inflammatory state in never-treated hypertensives, as they are independently linked to CRP levels. This may have important implications for risk stratification and pharmacotherapy; prospective studies should elucidate the interplay of subclinical peripheral artery disease, inflammation and hypertension and the impact of anti-inflammatory therapies on risk.

IMAGING FOR PERIPHERAL DISEASE

P4669 | BEDSIDE
Near-infrared spectroscopic hand imaging: a new tool to assess microcirculatory impairment in systemic sclerosis
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Background: Systemic sclerosis (SSc) causes functional and structural microcirculatory dysfunction, affecting also distal extremities. Optical Near-Infrared Spectroscopy (NIRS) of blood HbO2 saturation (stO2) is able to evaluate O2 delivery/consumption balance in the explored tissue. The NIRS-sensitive camera non-invasively detects stO2 values in superficial tissues, automatically generating 2D imaging maps in real time.

Objectives: Whether NIRS hand imaging may evaluate peripheral microcirculatory dysfunction and its spatial heterogeneity in SSc pts compared to controls.

Methods: Fifty-four SSc pts (age 55±16 yrs) and twenty-one healthy controls (mean age 51±14 yrs, p = 0.29) were studied by palmar NIRS 2D imaging. A blood pressure cuff was applied to the forearm and 3-min ischaemia was induced. Images were acquired at basal conditions and each 10 secs during 3 mins of ischemia and 5 mins of reperfusion. Five regions of interest were positioned on each fingertip, from the second to the fifth finger and one on thenar eminence.

Results: A significant difference was found between controls and SSc in basal stO2 (84.3±7.5 vs 75.4±10.9%, p < 0.001), minimum stO2 (65.2±8.0 vs 53.4±10.1%, p < 0.001) and time to maximum stO2 during hyperaemia (63±38 vs 85±49 sec, p < 0.05). Patients with ScI-70 antibodies had lower basal stO2 compared to pts without (69.3±12.7 vs 78.8±11.7%, p < 0.05), as well as pts with diabetes mellitus (69.3±12.7 vs 78.8±11.7%, p < 0.05). Conversely, no significant differences were found among the same SSc subgroups at nailfold capillaroscopy.

Conclusions: NIRS hand imaging is a simple, automated tool to non-invasively detect regional microcirculatory defects in SSc, which seems to add significant functional information to current morphological picture of nailfold capillaroscopy.

P4670 | BEDSIDE
Ultrasound evaluation of the forearm arteries anomalies in patients undergoing percutaneous coronary intervention via radial artery access
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Background: A proven advantage of radial over femoral artery access has led to an increase in the number of interventions via radial artery access in patients with acute coronary syndromes. Transradial procedure failures can sometimes be due to variation in radial artery anatomy. An ultrasound examination of the forearm arteries provides important information about the anatomy of the forearm vasculature.

Objective: The aim of this ultrasonographic study was to assess the morphology and identify potential vascular abnormalities of arteries of the lower arm.

Methods: An ultrasound evaluation of forearm arteries was performed in 110 patients prior to intervention and then vascular anatomy was verified by angiography during the procedure.

Results: The mean age of participants was 59.2±7.9 years. 27% of the study population were females. The population mean for the right radial artery was 2.17±0.54 mm, and for the left radial artery was 2.25±0.43 mm. The measurements revealed sex-related differences in diameters of arteries forearm (p < 0.001). Vascular abnormalities of the radial artery were identified in 11 patients (10%) on an ultrasound examination and confirmed in subsequent angiography. 8 patients had a high-bifurcating radial origin, 3 patients anomalous branching of radial artery. Procedural failure was more common in patients with anomalous anatomy than in patients with normal anatomy (18% vs 1%, p = 0.001).

Conclusions: Ultrasound imaging is a reliable method of evaluation that enables to determine the size and enables reliable evaluation of abnormalities of the radial artery, especially in the distal forearm.

P4671 | BEDSIDE
Facies of hypertension and renal microcirculation
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Purpose: The present study sought to determine the relationship between renal resistive index (RI) and type of hypertension.

Methods: We studied 275 consecutive, newly diagnosed, never treated hypertensives (51±14 year, 55% male). Diabetic individuals and those with overt cardiovascualr or renal disease were excluded. The evaluation of target organ damges (OD) was performed in accordance to the European Society of Hypertension guidelines. Moreover, all patients underwent renal Doppler ultrasound with RI measurement. The mean value of RI from both kidneys was used for the analysis. Based on office and ambulatory blood pressure (BP) levels, the population was split in four groups: masked (17%), isolated systolic (ISH, 15%), isolated diastolic (IDH, 13%) and mixed (systolic-diastolic, SDH, 55%) hypertension.

Results: Patients with ISH were older, predominantly male, with more severe OD, less fit and with the highest RI (Table). Patients with IDH were younger, predominantly female with excellent OD profile, physically active and with the lowest RI. Between these two extreme clinical profiles were patients with masked and SDH, who were middle-aged with intermediate OD profile, moderately active and intermediate RIs. Multinomial logistic regression analysis (reference category IDH) revealed that RI (ISH vs. IDH: OR 1.24 with 95% CI 1.08–1.40 - p<0.001, Masked vs. IDH: OR 1.13 with 95% CI 1.03–1.25 - p<0.008, SDH vs. IDH: OR 0.94 with 95% CI 0.84–1.04 - p=0.263), pulse pressure and heart rate were independent determinants of hypertension type after adjustment for age, gender, abdominal obesity and glomerular filtration rate.

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<td>Masked</td>
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<td>0.001</td>
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<td>Age, years</td>
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<td>24-hour systolic blood pressure, mmHg</td>
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<td>24-hour diastolic blood pressure, mmHg</td>
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<td>Carotid femoral pulse wave velocity, m/sec</td>
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<td>Left ventricular mass index, kg/m2</td>
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<td>Mean common carotid intima-media thickness, mm</td>
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Conclusions: Renal resistive index is closely associated with systolic and diastolic BP and is an independent determinant of hypertension phenotype.
**P4672 | BEDSIDE**

Correlation between arterial stiffness as measured by progression of cardiac aneurysm index and long term hypertension control status

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**Background:** Hypertension plays an important role in the development of arterial stiffness and is well known as a vascular risk factor associated with atherosclerosis. Arterial stiffness can be noninvasively measured by various methods including cardiac aneurysm index (CAVI). This index can reflect the stiffness of the aorta and peripheral vessels eg., temoral and tibial artery. We sought to identify the correlation between arterial stiffness as measured by progression of CAVI and long-term hypertension control status.

**Methods:** Participants with complete CAVI data from Electricity Generating Authority of Thailand (EGAT study in 2007 and 2008) were longitudinally studied. CAVI measurement was performed in 2007–2008 survey with repeated measurement in 2012–2013 survey. Status of hypertension (HTN); awareness, treatment and control; of participants in 2007, 2008, 2012 and 2013 was extensively reviewed.

**Results:** Correlation between status of hypertension during 5-year period and progression of CAVI were statistically analyzed.

**Conclusion:** CAVI progression as a marker for hypertension may be helpful for early detection of the patients who are at risk of developing hypertension.

**P4673 | BEDSIDE**

Magnetic resonance angiographic follow-up of denervation-induced renal artery dissections

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**Background:** Renal denervation has been associated with acute vascular trauma, including the development of minor dissections in the treated vessels, identified by intravascular imaging. The long-term consequences and clinical significance of such dissections are unknown.

**Purpose:** To investigate by magnetic resonance angiography (MRA) the natural history of denervation-induced renal artery dissections detected by optical coherence tomography (OCT), 6 months after the procedure.

**Methods:** Twenty-five patients, that had undergone MRA of the renal arteries, underwent bilateral renal denervation with 4 different systems: Symplicity™ (n=3), Paradise™ (n=5), OneShot™ (n=3) and Vessix V2™ (n=2), and underwent OCT after the procedure. OCT studies were reviewed for presence of dissection. Dissection was identified in 7/13 patients and 5/20 studied vessels. Six-month follow-up by MRA was performed in 6/7 patients (6/8 vessels) with dissection, and quantitative measurements were performed at the baseline and follow-up examinations.

**Results:** Images were successfully retrieved from all 6 vessels. Mean diameter stenosis was 16.4±9.6%, and there was no binary restenosis. There was no significant difference in any luminal measurements between pre-procedure and 6-month follow-up (Lumen volume: 1057±468mm³ vs. 1012±475mm³, p=0.02; mean luminal area: 22.6±6.8mm² vs. 21.1±6.0mm², p=0.26; minimal luminal area: 15.9±3.8mm² vs. 14.7±3.3mm², p=0.04; area stenosis: 34.0±21.0% vs. 29.2±16.3%, p=0.66). An example is illustrated in the figure.

**Conclusion:** Six-month MRA follow-up of patients with OCT-detected, denervation-induced renal artery dissections did not reveal any obstructive steno.

**SAFETY AND EFFICACY OF SECONDARY PREVENTION MEDICATIONS**

**P4674 | BEDSIDE**

Impacts of age on coronary atherosclerosis and vascular response to statin therapy

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**Background:** Age is a well-established risk factor for cardiovascular disease. In addition to the high likelihood of other cardiovascular risk factors being present in the elderly, aging process itself induces structural and functional changes in the vascular wall. Recent trials using intravascular ultrasound (IVUS) have shown that lipid-lowering therapy with statins halts the progression or induces the regression of coronary artery plaques. However, not all patients show regression of coronary atherosclerosis after statin therapy. We speculate that the residual risk for cardiovascular events after statin therapy can be explained in part by age.

**Purpose:** To examine the impacts of age on coronary atherosclerosis and vascular response to statin therapy.

**Methods:** The effects of 8-month statin therapy on coronary atherosclerosis were evaluated using virtual histology intravascular ultrasound from 119 patients who were divided into two groups according to age: elderly patients (≥65 years, n=72) and non-elderly patients (≤65 years, n=47). No patients were taking statins or other lipid-lowering therapies at baseline.

**Results:** At baseline, external elastic membrane (EEM) volume (17.27 vs. 14.95 mm³/mm, p<0.02) and plaque volume (9.49 vs. 8.11 mm³/mm, p<0.03) in the elderly patients were significantly greater than in the non-elderly patients. The EEM volume (−2.4% vs. 0.007) and plaque volume (−3.1%, p=0.007) after 8-month of statin therapy had significantly decreased in the non-elderly patients but not in the elderly patients. A significant positive correlation was observed between age and percentage change in plaque volume (r=0.265, p=0.004). A multivariate re-

**Conclusion:** Adverse events of statin therapy were not observed. Statin effects on coronary atherosclerosis were more pronounced in elderly patients than in non-elderly patients.

**P4675 | BEDSIDE**

Clinical presentation and outcome of bleeding in patients on treatment with new oral anticoagulants or vitamin K antagonists in real-life

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**Background:** In clinical trials, different safety profiles have been shown for new oral anticoagulants (NOACs) compared with vitamin K antagonists (VKAs).

**Purpose:** The aim of this study was to compare clinical presentation, management and outcome of VKAs and NOACs-associated bleedings in real-life.

**Methods:** Patients admitted to the Emergency Department of 8 Italian hospitals for major (MB) or clinically relevant non-major bleeding while on oral anticoagulant treatment from September 2013 to January 2015 were included in a prospective, cohort study. In-hospital death was the primary clinical outcome.

**Results:** 318 patients were included in the study, 61 (19%) on treatment with NOACs and 257 (81%) with VKAs.

**Patients admitted for bleeding while on NOACs were similar to those on VKAs in terms of age (mean 77.9 vs 78.8 years) and prevalence of comorbidities (diabetes, liver or renal failure, vascular disease). A history of bleeding was more common in patients on NOACs in comparison to those on VKAs (31 vs 17%, p=0.017). Shock at presentation was more common in patients on NOACs in comparison to those on VKAs (2 vs 10%; p=0.006).

**Conclusions:** Our study is the first to compare the safety profiles of NOACs and VKAs in routine practice. The increased risk of bleeding in patients on NOACs in comparison to those on VKAs was highly significant (OR 10.95; 95% CI 3.25–36.89; p<0.001)

**Patients admitted for bleeding while on NOACs were similar to those on VKAs in terms of age (mean 77.9 vs 78.8 years) and prevalence of comorbidities (diabetes, liver or renal failure, vascular disease). A history of bleeding was more common in patients on NOACs in comparison to those on VKAs (31 vs 17%, p=0.017). Shock at presentation was more common in patients on NOACs in comparison to those on VKAs (2 vs 10%; p=0.006).

**MB was observed in 77% of patients on NOACs as compared with 87% of patients on VKAs (OR 0.49; 95% CI 0.25–0.99, p=0.045). Among patients with MB, intracranial hemorrhage (ICH) was more common in patients on VKAs compared with patients on NOACs (48% versus 32%, OR 0.51; 95% CI 0.26–0.99, p=0.047) while gastrointestinal bleeding was more common in patients on NOACs as compared to patients on VKAs (OR 2.59; 95% CI 1.35–4.94; p=0.003).

**Conclusion:** No differences were observed in the outcome of patients on NOACs or VKAs.

**Disclosures:** The authors have nothing to disclose.

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while no difference was observed in the use of fresh frozen plasma (FFP) or prothrombin complex concentrates (PCCs). In-hospital death occurred in 40 patients (13%), 35 of whom were on VKAs and 5 on NOACs at admission (14% versus 8.2%; p<0.05). ICH (OR 3.03; 95% CI 1.08–8.47; p=0.035) was an independent predictor of in-hospital death while the use of ASA (OR 0.4; 95% CI 0.20–0.81; p=0.001) was associated with survival. Treatment with NOACs was associated with a not significant decrease in the risk for in-hospital death (OR 0.87; 95% CI 0.30–2.47).

Conclusions: Our real-life data supports the findings from clinical trials of a reduction in the risk of intracranial bleeding in patients on NOACs in comparison to patients on VKAs. Whether these differences will account for a reduction in case-fatality rate of anticoagulants-associated bleeding in favor of NOACs is still undefined.

P4676 | BEDSIDE
Is it necessary to use new antiplatelet agents in patients who are treated with a biore sorbable vascular scaffold?
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Background: During the last months a few cases of late and very late biore sorbable vascular scaffold thrombosis have been reported. Optimal duration and strategy of dual antiplatelet therapy after BVS implantation remain unclear.

Aim: To know the impact of different strategies of dual antiplatelet therapies (DAT) after BVS implantation at immediate and long term follow up.

Methods: Our study includes a group of 556 patients (p) with 680 coronary lesions treated with BVS. All patients were discharged free of symptoms under dual antiplatelet therapy (100 mg of aspirin, plus one or two P2Y12 inhibitors, establishing two groups clopidogrel 75 mg od (n=244 42%), and new antiplatelets agents, prasugrel 10 mg od, or ticagrelor 90 mg bd (n=312 58%) for at least 12 months. Beyond this period discontinuation of the P2Y12 inhibitor was based on their physicians’ decision. Major adverse cardiac events and significant bleedings during the follow up were recorded. The study was designed as a retrospective observational study.

Results: The mean age was 56±9 years. Most of the patients were male (84%) and 24% were diabetics. In terms of complex lesions, 230 bifurcations coronary lesions, 236 diffuse coronary lesions and 30 in-stent restenosis were treated with BVS. The scaffold length was 24±12 mm and the mean BVS diameter was 3.14±0.36 mm. Clinical follow up was obtained in patients. After mean follow up of 15±5 months the cumulative MACE was 5%. There were 5 cardiac deaths (1%), 10 target lesion revascularization (3,5%) and 7 myocardial infarction (1,2%). Three subacute BVS thrombosis (days 2, 3, 7) and 3 late BVS thrombosis (days 57, 224, 359) were documented. Nine major bleedings (1,6%), and one fatal intracranial hemorrhage were reported.

Conclusion: New P2Y12 inhibitors seems to reduce major adverse cardiac events in patients treated with BVS, without increasing episodes of major bleeding. Further and randomized studies are required to establish an optimal strategy and duration of dual antiplatelet therapy.

P4677 | BEDSIDE
SAME-TT2R2 score and the time in therapeutic range in anticoagulated elderly with atrial fibrillation
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Background: The efficacy and safety of vitamin-K antagonists (VKA) depends on the quality of anticoagulation control which can be measured as the time in therapeutic range (TTR). Recently, the SAME-TT2R2 risk stratification scheme was developed as a tool to assess which patients are likely to have a high or a low TTR. However, this scheme was designed from a relatively young population.

Purpose: To study the association between the SAME-TT2R2 scheme and the time in therapeutic range in the very elderly.

Methods: In May 2011, patients with atrial fibrillation (AF) from the outpatient anticoagulation clinic aged 80 years or above were asked to participate in a clinical registry. Baseline characteristics of all included patients were derived from the medical charts and INR measurements were recorded using the international normalized ratio (INR) August 2012. In the Netherlands, the therapeutic INR range is set at 2.0–3.5. Using these boundaries, TTR was calculated using the Rosendaal method. Patients were categorized according to the SAME-TT2R2 score into low risk (0–1 points) or high risk (≥2 points) for stable INR control.

Results: In total 852 patients were included with a median age of 84 years (IQR 82–87). The median SAME-TT2R2 score was 1 (IQR 1–2). Patients with a higher SAME-TT2R2 score were older and comorbidities were more often present. Mean follow up was 1.2 years with no difference between groups. The median TTR was significantly lower in patients with high risk (score ≥2 points; p=0.006). With regard to stable TTR <60% or highly stable TTR >95% INR control, no difference was observed between groups.

P4678 | SPOTLIGHT
Antplatelet drug resistance in Indian population
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Background: Stent thrombosis and consequent post PCI complication are being reported from many centres in India. There is very little data on Aspirin and Clopidogrel resistance in Indian population.

Aim: The study is to estimate the Prevalence of Aspirin and Clopidogrel resistance in Indian patients after Percutaneous Coronary Intervention. The study in-
includes total of 200 consecutive Percutaneous Coronary Intervention (PCI) pa-
tients who consented for the study.
Methods: Anti-platelet drug resistance was evaluated on day seven using Verity
now RPFPT point of care system.
Results: 174 patients (87%) are males and 26 (13%) patients are female in the
age group 35 to 83 years. The study shows that 43 patients (22%) are resis-
tant to Aspirin and 157 patients (78%) are Sensitive to Aspirin. There is signif-
icant (P<0.03) difference in male and female patients in Aspirin sensitive 124/11
(71.42%) and resistant 50/15 (29.58%) patients. There is no significant differ-
ence (P>0.450) in Aspirin resistance/sensitivity and age distribution. This study did not
show any statistically significant (P<0.973) in Aspirin sensitive/resistance in DM
patients. Our study shows 65 patients (32.%) are resistant to Clopidogrel and
135 patients (68%) are sensitive to Clopidogrel. There is significant (P<0.003) dif-
ference in Clopidogrel sensitivity/resistance in male/ female patients. Our study
did not showed statistically significant (P<0.07) difference in Clopidogrel Sensitiv-
ity/resistance in Age distribution. There was no statistically significant difference
(P<0.141) in Clopidogrel sensitive/resistance in diabetes patients. Our study also
shows 6.5% of the patients are resistant to both Aspirin and Clopidogrel.
Conclusion: The prevalence of Aspirin and Clopidogrel resistance is similar to
finding reported from Caucasian population.
Acknowledgement/Funding: Hospital Institute Support

P4680 | BEDSIDE
The assessment of anti-coagulant activity to predict bleeding outcome in atrial fibrillation patients receiving dabigatran etexilate
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Introduction: Special circumstances may require the measurement of the an-
ticoagulant effect of dabigatran etexilate (DE). No data currently link any given
coaulation test to bleeding outcomes in patients receiving DE for atrial fibrilla-
 tion (AF).
Purpose: To correlate different coagulation tests to the bleeding outcomes in AF patients receiving DE.
Methods: Non-valvar AF patients receiving DE of 110 mg (DE110) or 150
mg (DE150) were consecutively enrolled. The hemoclot thrombin inhibitor ass-
say (HTI), prothrombin time (PT), international normalized ratio of PT (INR), and
activated partial thromboplastin time (APTT) measurements were correlated with
bleeding events during a prospective follow-up.
Results: There were 17 bleeding events (8.2%) in 208 patients (74.7±10.3 years
old, 67.9% male, median follow-up: 364 days). Compared with DE110, the pa-
tients receiving DE150 were younger and more often male and had lower HAS-
BLEED and CHADS2VASc scores and better renal function. Subjects: HTI levels
were very variable (DE110, 10–90th percentile: 20.5–223.9 ng/ml). A receiver-
operator characteristic curve gave a median cutoff HTI level of 117.7 ng/ml to
predict bleeding events (C-statistics: 0.65; p=0.036), but no cutoff could be de-
determined for PT, INR or APTT. Based on the Kaplan-Meier analysis, a DE level
>117.7 ng/ml was associated with a higher bleeding rate (15.4% vs. 4.9%,
P=0.01). After multivariate Cox regression analysis, HTI levels, history of stroke
and male gender were independent risk factors for bleeding events.
Conclusions: The independent correlation between DE-HTI levels and bleeding
in patients receiving routine clinical care suggests that monitoring of DE to opti-
mize the risk-benefit ratio is feasible.
Acknowledgement/Funding: Sysmex

P4681 | BEDSIDE
Outcome of transcatheter closure using the amplatzer devices in largest series of patients with isolated aorto-pulmonary window (APW) defect
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Background: Isolated Aortopulmonary window (APW) defect is a very rare con-
genital condition presenting with symptoms of heart failure. There is scant data
about transcatheter closure (TCC) of APW. We present the largest series of pa-
tients undergoing APW-TCC.
Aims: To assess the outcome of transcatheter closure using the Amplatzer de-
vices. Amplatzer duct occluder 1 (ADO I) and Amplatzer septal occluder (ASO) in
patients with APW defect.
Methods and results: Seven patients, aged 07 months to 11 years (median 01
year) with isolated APW were selected for TCC. All patients were symptomatic for
effort intolerance. On examination three patients had continuous to and fro mur-
mur while four had systolic murmur. Transhcoracic echocardiography was used to
size the defect, profile the anatomy of defect with respect to the great arteries
and coronaries and defects deemed suitable were taken up for cardiac catheterizer-
tion and TCC. At cardiac catheterization, the defect size was 3.5–6.5mm (mean 5.4
mm) at its aortic end as measured by angiography. In all patients, the defect was
closed from the venous side, using ADO devices 2.4–8 mm larger than the defect.
The ADO sizes ranged from 8/6 to 10/8mm (median 10/8 mm). An ASO device
was put in one patient. The procedure was successful with no residual shunt in all
patients except one who developed severe hemolysis requiring blood transfusion.
One patient had significant aortic regurgitation (AR) immediate post procedure
which was not related to device, postulated to be due to afterload mismatch & di-
minished to grade I on subsequently. All the patients were asymptomatic on follow
up.
Figure showing pre and post APW-TCC
Conclusion: In appropriately selected patients with isolated APW-TCC is a safe,
effective & attractive alternative to surgery with encouraging outcomes.

P4682 | BEDSIDE
Comparison of hybrid endovascular and open surgical repair for thoracic aortic disease involving arch
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Objectives: To compare the outcomes of hybrid endovascular (Hybrid) and open surgical repair (OR) for thoracic aortic disease involving arch
Methods: A total 83 consecutive patients (men: 59 patients, mean age: 62.4±14.6 years) with thoracic aortic disease involving arch who underwent Hybrid (N=50)
or OR (N=33) were analyzed.
Results: In the Hybrid, patients were older and more combined with COPD. While increased aneurysm and pseudoaneurysm were more common in the Hybrid,
aortic dissection was more common in the OR. In all patients in the Hybrid, supra-aortic vessel transposition and stent-graft implantation were achieved. In the
OR, total arch replacement was performed in 30 patients (91.9%), partial arch replacement in 3 patients (9.1%). Perioperative complications affected 15
patients (30.0%) in the Hybrid and 15 patients (45.5%) in the OR. In-hospital death was more common in the OR (27.3% vs. 6.0%, p=0.010). Primary success
was achieved in 33 patients (66.0%) in the Hybrid. Five patients died after dis-
charge during follow-up (mean: 73.8±76.7 months) in the Hybrid and three patient
died in the OR. In 12 patients, reintervention was necessary in the Hybrid and 2
patient in the OR. Although the reintervention-free survival rate was lower in the
Hybrid (p=0.012) the death-free survival rate during follow-up was not different
between both groups (p=0.164).

Conclusions: Considering higher risk patients allocated and lower perioperative
mortality in the Hybrid group, for thoracic aortic disease involving arch, hybrid
endovascular repair may be an alternative option in frail patients who in open pro-
cedures is too risky. However, higher reintervention rate of hybrid endovascular
repair should be considered for careful selection of treatment modality.

P4683 | BEDSIDE
Percutaneous repair of prosthetic paravalvular leaks: acute and short-term outcomes
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Background: Transcatheter closure has recently emerged as a promising, lower
risk alternative to reoperation for patients with prosthetic paravalvular regurgita-
tion. The aim of this study was to report our experience with the percutaneous repair of
paravalvular leaks.
Aim: To assess the efficacy and the acute and short-term clinical outcomes of
percutaneous mitral and aortic paravalvular leak repair.
Methods and results: Percutaneous repair of paravalvular leaks was at-

Safety and efficacy of secondary prevention medications / Percutaneous/endovascular treatment 819

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tented in 36 patients (age 58.4±14.1 years; 66% males) with heart failure and/or haemolytic anaemia, considered at high surgical risk. Most of the treated defects were in peripheral position (68%). A total of 55 devices (50 Amplatzer Vascular Plug type II, 2 Amplatzer Vascular Plug type IV, 3 Amplatzer Duct Occluder type II AS) was implanted, with 17 patients (47%) requiring 2 or more plugs. The device was successfully implanted in 34 (94.4%) patients and successful closure (defined as regurgitation reduction ≥ 1 grade) was achieved in 29 (80.5%) patients. Overall, the in-hospital complication rate was 8.3% (death, 2.8%; bleeding, 5.5%). No procedural deaths occurred, but 1 (2.8%) patient died 2 days later. The median length of hospital stay was 5 days (IQR 4–7). During a median follow-up of 8 months (IQR 3.5–14.5) no further deaths were encountered. Two patients underwent elective surgery, of whom one had valve replacement after an unsuccessful percutaneous closure attempt, and one had surgical closure of a femoral artery aneurysm in an accessory vascular access site. Symptom improvement during the follow-up (defined as reduction of NYHA Class ≥ 1 grade) was observed in 62% of cases.

Conclusions: Percutaneous repair of mitral and aortic paravalvular leak represents a viable option in selected patients at high surgical risk, with a reasonable rate of procedural success and a satisfactory clinical outcome.

P4684 | BEDSIDE
Deficiency of endothelial progenitor cells is associated with subacute thrombosis after angioplasty in hemodialysis patients
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Purpose: The outcome of renal artery stenting in angiographically borderline stenosis, and then to evaluate blood pressure response to renal artery stenting (PTA).

Methods: 45 renal arteries with mean RAS degree of 55.8±6.4% (50–69%) on angiography were evaluated for functional severity in 40 subjects, aged 65±4.8±4.8, 26M. Criteria for functionally significant RAS were: MLA >8.6mm2, or either peak RPP>20mmHg, or dopamine and papaverine HPG -21mmHg, or RFRR<0.8. Patients with significant RAS were referred to PTA. The impact of systolic and diastolic BP was assessed with a 24-hour ABPM and the number of blood lowering agents, as well as RF (eGFR) during 12 months following PTA. The improvement of BP was defined as SBP reduction of >15mmHg and/or DBP of >7mmHg, and/or a number of blood lowering agents reduction. RF improvement was defined as eGFR increase by 12.5% of the initial value.

Results: Mean MLA was 9.7±4.34mm2 (range:2.4–20.9), mean reference area 27.4±8.3mm (range:15.5–45) and mean stenosis area 70±12.5% (range:39.5–88.6) on IVUS, while mean dopamine RFRR was 0.84±0.1 (range:0.66–1.0). Dopamine was used in 96.7% of cases. Symptom improvement during the follow-up (defined as reduction of NYHA Class ≥ 1 grade) was observed in 62% of cases.

Conclusions: Percutaneous repair of mitral and aortic paravalvular leak represents a viable option in selected patients at high surgical risk, with a reasonable rate of procedural success and a satisfactory clinical outcome.

P4685 | BEDSIDE
Impact of age on the long-term clinical outcomes after carotid artery stenting: a single centre registry
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Background: Carotid artery stenting (CAS) is an accepted alternative strategy to carotid endarterectomy primarily in high risk patients (pts). Although the elderly are a growing population with significant comorbidities and surgical risk, CAS presents a controversial procedure due to scarce clinical data.

Purpose: To evaluate the impact of age on clinical outcomes of CAS in a single centre retrospective analysis.

Methods: From October 2000 to August 2014, 279 pts underwent CAS (285 procedures). Age groups (gp) were established based on the distribution of the population: gp 1 (<73 years, n=140, mean age 64.9±6.2) and gp 2 (>73 years, n=139, mean age 77.9±3.3). Embolic protection devices were used in 99.3% of cases. All patients had a 24-hour in-hospital surveillance post procedure. Mean follow-up (FU) was 33±20 months (M). Primary endpoint was major adverse cardiovascular events (MACE) which included stroke, acute coronary syndrome and surgical risk, CAS remains a controversial procedure due to scarce clinical data.

Results: Baseline characteristics were similar in both gups, except for the presence of smoking, which was higher in gp 1 (p <0.001) and severe valvular disease (SVD) (gp 1: 4.3 vs 17.4%, p <0.001, OR 4.7 CI 1.8–11.9). Procedural success was achieved in 100% of the cases in both gups. In gp 2, proximal flow blockage was used in 12.3 vs 15.7% (p=NS), distal protection filter in 87.0 vs 83.6% (p=NS) and aspirin, clopidogrel and ticagrelor were more frequent in gp 1 (93.7 vs 47.9%, p=0.04). Univariate analysis showed that ACS at 6 M (5.2 vs 0%, p=0.007, OR 1.05 CI 1.01–1.1), MACE at 6 M (8.9 vs 2.9%, p=0.03, OR 3.3 CI 1.03–10.4), ACS at 1 year (63 vs 0.7%, p=0.02, OR 9.1 CI 1.1–73.6) and MACE at 1 year (11.1 vs 3.7%, p=0.02, OR 3.2 CI 1.1–9.3) were more frequent in the older gp (gp 2). This significance, however, did not persist at 2 years FU. All-cause mortality was similar in both gups. Multivariate logistic regression analysis comprised several variables with known prognostic value (prior neurologic symptoms, prior ACS, dyslipidemia, diabetes, smoking, coronary artery disease, SVD) but the model only included age >73 (Exp(B)=3.25, p=0.028), thereby confirming its powerful independent value to predict the primary endpoint at 1 year FU. Notwithstanding the prognostic value of age in our population, all-cause mortality was similar in both gups.

Conclusions: Our data support the statement that older pts are at higher risk for MACE in the first year post procedure, mostly driven by ACS. Therefore, CAS is safe and feasible in an older population with frequent SVD, as long as the pt selection is appropriate and performed by experienced operators.

P4677 | BEDSIDE
Balloon pulmonary angioplasty as treatment option for patients with unoperable chronic thromboembolic pulmonary hypertension
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Background: The natural course of chronic thromboembolic pulmonary hyper-
tension (CTEPH) is similar to a malignant disease. For operable patients pulmonary endarterectomy (PEA) provides a safe and often curative treatment option. Inoperable patients are usually treated with specific medication, often leading to an insufficient improvement. Dependent on the experience of the centre, the proportion of inoperable patients ranges from 10 to 37%. Balloon pulmonary angioplasty (BPA) is alternative treatment for these patients, but presently there are only limited data available that address the outcome of this procedure.

**Purpose**: This study was designed to determine the success rate of a select group of CTEPH patients undergoing BPA at our centre.

**Methods**: A total of 267 CTEPH patients were discussed regarding the treatment options in an interdisciplinary conference consisting of thoracic surgeons, cardiologists, pulmonary specialists, radiologists, and anaesthesiologists. All patients were characterized by technically operable findings according to several imaging modalities. Clinical history, physical examination, 12-lead ECG, laboratory tests, echocardiography, cardiopulmonary exercise test, 6-minute walk, coronary angiography, right heart catheterization, ventilation and perfusion scintigraphy, CT angiography, and pulmonary angiography were assessed for all patients. Seventy-eight (29.2%) patients were classified as being unsuitable for PEA. Out of these 40 patients were designated for BPA, which was planned as a staged procedure via femoral access.

**Results**: All patients undergoing BPA (mean age 64.7±13.5 years) were in WHO functional class III with depressed right ventricular function (TASSP 16.4±8.9) and elevated systolic right ventricular pressure (68.2±14.7 mmHg). Almost half (46.2%) of the patients had been previously treated medically for pulmonary hypertension. After BPA the mean pulmonary artery pressure decreased significantly (40.5±12.3 mmHg vs. 29.6±9.2 mmHg; P<0.001). During BPA we observed 3 dissections of a segment artery, which was treated conservatively. Two patients developed reperfusion oedema with the need for non-invasive ventilation. After BPA 85% of the patients showed a better WHO functional class (P<0.01), increased 6-minute walk distance (P<0.01), and better right ventricular function (P<0.01).

**Conclusion**: BPA for well-selected high-risk CTEPH patients is a useful addition to the surgical and interventional procedure spectrum in high-volume centres performing both BPA and PEA. The long-term outcome following BPA needs to be evaluated in further clinical studies.

**P4689 | BEDSIDE**

**Early release kinetics of N-terminal pro-B-type natriuretic peptide in patients after percutaneous transluminal septal myocardial ablation**

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**Background and introduction**: In symptomatic patients with obstructive form of hypertrophic cardiomyopathy (HCM), septal alcohol ablation (SAA) has been shown to be an effective treatment of HCM. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a powerful biomarker in various cardiovascular diseases as well as in HCM. The aim of present study was to examine the effect of the SAA caused left ventricular outflow gradient and wall stress reduction on serum NT-proBNP levels.

**Methods**: We analysed the early release kinetics of NT-proBNP in 9 patients with hypertrophic obstructive cardiomyopathy undergoing SAA from June 2011 to January 2014. Serum samples were collected in gel tubes tubes prior to and at 1, 2, 3, 4 and 6 hour after SAA. An electrochemiluminescence immunoassay using monoclonal antibodies was used to measure serum NT-proBNP levels (NT-proBNP assay, Elecsys Analyzer Cobas 4010, Roche Diagnostics, Mannheim, Germany).

**Results**: The SAA in nine patients resulted in complete success in eight and partial success in one. In all but one of the cases the serum NT-proBNP values decreased during the first 4 hours. Decreasing mean serum NT-proBNP concentrations were observed at all time points post procedure. The change compared to baseline value was significant at 1, 2 and 4 hour after SAA (P value 0.040, 0.042, 0.038, respectively).

**Conclusions**: Our results show decreasing serum NT-proBNP levels after induction of myocardial infarction during septal alcoholic ablation. These findings suggest that the observed changes in serum NT-proBNP levels may be related to the decrease of the left ventricular wall stress due to the procedure related reduction of the left ventricular outflow gradient.

**P4690 | BEDSIDE**

**Stent implantation jailing deep femoral artery does not worsen clinical outcomes 6 months after endovascular treatment in patients with peripheral arterial disease**

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**Purpose**: The present study evaluated the effect of stent-jail of the ostium of the deep femoral artery (DFA) on clinical outcomes in patients with peripheral arterial disease.

**Methods**: This retrospective study included 143 patients who had undergone successful endovascular procedures for the superficial femoral artery (SFA) that involved the ostium of the SFA or the common femoral artery (CFA). They were classified in 2 groups whether the ostium of the DFA was jailed after stenting (n=79) or not (n=64). Critical limb ischemia (CLI) status, major adverse limb events (MALE) defined as major amputation, target lesion revascularization, and bypass surgery for the target limb was assessed. Amputation free survival in CLI patients and incidence of target lesion revascularization (TLR) in non-CLI patients at 6 month were also evaluated.

**Results**: There were 24 (30.4%) and 22 (34.4%) CLI patients in the jailed and non-jailed group, respectively (P=0.61). Patient and lesion characteristics were similar in both groups, except the higher incidence of chronic total occlusion of the ostium of the SFA (70.9% vs. 20.3%, P<0.001) in the jailed group. There were no significant differences in the incidence of CLI (7.8% vs. 6.3%, P=0.76) and MALE (11.4% vs. 7.8%, P=0.47) between the 2 groups. Amputation free survival in CLI patients (79.2% vs. 77.3%, P=0.88) and freedom from TLR in non-CLI patients (89.1% vs 90.5%, P=0.82) were similar in both groups.

**Conclusion**: Stent implantation jailing the DFA entry does not worsen clinical outcomes in patients with peripheral arterial disease.

**P4688 | BEDSIDE**

**New insights into the rate of percutaneous transluminal coronary angioplasty in patients with peripheral artery disease**

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**Background**: Owing to increasing implantation rates and patients’ longer life expectancy, the need for transvenous lead extraction (TLE) as a specialized procedure has exhibited a significant growth over years.

**Objective**: Herein, we aimed to present our initial experience in TLE by using a novel TighTroll™ Rotating Mechanical Dilator Sheath.

**Methods**: Between October 2014 and February 2015, a total of 34 leads in 19 patients were removed at our tertiary referral centre. All of the extracted leads were >12 months old and indications for extraction were based on the recommendations of the HRS. The leads were removed by using the TighTroll™ Mechanical Dilator Sheath (Spectranetics Corporation) with the rotational cutting force only.

**Results**: Indications for lead removal included cardiac device infection in 9 (47.4%) cases, lead malfunction in the 9 (47.4%) cases and upgrade to CRT-D in the remaining 1 case (5.3%). The extracted devices were pacemaker in 8 (42.1%) cases, ICD in 6 (31.6%) cases and CRT in the remaining 5 (26.3%) subjects. Among 34 leads, 8 (23.5%) were right ventricular, 11 (32.4%) were atrial, 11 (32.4%) were defibrillator coil and 4 (11.8%) were coronary sinus electrodes. The median implantation time (insertion to extraction) was 72 (24–216) months. Complete procedural success with TighTroll™ system alone was achieved in all 19 patients (34 leads, 100%). Clinical success was 100% and all of the patients discharged uneventfully without any complication.

**Conclusions**: Our preliminary data in a small series shows that the mechanical
Endovascular treatment for subacute deep vein thrombosis

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Background: Deep vein thrombosis is a serious disease that causes complications such as pulmonary embolism and post-thrombotic syndrome (PTS). Generally, although thrombolytic therapy and anticoagulation therapy is performed, treatment for patients drug is not effective has not been established. Here, we investigated the effect of endovascular treatment for anti-thrombotic therapy resistance of subacute deep vein thrombosis.

Methods: The target is 11 people who resisted the drug treatment have symptoms such as swelling and pain by the proximal portion deep vein thrombosis (4 male, mean 55.5 years). From onset until the endovascular treatment, an average of 16 days had passed. Until endovascular treatment is performed, unfractionated heparin, warfarin, Xa inhibitor, urokinase was administered. Before performing endovascular treatment, IVG filter was placed to prevent pulmonary embolism in all cases. The sheath (6–8 Fr) is inserted into the popliteal vein or contralateral femoral vein and passed through a wire in the blood vessel. We repeated the aspiration of thrombus using a guide catheter 6–8 Fr. After removal of the thrombus, urokinase was administered using a Fountain-infusion catheter, balloon dilation was performed for venous stenosis. After endovascular treatment, we examined the therapeutic effect in the image examination and clinical findings.

Results: Improved blood flow to the inferior vena cava is obtained in all cases, and needed to balloon dilation in 6 cases, stents were not used. Pulmonary embolism after endovascular treatment did not occur. Edema was improved in all patients, but formation of thrombus within one week was observed in two cases. Other cases did not develop PTS after more than 6 months.

Conclusions: Endovascular treatment for subacute deep vein thrombosis is an effective therapy for venous patency.

Endovascular treatment of aortic coarctation


Background: Coarctation of the aorta (CAO) is a congenital cardiovascular malformation of high prevalence, characterized by a narrowing of the thoracic aorta usually just distal to the left subclavian artery. Untreated, it leads to early death predominantly because of hypertension and its cardiovascular sequelae. The traditional treatment is open surgical repair. More recently, endovascular techniques have been employed as an alternative to traditional open repair, with good results particularly in adults and older children.

Objective: The aim of this study is to report the results of our beginning experience on balloon angioplasty and stenting of native and recurrent CAO.

Methods: Since 2009, a total of 17 patients who underwent transcatheter intervention for COA in our faculty were assigned retrospectively. Procedural Success is defined as peak systolic pressure gradient after balloon therapy or stent implantation <20 mm Hg.

Results: There were 11 males and 6 females. The mean age was 11.47 years (3 months to 39 years old). There were 12 native COA. 9 patients underwent stent implantation and balloon angioplasty was the treatment in 7 cases. Procedural success was achieved in 14 cases (82%). 1 case was complicated with stent migration to the left iliac artery. The peak systolic pressure gradient decreased from 58±20 mmHg to 12±11 mmHg immediately after the procedure. There were no deaths related to the procedure. On follow-up, 3 patients (17%) aged 17, 18 and 24 years old, treated with initial stent implantation underwent balloon angioplasty for recoarctation. The mean time course to restenosis was 7 months. Aneurysm of the left subclavian artery was found in one patient and was treated with the implantation of a covered stent.

Conclusion: Our small and beginning experience in endovascular management of CAO reinforce the impression of an effective and safe therapeutic option, with low rate of complications and less invasive particularly in adults and older children.

Endovascular treatment for subacute deep vein thrombosis

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P4694 | BEDSIDE

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Conclusion: Our small and beginning experience in endovascular management of CAO reinforce the impression of an effective and safe therapeutic option, with low rate of complications and less invasive particularly in adults and older children.

Endovascular treatment for subacute deep vein thrombosis

P4696 | SPOTLIGHT

Methods: We retrospectively analyzed the data of 152 consecutive patients with RASTA undergoing endovascular treatment in our hospital between 2005 and 2012.

Results: At two-year follow-up, the proportion of hypertension cure, improvement, and failure was 27.4%, 63.4% and 12.3% in PTA group (n=93), 22.4%, 62.1%, and 15.5% in stent group (n=59), respectively, p=0.795. Primary patency rate was 90.1% in renal arteries (125 lesions) treated with PTA, 75.6% in renal arteries (64 lesions) treated with stent, p=0.008. Female, active disease in need of balloon dilation and/or immunosuppressant agents, residual stenosis, residual stenosis and stent were significantly associated with the restenosis. In patients with restenosis, renal artery occlusion occurred more frequently in stent group (8/15), compared with that in PTA group (1/12), p=0.019. Reintervention was more common in stent group (13/63), including nephrectomy in 3 patients, than that in PTA group (8/125), p=0.003. In stent group, progressive renal insufficiency occurred in 2 patients (3.4%).

Conclusions: Though, PTA alone and selective stenting had no significant difference in terms of the effect on blood pressure, stenting resulted in inferior 2-year primary patency rate, higher occlusion rate and higher reintervention rate. It should be seriously considered before stenting was undergone in patients with RASTA, particularly in patients with high risk for restenosis.

Endovascular treatment of aortic coarctation


Background: Coarctation of the aorta (CAO) is a congenital cardiovascular malformation of high prevalence, characterized by a narrowing of the thoracic aorta usually just distal to the left subclavian artery. Untreated, it leads to early death predominantly because of hypertension and its cardiovascular sequelae. The traditional treatment is open surgical repair. More recently, endovascular techniques have been employed as an alternative to traditional open repair, with good results particularly in adults and older children.

Objective: The aim of this study is to report the results of our beginning experience on balloon angioplasty and stenting of native and recurrent CAO.
women undergoing percutaneous coronary intervention (PCI) with DES, and (ii) the effect of new-generation DES on the risk of major adverse cardiac events (MACE) in women with or without ACS.

Methods: We pooled patient-level data for women enrolled in 26 randomized trials. Study population was categorized according to the clinical presentation: stable angina (SA), unstable angina (UA) or NSTEMI and STEMI. MACE were defined as the composite of death, myocardial infarction, definite or probable stent thrombosis or target lesion revascularization. Outcomes were reported at 3 years of follow-up. Women who received BMS were excluded from this study.

Results: Of 11,090 women included in the pooled database, 10,133 received a DES. A new-generation DES was used in 6,190 (61.1%). Overall, 5760 (57%) women had a SA, 3954 (35%) had a UA/NSTEMI and 779 (8%) had a STEMI as clinical presentation. Women presenting with STEMI were younger, more commonly men, and had a higher prevalence of diabetes mellitus and hypertension. Female sex was an independent predictor of higher rates of death (HR: 3.45; 95% CI: 1.99–5.98; p<0.001). The mortality risk was associated with STEMI was highest in the first year to then attenuate over time. Use of new-generation DES was associated with a significant benefit on the risk of the death at 3 years in both ACS (HR: 0.58; 95% CI: 0.34–0.98) and non-ACS women (HR: 0.49; 95% CI: 0.30–0.80) without evidence of interaction.

Conclusion: Presentation among women undergoing PCI confers a significantly higher risk for long-term mortality. New-generation DESs provide improved clinical outcomes in women with acute myocardial infarction.

Acknowledgement/Funding: Women in Innovation Initiative of the Society of Cardiovascular Angiography and Interventions.

P4697 | BEDSIDE
Impact of the American College of Cardiology/American Heart Association lesion classification for outcomes in patients with acute myocardial infarction undergoing percutaneous coronary intervention

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Background: Previous studies have reported lesion complexity is predictive of clinical events after balloon angioplasty. However, it is unclear whether complex lesions continue to indicate a worse prognosis in the contemporary era of acute myocardial infarction (AMI).

Purpose: We sought to determine the frequency and the prognostic value of lesion complexity assessed using the modified American College of Cardiology/American Heart Association (ACC/AHA) lesion morphology classification for 1-year outcome comparison with AMI undergoing contemporary percutaneous coronary intervention (PCI) and pharmacologic therapies.

Methods: Data of 18,348 patients were pooled from 2 prospective national AMI registries. Patient characteristics and outcomes were compared based on lesion complexity defined by the modified ACC/AHA classification. The primary endpoint was 1-year all-cause death.

Results: Lesions were classified as type A (n=802 [4.4%]), B1 (n=3,478 [19.0%]), B2 (n=5,577 [30.4%]), or C (n=8,491 [46.2%]), and lesion type A or B1 was considered as simple (23.4%), and type B2 or C, complex (76.6%) lesions.

Conclusions: Type B or C lesions defined by the modified ACC/AHA classification were relatively frequent in patients with AMI, and patients with AMI and type B2 or C lesion characteristics have an adverse 1-year prognosis even after adjustment for clinical covariates. The use of new-generation DES was associated with lower risk of LVD (adjusted HR: 0.73, 95% CI: 0.60–0.89). There were no significant differences in short-term major cardiovascular outcomes between women and men. Women undergoing PCI have a lower risk of LVD than men. There was no association between sex and stent type on short-term outcomes.
Impact of successful recanalization of chronic total occlusions using conventional techniques on long-term clinical outcomes: a meta-analysis


Background: Although coronary stent implantation dramatically reduced the occurrences of restenosis and the need for repeat revascularization, there is still uncertainty as to the prognostic impact of successful recanalization of chronic total occlusion (CTO) lesions.

Methods: Databases were searched for clinical studies that compared outcomes after successful recanalization of CTO lesions using coronary stent deployment with those of unsuccessful recanalization from January 2003 to October 2014. The end points of this study were mortality; myocardial infarction (MI); major adverse cardiac events (MACE); and the need for coronary artery bypass graft surgery (CABG) within a 3-year period.

Results: We identified 18 studies encompassing 11,425 patients with a median follow-up period of 12–60 months after successful vs. unsuccessful CTO recanalization using coronary stent. There were 396 (4.9%) deaths of 8,037 patients after successful recanalization compared to 329 (10.6%) among 3,111 patients after unsuccessful recanalization (odds ratio [OR] 0.46, 95% confidence interval [CI] 0.37 to 0.58). Successful CTO recanalization significantly reduced the incidence of MI (OR 0.67, 95% CI 0.45 to 0.99) and MACE (OR 0.58, 95% CI 0.43 to 0.77). The need for subsequent CABG was significantly lower after successful recanalization (OR 0.16, 95% CI 0.12 to 0.21). There was no evidence of publication bias, as evidenced by a symmetrical funnel plot (Figure).

Conclusions: Successful recanalization of CTO lesions using coronary stent deployment appears to be associated with improvement in mortality and reduced needs for CABG as compared with unsuccessful PCI.

Adjunctive balloon post-dilatation in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

P. Song1, J.Y. Hahn2, E.K. Kim1, Y.B. Song2, S.H. Choi3, J.H. Choi3, H.C. Gwon4 on behalf of the Effects of Postconditioning on Myocardial Reperfusion in Patients with ST-segment Elevation Myocardial Infarction (POST) trial. 1Pohang University of Science and Technology, Division of Biomedical Engineering, Pohang, South Korea; 2Kaesong Paik Hospital, Inje University College of Medicine, Division of Cardiology, Department of Internal Medicine, Busan, Korea, Republic of; 3Samsung Medical Center, Cardiovascular Center, Seoul, Korea, Republic of Latvia; 4Universit"{a}t Z"{u}rich, Zurich, Switzerland.

Background: Adjunctive balloon post-dilatation has been shown to improve both post-procedural stent dimensions and stent apposition, but the relation to outcomes is not clarified. Furthermore, there have been some concerns regarding the risks of this practice, particularly in the setting of acute myocardial infarction (AMI).

Purpose: Our aim was to evaluate how adjunctive balloon post-dilatation influences procedural and 1-year clinical outcomes following primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: Outcomes were assessed in 679 patients undergoing stent implantation for STEMI in the Effects of Postconditioning on Myocardial Reperfusion in Patients with ST-segment Elevation Myocardial Infarction (POST) trial. We used multivariate logistic regression and Cox proportional hazard modeling to estimate risk of outcomes with vs. without adjunctive balloon post-dilatation. The procedural outcomes included the rate of no-reflow after adjunctive balloon post-
P4703 | BEDSIDE
Feasibility and safety of percutaneously inserted emergency VA-ECMO in cardiac catheterisation laboratory in acute MI with severe cardiogenic shock
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Background: Survival in patients suffering from cardiogenic shock is poor. The literature reports conflicting results for survival after extracorporeal membrane oxygenation support in adult. Data on use of veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support initiated by interventional cardiologist in cardiac catheterization laboratory is lacking. We present our institutional experience of VA-ECMO in patients with acute STEMI suffering severe cardiogenic shock.

Purpose: To demonstrate feasibility, safety and effectiveness of rapid initiation of VA-ECMO support by interventional cardiologists in cardiac catheterisation laboratory.

Methods: ECMO database between November 2013 and January 2015 was used to identify patients who underwent emergency VA-ECMO support. All patients treated using the VA-ECMO protocol were included.

Results: A total of 8 patients underwent emergency VA-ECMO support initiated in the Cardiac catheterization laboratory. All 8 patients were male, aged 33–56 (mean 45). 7 presented with STEMI and 1 was an iatrogenic left main coronary dissection. Of the 7 STEMI patients 5 were primary PCI and 2 were rescue PCI, 4 were anterior infarcts (2 left main occlusion) and 3 were inferior. All 8 were profoundly hypotensive on high inotropic support, and 4 were undergoing CPR at the time of cannulation. Cannulation of the femoral artery and vein performed percutaneously by the interventional cardiologist while the ECMO device was set up. Mean ECLS (ECMO support team) time was 20 minutes. Elective hypothermia (32–34°C) was used in the 4 patients who were receiving CPR. After ECMO was established maximal revascularization was carried out including the use of rotational atherectomy in one patient. One patient had a STEMI with non-culprit coronary artery disease. VA-ECMO support was maintained at 3.7 – 4.8 l/min and continued for 42–121 hours. All 8 patients were successfully weaned from ECMO and survived > 30 days. Seven patients were discharged from the hospital. One patient had neurological damage and suffered late death at 12 months after PPCI.

Conclusions: VA-ECMO is a feasible and safe approach to managing residual disease based on predicted outcomes. In the PPCI setting, calculating rSS is more practical than calculating the baseline SYNTAX score. In patients treated using the VA-ECMO protocol, mortality, nonfatal myocardial infarction and stroke during the follow up in group of patients treated with staged PCI in comparison with patients treated conservatively, an intention-to-treat analysis was used. Patients were followed for 38 months (median). Composite primary endpoint appeared in 15 (13.9%) patients in no PCI group and 17 (16.0%) in PCI group with hazard ratio in staged PCI group 1.35; 95% confidence interval [0.66 to 2.74]; p=0.681. Hazard ratio for all cause mortality was 0.91 (95% CI, 0.30–2.70) and for non-fatal myocardial infarction 1.71 (95% CI, 0.66–4.41) in staged PCI group. 19 (17.6%) patients from no PCI group had PCI of non-culprit coronary artery during the follow up due to progression of angina symptoms or myocardial infarction. Only 13 (6.1%) patients had non-culprit artery stenosis ≥95% and the non-culprit artery in 2 patients was medial or circumflex coronary artery.

This trial found no difference (not even a trend) favouring staged multivessel PCI over culprit-only PCI in STEMI. Larger trials are needed to clarify the revascularisation strategy in STEMI patients with multivessel disease.

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P4704 | BEDSIDE
A comparison of baseline and residual SYNTAX scores in prediction of mortality after primary percutaneous coronary intervention for STEMI
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Background: There is renewed interest in complete revascularisation after primary percutaneous coronary intervention (PCI) for STEMI elevation myocardial infarction (STEMI), recent studies suggest that pre-emptive treatment of non-infarct related arteries (IRA) improves cardiac outcomes. Calculation of the residual SYNTAX score (rSS) after PCI of the IRA may help to standardise the approach to managing residual disease based on predicted outcomes. In the PPCI setting, calculating rSS is more practical than calculating the baseline SYNTAX score (bSS). However, rSS has not been compared with any prognostic utility of the bSS in this patient group.

Purpose: We therefore compared the ability of bSS and rSS in predicting mortality at 12 months after PPCI.

Methods: 590 patients presenting for PPCI from Jan 2012 to Dec 2013 were identified from the prospective database of our high-volume tertiary centre. Of these, 168 were excluded from analysis because they had presented > 12 hours after the onset of major pain, required intubation or cardiopulmonary resuscitation before arrival at the hospital, had had previous CABG or did not actually receive PCI. APRI prediction was used to examine the relationship between bSS, rSS and the primary end-point of 12-month mortality.

Results: Of the 422 patients (mean age 59) analysed, 81% were male and 18% had known diabetes. At 12 months, the mortality rate was 5.4% (23/422). Logistic regression revealed an odds ratio (OR) for mortality of 1.05 (95% CI: 1.02–1.10, P=0.007) for bSS and 1.06 (95% CI: 1.02–1.11, P=0.009) for rSS.

Conclusion: Both baseline SS and residual SS at primary PCI can predict mortality at 12 months. The higher the bSS or rSS, the worse the prognosis. After PPCI, revascularised and the used for assessing the relationship between bSS, rSS and the primary end-point of 12-month mortality.

P4705 | BEDSIDE
Multivessel disease diagnosed at the time of primary PCI for STEMI: complete revascularization versus conservative strategy
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Primary percutaneous coronary intervention (PCI) of the occlusion or significant stenosis of infarct (culprit) artery is a method of choice in treatment of acute myocardial infarction with ST segment elevation with ST segment elevation (STEMI). The purpose of this study was to find out the optimal management of patients with STEMI treated by PCI who have at least one significant (>70%) stenosis of non-culprit coronary artery. From 2009 till 2013 214 patients with STEMI and multivessel coronary disease, successfully treated with infarct related artery PCI, were enrolled into the trial in six centers. 108 patients were randomly assigned to no PCI group and 106 to staged PCI group. Outside others patients with limiting angina pectoris present more than 1 month prior to STEMI were excluded from the trial. There were no significant differences between baseline characteristics in both groups. The primary endpoint of the study was the incidence of combined endpoint of all cause mortality, nonfatal myocardial infarction and stroke during the follow up in group of patients treated with staged PCI in comparison with patients treated conservatively.

Results: Patients were followed for 38 months (median), Composite primary endpoint appeared in 15 (13.9%) patients in no PCI group and 17 (16.0%) in PCI group with hazard ratio in staged PCI group 1.35; 95% confidence interval [0.66 to 2.74]; p=0.681. Hazard ratio for all cause mortality was 0.91 (95% CI, 0.30–2.70) and for non-fatal myocardial infarction 1.71 (95% CI, 0.66–4.41) in staged PCI group. 19 (17.6%) patients from no PCI group had PCI of non-culprit coronary artery during the follow up due to progression of angina symptoms or myocardial infarction. Only 13 (6.1%) patients had non-culprit artery stenosis ≥95% and the non-culprit artery in 2 patients was medial or circumflex coronary artery.

This trial found no difference (not even a trend) favouring staged multivessel PCI over culprit-only PCI in STEMI. Larger trials are needed to clarify the revascularisation strategy in STEMI patients with multivessel disease.

Acknowledgement/Funding: Research Grant IGA MZ CR NT1142-5/2010 and Project FNUSA-ICRC (CZ.1.05/1.1.00/02.0123)

P4706 | BEDSIDE
Beneficial effects of an old drug - intracoronary verapamil improves left ventricular function in acute anterior STEMI
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Objectives: Coronary microvascular dysfunction is frequently observed in patients with acute STEMI, leading to a suffering ischemic cardiomyopathy. Intracoronary adenosine is recommended by guidelines for improvement of myocardial reperfusion. However, side effects including bradycardia and hypotension are frequent, limiting its use. We evaluated the effects of intracoronary administration of verapamil on left ventricular function in patients with acute anterior STEMI after PCI. Long-term follow up (6 months) and 1 year.

Material and methods: This prospective study included 98 consecutive patients diagnosed with acute anterior STEMI, randomized into two groups: CON-control (n=47) and VER-verapamil (n=51). In the VER group, 250–500 mcg verapamil diluted in 1 ml, improves e 2 ml NaCl solution were injected into the infarct-related artery immediately after stenting, while 2 ml NaCl were injected in the CON group. Left ventricular function was assessed by echocardiographic parameters (EDV, ESV, EDD, EF) at admission, at 6 weeks and after 1 year. Wall motion of the LV segments were assessed in segments 7, 8, 13, 14, 15 and 16, and according to the AHA Consensus. Statistical analysis was performed using Mann-Whitney and X2 tests for nominal variables.

Results: The groups were homogeneous regarding age, gender, heart rate, SBP.
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Natural history of stent malapposition in patients treated by primary percutaneous coronary intervention: Subanalysis of ROBUST trial

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Background: Stent malapposition is anticipated to be associated with unfavorable clinical outcomes, but data from patients treated by primary percutaneous coronary intervention (PCI) are rare.

Purpose: To evaluate association of baseline stent malapposition to minimal lumen area, area stenosis, and percent of uncovered struts in 9-months follow-up.

Methods: 105 patients with acute ST segment elevation myocardial infarction underwent OCT-guided PCI. Either biolimus A9 or everolimus eluting stents were used in the trial. The OCT study was performed with C7-XRTM intravascular imaging system employing a non-occlusive technique. It was intended to maintain complete stent apposition, if feasible. Subsequent offline pullback analysis was performed using OCTival-Stent software. According to post-PCI OCT finding patients were divided in groups with 0–1%, 1–2%, 2–3% and >3% of malapposed struts. Data in groups were compared by Kruskall-Wallis test with Holm correction.

Results: With increasing percent of malapposed struts in baseline OCT, there was significant increase in area stenosis in follow-up. Trend towards increased percent of uncovered struts and decreased minimum lumen area was insignificant (see Table 1).

Conclusion: More pronounced stent malapposition in primary PCI is associated with increased area stenosis in 9-months follow-up.

Acknowledgement/Funding: The work was supported by a long-term organization development plan 1011 (FmHS).

P4708 | BEDSIDE

Intracoronary nitropusside versus verapamil for the prevention of no/slow reflow phenomenon in patients undergoing primary percutaneous coronary intervention

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Background: No/Slow reflow is a serious complication of percutaneous coronary intervention (PCI) performed for acute myocardial infarction that increases mortality and decreases left ventricular functional recovery. Furthermore, this phenomenon is also linked to ventricular arrhythmias, early congestive heart failure and ventricular remodeling. Once it occurs, there are limited treatment options which is not as effective as prophylaxis.

Objective: To compare between the efficacy and safety of intracoronary verapamil versus nitropusside in the prevention of the no/Slow reflow phenomenon in patients with acute ST segment elevation myocardial infarction (STEMI) undergoing primary PCI.

Methods: A total of 60 STEMI patients with Thrombolyis In Myocardial Infarction (TIMI) flow grade 0/1 were randomly allocated 1:1 to receive verapamil (n=30) or nitropusside (n=30) given to the occluded site using local drug infusion balloon catheter. The primary endpoint was the incidence of ST-segment resolution (STR) - 70% on electrocardiogram at 90 min after PCI. Secondary endpoints were angiographic Microvascular obstruction (MVO) incidence (TIMI flow grade ≤2 or 3 with a myocardial blush grade ≥2), echocardiographic evaluation (left ventricular ejection fraction (LVEF) and wall motion index score (WMIS)), occurrence of hypotension, and major adverse cardiac event (MACE) rate at 30 days as a composite of cardiac death, myocardial infarction, target lesion revascularization, and heart failure requiring hospitalization.

Results: STR - 70% for single lead showing maximal ST elevation occurred in 33.3% of verapamil -treated patients and in 6.7% of nitropusside-treated patients (p<0.009), and for the sum of multiple leads showing ST elevation occurred in 43.3% and in 13.3% respectively (p<0.04). Angiographic MVO occurred in 10% of verapamil -treated patients and 30% of nitropusside-treated patients (p<0.04). The mean LVEF was 42.6±4.9 and 40.4±4.7 for verapamil and nitropusside-treated patients respectively (p=0.086). Likewise, the mean WMIS was 1.43±0.13 and 1.45±0.16 for verapamil and nitropusside-treated patients respectively (p=0.145). Proporional hypotension occurred in 3.3% and 20% respectively (p<0.04), MACE occurred in 3.3% and 6.6% respectively (p<0.09).

Conclusion: In STEMI patients treated by PCI, intracoronary verapamil achieved a significantly better myocardial reperfusion with a significantly less occurrence of hypotenion in comparison to nitropusside. However, there was no significant difference in MACE at 1 month follow up.

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P4709 | BEDSIDE

Effect of guidewire passage and mechanical thrombus aspiration on ST segment displacement in primary percutaneous coronary intervention for STEMI

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Background and purpose: We studied the effect of guidewire passage and thrombus aspiration on ST segment resolution in patients treated by primary percutaneous coronary intervention (PCI) for acute STEMI.

Methods: A Witt biomedical ECG system was used for all ECGs. A 12 lead trace was recorded in the angiography laboratory at the start of the case and further ECGs were recorded after a guidewire had been passed down the occluded coronary artery, after mechanical thrombus aspiration and at the end of the case whilst the patient was still on the cath lab table. ST segment deviation was evaluated in the lead with maximum elevation, measured 75 msec after the J point. ECGs with left bundle branch block were excluded. A proportion of the ECGs were independently assessed by a second individual to evaluate reproducibility and good concordance was found. A repeated analysis of variance was used to compare the absolute ST segment elevation means at different stages.

Results: The mean ST segment elevation at the beginning of the case was 5.1mm and this fell to 4.2mm after guidewire passage (p<0.001). When thrombus aspiration was performed the mean ST segment elevation was 4.1mm (not significantly different from guidewire passage). Mean ST segment elevation at the end of the case was 3.4mm. The proportion of patient who achieved more than 50% resolution of the original ST elevation was 15.7% cases after guidewire passage, 23.6% after thrombus aspiration and 43.0% at the end of the case. Adverse ST segment changes (defined as ST elevation greater than the initial ECG) was seen in 14.6% cases after guidewire passage, 21.4% cases after thrombus aspiration and in 14.0% patients at the end of the case.

Conclusion: In this series of patients the mean resolution of ST segment elevation during PCI was not significantly greater after thrombus aspiration compared to simple passage of the guidewire. We propose that guidewire passage could be used as the "device time" to assess PCI services. Thrombus aspiration appears to exert a mixed effect on ST resolution in STEMI in that more patients achieve more than 50% resolution compared to guidewire passage alone, however, more patients exhibit a worsening of ST segment displacement with thrombus aspiration. These data are consistent with the uncertain role of routine thrombus aspiration in PCI for STEMI.
P4710 | BEDSIDE

Safety and effectiveness of deferring definitive treatment of the culprit lesion in major myocardial infarction

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Background: In selected patients (p) with ST segment elevation myocardial infarction (STEMI), deferring treatment of the culprit lesion after achieving reperfusion might be a better option. There is lack of strong evidence about the safety and the effectiveness of this strategy.

Methods: Retrospective study was performed comparing STEMI p with deferring definitive treatment after reperfusion (Group A) versus STEMI p with immediate stenting (Gr B) during primary percutaneous coronary intervention (PPCI).

Results: There were no difference either in the ischemic (rotational atherectomy was performed in 14%). There is a trend of reduction in significant residual lesion. A delayed stent implantation was needed in 48% of Gr A (0.30%), 3 (0.30%) and 18 (1.80%) respectively. At 6-month, TLR was found in 5 (0.5%) patients, indicating their high reinfarction, and 5 (0.5%) target-lesion revascularizations, and 0 (0%) target-vessel revascularization.

Conclusions: In selected STEMI p who underwent a PPCI, the deferred treatment of the culprit lesion showed similar results in effectiveness (ischemic MAC), and safety (bleeding) compared with immediate stenting, with a trend of reduction in infarct size measured by CK.

P4711 | BEDSIDE

In-hospital, thirty-day and six-month result of bidegradable polymer coated sirolimus eluting stent in coronary artery lesions (i-TRIAL study)

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Background and introduction: The i-TRIAL study was a multi-centre, retrospective, non-randomized, single-arm study, which enrolled 1008 consecutive patients treated with Indolimus, between April 2012 and June 2014. The only exclusion criteria was patient’s refusal to provide written informed consent. The primary-end point of the study was major adverse cardiac events (MACE), which is an aggregate of cardiac death, myocardial infarction, target-lesion revascularization and stent thrombosis (ST). The clinical follow-ups were scheduled at 30-day and 6-month.

Results: The mean age of enrolled patients was 52.6±11.0 years. A total of 1137 lesions were intervened successfully with 1242 stents (1.09±0.30 stent per lesion). The average stent length and diameter was 27.4±20.9 mm and 3.12±0.36 mm respectively. There were 740 (73.40%) male patients, indicating their high prevalence. Diabetes, hypertension and chronic totally occluded lesions were found in 372 (36.90%), 408 (40.47%) and 170 (16.86%) patients, respectively. These shows that study also included high risk complex lesions and not ideal revascularized lesions. The incidence of MAC at in-hospital, 30-day and 6-month was 3 (0.30%), 3 (0.30%) and 18 (1.80%) respectively. At 6-month, TLR was found in 5 (0.5%) patients. The were 2 (0.20%) cases of ST and 7 (0.70%) cases of MI at 6-month follow-up.

Conclusions: The use of Indolimus is associated with lower incidence of TLR, ST and consequent MAC. Thus, the i-TRIAL study gives an idea about favorable safety, efficacy and clinical performance of the Indolimus in the real world of interventional cardiology.

P4712 | BEDSIDE

The role of thrombus aspiration for primary angioplasty in patients >75 years with ST elevation myocardial infarction: the ESTROFA MI+75 study

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Purpose: Primary angioplasty is the best reperfusion treatment in ST elevated myocardial infarction. The prevalence of very elderly patients (>75 years) undergoing primary angioplasty is progressively increasing as population is ageing. The benefit of thrombus aspiration is unknown for this important subgroup of patients.

Methods: Retrospective consecutive registry conducted in 21 centers of patients >75 years with ST elevation myocardial infarction undergoing primary angioplasty.

Results: A total of 2,146 pts have been included, and among them, 1,064 (49.5%) underwent thrombus aspiration and 1,082 (50.5%) did not. A propensity score matching was performed yielding two comparable groups of 432 patients each without significant differences in baseline clinical or angiographic characteristics. All patients had completed one year follow up. Outcomes at 12 months were: cardiac death, major adverse cardiac event and TLR with or without aspiration vs. 16.5% with aspiration (p=0.03). TLR 3.9% vs. 1.8% (p=0.01) definitive or probable stent thrombosis 3.6% vs. 1.1% (p=0.08) respectively.

Conclusions: In this registry half of patients over 75 years underwent thrombus aspiration during primary angioplasty. A propensity score matching analysis of the use of thrombus aspiration was associated to a significant improvement in clinical outcomes at 12 months.

P4713 | BEDSIDE

Real-world experience with ultra-thin bidegradable polymer coated sirolimus-eluting coronary stent: Six-month clinical outcomes of FLEX-Registry

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Background and introduction: FLEX-Registry is a retrospective multicenter registry, sought to examine safety and efficacy of ultra-thin bidegradable polymer-coated sirolimus-eluting Supraflex (Sahajanand Medical Technologies Pvt. Ltd, India) coronary stent for the treatment of coronary artery disease across a wide range of unselected patients treated in routine clinical practice, including those with high-risk characteristics and complex lesions.

Methods: FLEX-Registry is a retrospective, non-randomized, single-arm and multicentre registry. A total of 995 consecutive patients who received 1,399 Supraflex stents for the treatment of 1,184 lesions between periods of July 2013 to May 2014 at 9 different tertiary care centres were enrolled. The patients were followed-up at 6 months after the index procedure by telephone contact or clinical visit. The primary end-point of the study was major adverse cardiac event, a composite of cardiac death, myocardial infarction, target-lesion revascularization and target-vessel revascularization at 6-month clinical follow-up.

Results: FLEX-Registry included high risk patients, among whom 441 (44.3%) were hypertensive and 231 (23.2%) were diabetics. Average number of stents per patient was 1.41±0.56. Clinical follow-up at six-months was completed in 986 (99.10%) patients. Major adverse cardiac event was reported in 4 (0.4%) and 11 (1.1%) patients at in-hospital and 30-day follow-up respectively. Major adverse cardiac event was observed in 22 (2.2%) patients at 6-month follow-up, comprising 11 (5.5%) cardiac death, 5 (5.5%) myocardial infarction, and 5 (0.5%) target-lesion revascularizations, and 0 (0%) target-vessel revascularization. Stent thrombosis occurred in 1.1% (11 patients) at 6-month clinical follow-up.

Conclusions: FLEX-Registry evaluated clinical outcomes in real-world and more complex cohorts and thereby provides evidence to the clinicians for safe and routine extended use of Supraflex, sirolimus-eluting stent, to a broader percutaneous coronary intervention population.
Background: Patients undergoing primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) are at high risk of femoral vascular complications (VC). In spite of the growing use of the radial approach, femoral remains the most common in primary PCI. The use of femoral vascular closure devices (VCDs) has expanded in recent years despite the controversial in previous trials. The objective is to evaluate safety and efficacy, and to compare these VCDs in primary PCI.

Methods: A total of 827 consecutive patients undergoing primary PCI for STEMI via femoral were studied for in-hospital and 6 months out-patient outcomes through a registry from January 2010 to October 2013. The primary end point was the presence of VC defined as a composited of hematoma ≥6 cm, recurrent bleeding, pseudoaneurysm, arteriovenous fistula, arterial thrombosis or reper-

tional bleeding.

Results: 404 (48.8%) patients received Angio-Seal® and 423 (51.2%) Exo-Seal®. 39 (4.7%) patients had a VC, with a similar incidence of events between the 2 VCDs (4.7% vs 4.8%, p=0.90). Gender, type of PCI (STEMI or NSTEMI) and TIMI flow prior to the procedure. We did not observe significant difference in the PPCI procedural technique (use of aspiration thrombectomy, pre dilatation, post dilatation or use of IVUS) or procedure outcomes (success rate, referral to CABG or mortality rate) between cases performed during day time vs. night time.

Conclusions: VC after femoral approach in patients undergoing primary PCI for STEMI rebleed in a high incidence despite the routine use of VCDs in our hospital. These VC were significantly associated with individual characteristics (BMI, CKD, PAD) and procedure-related (sheath size). The safety and efficacy of both VCDs is similar after primary PCI in patients with STEMI.

P4717 | BEDSIDE

ST-elevation myocardial infarction and multivessel disease: predictors of non-culprit lesion revascularization


Introduction: In patients with multivessel disease (MVD) undergoing primary percutaneous intervention (PCI), revascularization of the non-culprit lesions within the first month is associated with a significant improvement in clinical outcome. Yet, it is not clear how to select non-culprit lesions and what is the right timing of revascularization.

Purpose: We investigated in our daily clinical practice the predictors of non-culprit lesion revascularization (percutaneous or surgical [CABG]) within 30 days from the primary PCI.

Methods: All consecutive patients undergoing primary PCI (pPCI) from 2010 to 2014 at our cath lab were included. Multivessel disease was defined as the presence of ≥50% stenosis in at least one non-culprit vessel. Study endpoint was any revascularization performed in the non-culprit lesion within 30 days from pPCI. Predictors related between clinical, angiographic and procedural factors with the study endpoint were explored with logistic regression analysis. Relationship between the study endpoint and clinical outcome was analyzed by Cox-regression analysis.

Results: We enrolled 299 patients of whom 192 (64%) presenting with MVD. Revascularization of the non-culprit lesion was performed within 30 days in 71 patients (68 with PCI, 3 with CABG) and 97 lesions: 1 LM (1%), 30 (30%) LAD, 35 LCX (36%), 31 RCA (32%) (p<0.01). Most of the non-culprit lesion revascularization (79%) occurred within the first 3 days from the pPCI. Dyslipidemia (p<0.01), % diameter stenosis of non-culprit vessels (p<0.01), MVD (p=0.01), and rate of 2-vessel disease with LAD involved (p<0.01) or 3-vessel disease (p<0.01) were significantly associated to the study endpoint at the univariate analysis. No asso-
ciation was found with left ventricular ejection fraction or diastolic volume. At the multivariate analysis, a significant association was observed only with the % diameter stenosis of the non-culprit lesion (OR 1.05, 95% CI 1.03–1.07). A mean follow-up of 16 months was obtained in 108 (36%) patients. At the Cox-regression, revascularization of the non-culprit lesion within 30 days was not as-

P4718 | BEDSIDE

The Impact of operator fatigue and sleep deprivation on primary percutaneous intervention procedure technique and outcomes

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Background: Studies have demonstrated that operator fatigue and sleep deprivation may impact the procedural performance and outcomes, but little information is available about this subject in Primary Percutaneous Intervention (PCI).

Methods: We compared the PCI procedural strategy and clinical outcomes between patients who present during night time (11:00 PM to 7:00 AM) vs. those who present during day time (7:00 AM to 11:00 PM) in high volume center using the PCI data registry.

Results: 721 patients underwent pPCI at our Heart Hospital between October 1, 2013 and September 15 2014. Among those 29% cases were performed during night time and 71% during day time. There was no significant difference in demographic and type of PCI and TIMI flow prior to the procedure.

Conclusion: Operator fatigue and sleep deprivation do not seem to have a significant impact on the PCI procedure technique or outcomes.
suffered a cardiac death (0.6%), 2 had MI (1.2%), 1 underwent TLR (0.6%) and overall TLF rate was 2.4% (4/168). No stent thrombosis occurred during 6-month of follow-up.

Conclusions: In day-to-day clinical practice, treatment of CTO with Indolimus SES showed favourable immediate, short and midterm clinical outcomes.

P4718 | BEDSIDE
Clinical outcomes of first and second generation drug-eluting stent implantation for unprotected left main coronary artery bifurcation

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Aims: To investigate the outcomes of first and second generation drug-eluting stent (DES) implantation for unprotected left main coronary artery (ULMCA) bifurcation lesions.

Methods and results: This is a single center, retrospective study. Between April 2007 and March 2013, a total of 1075 percutaneous coronary intervention were performed in our hospital. Among these, we performed elective DES implantation for 241 stable angina patients with ULMCA bifurcation lesions. 86 Sirolimus-eluting stents and 32 Paclitaxel-eluting stents were implanted. (116 patients in first generation group) 4 Zotarolimus-eluting stents, 82 Everolimus-eluting stents and 37 Biolimus A9-eluting stents were implanted. (123 patients in second generation group). We evaluated their backgrounds and clinical outcomes. The end points were the occurrence of major adverse cardiac events (MACE) and target lesion revascularization (TLR). First and second generation groups were followed up for 1389±532 days and 583±381 days. Backgrounds are similar in both groups. Kaplan-Meier survival curves showed that freedom from MACE at 1 and 3 years was 97% and 96% in second generation group compared with 95% and 91% in first generation group (p=0.24). Freedom from TLR at 1 and 3 years was 95% and 92% in second generation group compared with 93% and 88% in first generation group (p=0.54).

Conclusion: Second generation DES offers no statistically significant advantage over first generation DES in long-term outcome after ULMCA bifurcation stenting.

P4719 | BEDSIDE
Influence of screen display in percutaneous coronary intervention: size does not matter


Background: Quantitative coronary angiography (QCA) is not used in routine clinical practice and stent size is chosen by visual reference. New radiological equipments of percutaneous coronary intervention (PCI) allow to create a custom and different sized display.

Purpose: To determine the influence of screen size in the number, diameter and length of implanted stents, the need of post-dilatation and the presence of intimal dissection.

Methods: 334 consecutive patients who underwent coronary intervention (449 lesions) were randomized into two groups. 162 patients group S (small) with 45x56cm display and 172 patients group L (large) with 70x87cm display. Those lesions) were randomized into two groups. 162 patients group S (small) with 70x87cm display and 172 patients group L (large) with 70x87cm display. Those lesions) were randomized into two groups. 162 patients group S (small) with 70x87cm display and 172 patients group L (large) with 70x87cm display. Those lesions) were randomized into two groups.

Conclusions: Second generation DES offers no statistically significant advantage over first generation DES in long-term outcome after ULMCA bifurcation stenting.

P4720 | BENCH
Catheter substrate mapping to guide left ventricle aneurysm exclusion in patients post myocardial infarction

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Background: Substrate of ventricular tachyarrhythmias (VTA) is caused by post infarct (MI) scar. The purpose of this single center study was to evaluate the efficacy of the electroanatomical mapping (EAM) prior aneurysmectomy to identify the arrhythmogenic areas and of the myocardium in order to guide the surgeons to navigate resection and cryoablation of the most critical areas of the myocardium.

Patients and methods: 69 pts (≥ age 64 years, 56 m/13 w, with documented post MI aneurysms (Echo, MRI, LV angiography) were included into the study. In all pts VTA induction was tested prior to surgery and electroanatomical mapping (EAM) with identification of specific late and fractionated potentials was performed. Surgeon used the predefined EAM to navigate the surgery to eliminated most of the arrhythmogenic zones by resection of the aneurysm plus cyaooablation. EAM with programmed ventricular stimulation was repeated 2–3 months after aneurysmectomy to evaluate the effect of the surgical procedure.

Results: In all 69 pts we created EAM as a guide for surgical LVAR plus cyaooablation of the most important areas. Prior surgery VT was inducible in 34 pts (49%), after surgery VT was induced in only 3 pts (4.3%). EAM was performed in 57 pts after LVAR procedure and in all we demonstrated significant change of the substrate including reduction of late and fractionated potentials. Average of follow-up is 31.8 months (3–47) with only 2 deaths due to noncardiac reasons.

Conclusion: EAM reconstruction prior LVAR could play important role: 1. arrhythmia surgery by cryo-ablation of very specific substrate leads to dramatic reduction of VTA induction; 2. guide accurate LV reconstruction.

P4721 | BENCH
A randomized comparison of subcutaneous “Z” stitch versus manual compression to achieve hemostasis after large caliber femoral venous access

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Background: With the growing number of interventions requiring large caliber venous access, there is need for a safe and effective method of achieving hemostasis post procedurally. Subcutaneous stitches have been introduced for this purpose but systematic data on their performance are lacking.

Purpose: The study sought to: 1. compare “Z” stitch to manual compression in attaining hemostasis after femoral venous access with large bore sheaths, and 2. assess vein patency with the stitch in place and after its removal.

Methods: In this single center, randomized study, 86 consecutive patients with 90 femoral venous access sites requiring >10F sheaths were randomly assigned to “Z” stitch or compression group for hemostasis in a 1:1 fashion. “Z” stitch is a modified figure-of-eight suture introduced at our centre that allows for performance of deep stitches longitudinally to the vein’s long axis for improved safety and efficacy. Participants underwent structured assessment at baseline, peri-procedurally, at discharge, and at target 30 days follow-up. Duplex ultrasonography of groins was performed at discharge, and also in a subgroup of 28 unselected participants with the stitch in place.

Results: Mean of study participants was 61.7±19.1yrs. 33.3% were males.

The mean sheath size was 13.8±2.6F, (range 10 to 22F). Baseline patients’ characteristics were distributed equally between the groups. In the stitch vs. the compression group hemostasis was achieved quicker (<1 min vs. 12.1±5.2 min resp.), patients were sooner able to ambulate (9.3±7.4 vs. 16.2±5.7 hours after the procedure resp.), there were less minor access site bleedings (10% vs. 33% resp.), (p=0.05 for all). At visual inspection, 20% of patients in each group presented groin bruises greater than 10cm up to the target 30 days follow-up. Discharge ultrasound showed groin hematoma in 3.3% of patients in the stitch group vs. 10% in the compression group (p=0.18). All veins were patent at discharge with similar lumen diameters between the groups (9.3mm for the stitch vs. 10.4mm for compression group, p=0.11). Ultrasound study before stitch removal showed similar lumen diameters between the groups (9.3mm for the stitch vs. 10.4mm for compression group, p=0.11). Ultrasound study before stitch removal showed similar lumen diameters between the groups (9.3mm for the stitch vs. 10.4mm for compression group, p=0.11).

Conclusions: The “Z” stitch is a safe, effective, and cheap method of achieving hemostasis after large bore venous sheath removal. The stitch saves cath lab teams’ time and allows for earlier patients’ ambulation when compared
to manual compression. It does not compromise vessel’s patency. It appears like the method of choice in the studied settings.

Acknowledgement/Funding: The trial was funded by the institutional grant of the Institute of Cardiology in Warsaw.

BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS III

P4722 | BEDSIDE
Cytotoxic serum activity is independent mortality predictor of patients with chronic heart failure
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Introduction: Elevated serum level of neurohormones, cytokines and other agents is a major determinant of prognosis in chronic heart failure (CHF). This circulating cytotoxic load damages endothelial cells and increases the risk of cardiac events.

Purpose: We aimed to determine whether the damaging activity of serum may predict prognosis of patients with CHF.

Methods: Fifty seven patients with CHF and left ventricular systolic dysfunction (ejection fraction <40%) participated in this study (mean age 59±8 years, 81% male). Ten sex- and aged-matched healthy subjects served as a control group. According to NYHA criteria 40 (70%) patients were in stable class II and 17 (30%) in class III. Ischemic etiology of CHF was confirmed by coronary angiography in 34 (60%) patients and ruled out in 23 (40%). Mean left ventricular ejection fraction was 25±8%. Endothelium-dependent flow-mediated dilatation (FMD) of the brachial artery was assessed by high resolution ultrasound. Human umbilical vein endothelial cells (HUVEC) were incubated for 72 hours with 20% serum of patients. Cell viability was detected using the fluorescein -annexin V-propidium iodide double-staining and analysis with a flow cytometer. Patients were monitored over a minimum follow-up of 30 months (median 35.5 months). All-cause mortality was a single endpoint.

Results: Serum from patients with CHF increased the level of dead endothelial cells when compared with healthy subjects (18% vs 7%, p<0.0001) and decreased the level of viable cells (respectively 82% vs 93%, p<0.0001). Rate of dead HUVEC cells was similar for serum from patients with ischemic and nonischemic CHF (respectively 17% and 19%, p=ns). There was a significant inverse correlation between percentage of dead endothelial cells in vitro and endothelium-dependent vasodilatation in vivo (r=-0.28, p<0.05). During follow-up 13 patients died. Serum from this group decreased the level of viable endothelial cells after incubation when compared with survivors (61% vs 83%, p<0.0001). Cox regression analysis revealed that high cytotoxic serum activity (Exp[B]=0.631, SE 0.039, p<0.001) was the independent predictors of death.

Conclusions: Circulating blood of patients with CHF damages endothelial cells. This action is irrespective of etiology of CHF and related to impaired FMD. Cytotoxic serum activity is independently associated with a worse prognosis in patients with CHF. Assessment of serum-induced cellular injury could provide important, integrative estimate.

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P4723 | BENCH
The accuracy of biomarker risk prediction score in patients with chronic heart failure
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Background: Glomerular filtration rate (GFR) is one of the potent prognostic markers in patients with heart failure. Recently, cystatin C-derived GFR has been proposed for more precise estimation for GFR. We aimed to test the prognostic value of cystatin C-derived GFR in patients with heart failure of acute decompen- sated heart failure.

Methods: This retrospective study included 262 patients with acute decompen- sated heart failure. Prognostic value of the estimated GFRs, derived from the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation containing cystatin C (CKD-EPI-cystatin C equation) and CKD-EPI-cystatin C-creatinine equation, were compared with estimated GFR derived from the clas- sic equations containing only serum creatinine levels (Modification of Diet in Re- nal Disease (MDRD) equation and CKD-EPI-creatinine equation). Prognosis was evaluated with the composite of all-cause mortality and readmission for decom- pensated heart failure within one year.

Results: Mean age was 65.8±14.9 and 126 (48.1%) were men. Among the patients, 106 (40.5%) were with ischemic etiology. During the follow-up (mean follow-up 264.0±136.1 days), 67 (25.6%) events occurred. Mean estimated GFRs were 67.1±32.2, 64.8±27.4, 54.2±26.2 and 57.2±24.1 [ml min–1 (1.73m2)–1] for MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation, respectively. Estimated GFR using CKD-EPI-cystatin C was the best for predicting 1-year outcome in receiver operating characteristic curve (AUC). This retrospective study included 262 patients with acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure.

Conclusion: Estimated GFRs, which were derived from cystatin C, predicted the prognosis more accurately in patients with acute decompenated heart failure, compared to those from creatinine-alone equations.

Acknowledgement/Funding: The trial was funded by the institutional grant of the Institute of Cardiology in Warsaw.

P4724 | BEDSIDE
Prognostic value of cystatin C-derived estimated glomerular filtration rate in the patients with acute decompened heart failure

Background: Glomerular filtration rate (GFR) is one of the potent prognostic markers in patients with heart failure. Recently, cystatin C-derived GFR has been proposed for more precise estimation for GFR. We aimed to test the prognostic value of cystatin C-derived GFR in patients with heart failure of acute decompen- sated heart failure.

Methods: This retrospective study included 262 patients with acute decompen- sated heart failure. Prognostic value of the estimated GFRs, derived from the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation containing cystatin C (CKD-EPI-cystatin C equation) and CKD-EPI-creatinine equation, were compared with estimated GFR derived from the clas- sic equations containing only serum creatinine levels (Modification of Diet in Re- nal Disease (MDRD) equation and CKD-EPI-creatinine equation). Prognosis was evaluated with the composite of all-cause mortality and readmission for decom- pensated heart failure within one year.

Results: Mean age was 65.8±14.9 and 126 (48.1%) were men. Among the patients, 106 (40.5%) were with ischemic etiology. During the follow-up (mean follow-up 264.0±136.1 days), 67 (25.6%) events occurred. Mean estimated GFRs were 67.1±32.2, 64.8±27.4, 54.2±26.2 and 57.2±24.1 [ml min–1 (1.73m2)–1] for MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation, respectively. Estimated GFR using CKD-EPI-cystatin C was the best for predicting 1-year outcome in receiver operating characteristic curve (AUC). This retrospective study included 262 patients with acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure. Prognostic value of cystatin C-derived estimated glomerular filtration rate in patients with heart failure of acute decompen- sated heart failure.

Conclusion: Estimated GFRs, which were derived from cystatin C, predicted the prognosis more accurately in patients with acute decompenated heart failure, compared to those from creatinine-alone equations.

Acknowledgement/Funding: The trial was funded by the institutional grant of the Institute of Cardiology in Warsaw.

P4725 | BEDSIDE
Right ventricular function is a powerful independent predictor of adverse heart failure outcomes

Background: There is significant heterogeneity in advanced heart failure disease trajectory related in part to the ability of the right ventricle to respond to the failing left heart.

Aim: To investigate the predictive value of clinical, biochemical, haemodynamic and echocardiographic indices in this setting.

Methods: 182 consecutive patients listed for heart transplantation were studied. Descriptive statistics performed, 118 patients died, 64 patients received a cardiac transplant and 60 patients required ventilator assist device (VAD) insertion. Median freedom from death, VAD or cardiac transplant was 236 days. Univariate factors associ- ated with death/ VAD/ transplantation included body mass index, left ventricular ejection fraction, right ventricular function, cardiac index, right ventricular stroke work index, pulmonary vascular resistance, pulmonary arterial wedge pressure (PAWP), glomerular filtration rate (GFR), bilirubin, albumin and sodium (P<0.05 for all). Excluding serum markers in multivariate analysis, the functional indices

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which remained significant included haemodynamic variables derived from right heart catheterisation including PAWP, pulmonary vascular resistance, right ventricular stroke work index, as well as right ventricular function on echocardiography (P < 0.01 for all). Right ventricular indices were closely associated with bilirubin, QFR, albumin (P < 0.03 for all), PAWP was associated with sodium (P = 0.02).

Conclusion: Echocardiographic and haemodynamic measures of left ventricular function do not have as strong an impact on prognosis as those of right ventricular function. The strong correlations between bilirubin, albumin and QFR with prognosis, as well as their close association with haemodynamic and echocardiographic markers of right ventricular function, suggest that right ventricular adaptation is important in determining outcomes in patients with heart failure.

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P4726 | BEDSIDE
Heart rate / systolic blood pressure ratio at discharge as a simple prognostic factor for adverse clinical outcomes in patients with acute heart failure
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Background: Increased heart rate (HR) and low systolic blood pressure (SBP) are associated with worse clinical outcomes in patients with acute heart failure (AHF). However, the clinical significance of pre-discharge HR/SBP ratio was not evaluated in patients with AHF. Therefore, the aim of this study was to investigate the impacts of pre-discharge HR/SBP ratio on early clinical outcomes in patients AHF following discharge.

Methods: A total of 5,660 patients (68.5±14.5 years, 3,019 males) with AHF were consecutively enrolled in Korean AHF registry (KorAHF) who had HR and BP measurement at discharge, and 279 patients who died during hospitalization were excluded. Receiver operating characteristics (ROC) curve analysis to predict mortality was performed to identify the optimal cut-off value of HR/SBP ratio before dividing groups. They were divided into two groups according to HR/SBP ratio; high HR/SBP ratio group (≥0.6, n=2,751, 66.9±14.9 years, 1,465 males) and low HR/SBP ratio group (<0.6, n=2,630, 69.9±13.9 years, 1,388 males). Composite endpoints including all-cause mortality, and rehospitalization at 3 months of follow-up were compared between the groups.

Results: Baseline clinical characteristics were not different between the groups except for the higher prevalence of hypertension (49.6% vs. 32.4%, P < 0.0001), diabetes (66.7% vs. 62.3%, P < 0.0001), and ischemic heart disease (76.6% vs. 67.8%, P < 0.0001) in high HR/SBP ratio group. ROC curve analysis identified BP/HR ratio ≥0.66 as the optimal cut-off value for prediction of mortality in patients with AHF (AUC=0.584, 95% CI 0.551–0.617, P < 0.0001). Moreover in patients who could not be prescribed BB at discharge, the incidence of endpoint was significantly higher in high HR/SBP ratio group than in low HR/SBP ratio group (26.4% vs. 21.8%, P=0.008). In patients with BB use, however, there were no significant differences between the groups (17.9% vs. 16.5%, P=0.333). This phenomenon is not shown for ACEI or angiotensin II receptor blocker. In multivariate analysis using Cox proportional hazard model, high BP/SBP ratio (≥0.66) turned out to be an independent predictor of composite endpoint (HR 1.35, 95% CI 1.20–1.53, P < 0.0001).

Conclusions: Pre-discharge HR/SBP ratio was a significant prognostic factor of adverse clinical outcomes in patients with AHF after discharge. AHF patients who have high HR/SBP ratio might have to be subscribed BB before discharge for better long-term clinical outcomes. Pre-discharge HR/SBP ratio would be useful in the risk stratification or predicting future clinical events after discharge in patients with AHF.

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P4727 | BEDSIDE
The presence of metabolic syndrome predicts long-term outcome in heart failure patients
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Background and aim: It has been shown that the Metabolic Syndrome (MeS) is independently associated with increased incidence of heart failure (HF) and coronary artery disease. We investigated the prognostic value of MeS in addition to other clinical and Doppler echocardiographic parameters on the clinical outcomes in HF patients.

Methods: This study included 188 consecutive patients (62±10 years) with congestive HF. The primary outcomes were cardiac events (CE = mortality or need for hospitalization) due to acute HF signs and/or symptoms. LV end-diastolic and end-systolic dimensions, ejection fraction (EF), mitral and tricuspid annulus peak systolic excursion (MAPSE and TAPSE), myocardial velocities (s, e' and a'), left atrial (LA) dimensions, LA volume and LA emptying fraction were all measured. Based on the on the NCEP-ATP III criteria, patients were divided into MeS (n=83) and non-MeS (n=105) groups.

Results: During the follow-up (18±6 months) period, 87 patients (47%) had CE. The creatinin level was higher (P < 0.01), LV mass index was higher (P < 0.01), LA was larger (P < 0.001), LV ejection fraction was less, E/e' lower (P < 0.001), septal MAPSE lower (P < 0.01), diabetes and MeS more prevalent (P = 0.03 and P = 0.01, respectively), NYHA ≥2 more frequent (P < 0.01), in patients with cardiac events compared to those without. Patients with HF and MeS were older (P < 0.008), had larger LA (P < 0.04), lower systemic arterial pressure (P < 0.006, respectively), and reduced LV ejection fraction (P < 0.01) compared to those with non-HF MeS. Multivariate analysis identified E/e' (OR=0.1, 95% CI 1.081–1.234; P=0.02) and MeS (OR=3.967, 95% CI 1.673–9.409; P=0.002) as independent predictors of CE.

Conclusions: In medically treated patients with chronic HF, the presence of MeS, in addition to increased LV filling pressure, was associated with increased risk of cardiac events. This finding highlights the need for better optimization of medical therapy in HF patients with MeS.

P4728 | BEDSIDE
Outcome of cardiac sarcoidosis patients treated with cardiac resynchronization therapy- comparison with other non-ischemic cardiomyopathy patients
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Background: Cardiac sarcoidosis (CS) is a progressive myocardial inflammatory disease. In a subset of patients with CS, cardiac resynchronization therapy (CRT) is often indicated due to severe left ventricular dysfunction. However, there has been no report examined the significance of CRT in CS patients compared with other non-ischemic cardiomyopathy (NICM) patients.

Methods and results: We retrospectively investigated 96 patients with NICM, including 6 patients with CS, treated with CRT. We compared several parameters and prognosis of CS patients with those of non-CS patients. Fourteen patients with CS received steroid therapy. Prednisolone was administered in all CS patients with positive inflammation confirmed with gallium-68 citrate scintigraphy. CS patients had a similar frequency of positive CRT response, compared to non-CS patients (P=NS). During follow-up, cardiac death occurred in 1 patient with CS and 21 patients with non-CS (P=NS). Appropriate ICD therapies occurred in 7 patients with CS and 27 patients without CRT (P=NS). In multivariate Cox proportional hazards analysis, the prognosis of CS patients was relatively better, but not significantly compared with non-CS patients (HR: 0.214, 95% CI: 0.028 to 1.161, P=0.135).

Conclusions: Although CS commonly progresses, CS patients, in whom steroid therapy was administered if inflammation is positive, showed similar frequency of positive CRT response, appropriate ICD therapy and cardiac death compared to non-CS patients with NICM.

P4729 | BEDSIDE
Transient systolic hypotension worsens the 2-year prognosis of chronic heart failure with preserved left ventricular ejection fraction
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Introduction: Although more than half of all patients with chronic heart failure (CHF) are patients with preserved ejection fraction, factors influencing the prognosis of CHF in such patients are not clear now.

Purpose: The aim of this study was to determine the prognostic value of two-year episodes of arterial hypotension in patients with chronic heart failure (NYHA Class II–III) and preserved left ventricular ejection fraction (LVEF>50%).

Methods: 169 patients with CHF (95 females and 74 males, mean age was 56.3±10.9 years) and preserved ejection fraction (LVEF>50%) were studied. Left ventricular ejection fraction was 60.6±5.4%. 105 patients had functional class II
of CHF, 64 - Class III according to NYHA classification. Causes of CHF were: arterial hypertension in 16 patients, coronary artery disease (CAD) - 9 patients, CAD and arterial hypertension - 144 patients. The follow up period was 2 years. Combined endpoint included nonfatal myocardial infarction (MI) and cardiovascular death (CVD death). Patients were treated according to the European Society of Cardiology guidelines. The 24-hour ABPM was performed using MxSDFP-2 and MxSDFP-3 BPLab devices. During ABPM arterial hypertention was diagnosed according to criteria P.E. Owens and E.T. O'Brien (1996).

Results: Episodes of systolic arterial hypertention during the 24-hour were revealed in 54 (28.6%) of systolic-diastolic hypertention - in 45 (26.8%), of systolic-diastolic hypertention - in 54 (32.0%), absence of arterial hypertention episodes – in 65 (38.4%) patients. There were 8 MI or CVD deaths: 2 – in the group of patients with episodes of diastolic arterial hypertention and 6 - in the group of patients with systolic-diastolic hypertention. Instead of these there were no combined endpoints were found in the group of patients with CHF without episodes of arterial hypertention (x²=2.48, p<0.3 and x²=5.46, p<0.01, respectively). Relative risk of nonfatal MI or CVD death in patients with CHF with episodes of systolic arterial hypertention was 9.5 (95% CI, 2.5 to 12.2).

Conclusions: Episodes of arterial hypertention are diagnosed in 61.6% of patients with chronic heart failure (NYHA Class II-III) with preserved left ventricular ejection fraction. The presence of episodes of systolic or diastolic hypertention in patients with chronic heart failure increased the 2-year risk for nonfatal myocardial infarction and total cardiovascular death.

P4730 | BEDSIDE

KIM-1 and NAG: new renal biomarkers for prognosis in acutely decompensated heart failure

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Background: Patients with acutely decompensated heart failure suffer often from cardiological syndrome (CRS). The aim of the present study was to assess whether novel kidney injury markers are relevant for prognostication in acute heart failure.

Methods: The new renal biomarkers Kidney injury molecule-1 (KIM-1), N-acetylated beta-D-glucosaminidase (NAG), Neutrophil Gelatinase-Associated Lipocalin (NGAL) and IL-18 (Interleukin 18) were assessed from urine samples of 58 patients with acutely decompensated heart failure at admission and at discharge, beside NT-proBNP and serum creatinine.

Results: Patients were followed for a median duration of 644 days (IQR 316, 837 days). Upon survival analysis, a total of 22 deaths and 34 events regarding the combination of death or rehospitalisation for congestive heart failure occurred. Admission and discharge NT-proBNP as well as admission serum creatinine and discharge KIM-1 and NAG were significant predictors for all-cause mortality and the combination of all-cause mortality and rehospitalisation for heart failure (all p<0.05). On a Cox regression analysis including EF, occurrence of acute kidney injury, NYHA stage > 2, BMI, age, serum creatinine and respectively one of the markers, KIM-1 and NAG at discharge performed as independent predictors for both endpoints beside NT-proBNP at begin and end of therapy (each p<0.05). Upon ROC analysis, especially discharge KIM-1 showed satisfying predictive values (AUC 0.68 for both endpoints).

Conclusions: KIM-1 and NAG offer important prognostic information in patients with acutely decompensated heart failure, opposite to admission values. Therefore, these findings allow new insights in kidney injury in patients with heart failure and the potential role of new tubular markers in prognostication of acute heart failure.

Acknowledgement/Funding: none

BASIC MECHANISMS

P4731 | BEDSIDE

Octadecatetralin and phosphatidylcholine as a potential new biomarkers in heart failure - novel insights from the analysis of serum metabolome in chronic heart failure patients


Background: Patients with chronic heart failure (CHF) exhibit increased oxidative stress, which is associated with mitochondrial dysfunction. A decrease in mitochondrial fatty acid oxidation (FAO) is a hallmark of mitochondrial dysfunction in cardiomyocytes and involves the increased activity of fatty acid synthase (FAS) and peroxisomal β-oxidation. In addition, the decreased expression of the PPARα/β/δ pathway is associated with FAS activity and FAO.

Methods: We prospectively studied 36 optimally treated patients with chronic heart failure (NYHA Class II-III) with preserved left ventricular ejection fraction (LVEF > 40%). The patients were divided into groups treated with AngII, norepinephrine (NE) or a sub-depressor dose of the AngII receptor blocker Irbesartan (IRB) with AngII for 2 wks. The mice from each group were subjected to echocardiography for our evaluation of the standard basic echocardiography measurements and calculations for the estimation of left ventricle (LV) morphology and function. We used immunohistochemistry to determine the expressions of pNF-κB, MCP-1 and the infiltration of monocytes/macrophages in the heart tissues. We evaluated the O2- content using fluorescent dihydroethidium for the in situ imaging of ROS generation in the myocardium. NADPH oxidase activities were determined by a luminoscence assay. Immunoblotting was performed by the ELISA method.

Results: AngII and NE resulted in similar significant increases in systolic blood pressure in all drug-treated groups compared to the control group in both the WT and Tlr4lps-d mice (P<0.05). In the WT mice, AngII induced cardiac hypertrophy, vascular remodeling, perivascular fibrosis of the intramyocardial arteries, and monocyte/macrophage infiltration into the heart (P<0.05). AngII also increased the LV diastolic function and induced a greater LV end-systolic dimension (P<0.05), and it produced a fivefold increase in NADPH oxidase activity, ROS content, and pNF-κB and MCP-1 expression (P<0.05). The Tlr4-deficient (Tlr4lps-d) and wild-type (WT) mice were randomized into groups treated with AngII, norepinephrine (NE) or a sub-depressor dose of the AngII receptor blocker Irbesartan (IRB) with AngII for 2 wks. The mice from each group were subjected to echocardiography for our evaluation of the standard basic echocardiography measurements and calculations for the estimation of left ventricle (LV) morphology and function. We used immunohistochemistry to determine the expressions of pNF-κB, MCP-1 and the infiltration of monocytes/macrophages in the heart tissues. We evaluated the O2- content using fluorescent dihydroethidium for the in situ imaging of ROS generation in the myocardium. NADPH oxidase activities were determined by a luminoscence assay. Immunoblotting was performed by the ELISA method.

Conclusions: AngII and NE produced a similar significant increase in systolic blood pressure in all drug-treated groups compared to the control group in both the WT and Tlr4lps-d mice (P<0.05). In the WT mice, AngII induced cardiac hypertrophy, vascular remodeling, perivascular fibrosis of the intramyocardial arteries, and monocyte/macrophage infiltration into the heart (P<0.05). AngII also decreased the LV diastolic function and induced a greater LV end-systolic dimension (P<0.05), and it produced a fivefold increase in NADPH oxidase activity, ROS content, and pNF-κB and MCP-1 expression (P<0.05). The Tlr4lps-d mice showed a smaller effect of AngII on these indices. In the WT mice, IRB treatment reversed these changes compared to the mice treated with AngII alone. NE produced little effect on any index in either the WT or Tlr4lps-d mice. Conclusions: TLR4 may be involved in the increased oxidative stress, selectively affecting the MCP-1, and cardiac hypertrophy and dysfunction seen in AngII-induced hypertension.

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P4734 | BENCH
Differentiation of fibroblasts into myofibroblasts during hypertensive-derived cardiac fibrosis is promoted by alpha-β-catenin integrin-mediated activation of TGF-beta1

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Introduction - TGF-β1 plays a key role in the hypertensive-associated cardiac fibrosis by acting on cardiac fibroblast differentiation to produce α-smooth muscle actin (α-SMA)-expressing myofibroblasts. Integrin-mediated mechanotransduction plays an important role in TGF-β1 activation via its release from latent TGF-β1 binding protein 1 (LTBP-1). Integrin αvβ5 is expressed in the heart tissue and is known to be involved in the TGF-β1 activation.

Purpose: We tested if the hypertensive stimuli present in a rat model of hypertension were sufficient to elicit TGF-β1 activation by integrin αvβ5-mediated traction.

Methods: Immunohistochemistry and Western blot analyses were conducted on heart tissue from Spontaneously Hypertensive Rats (SHR, n=10) and normotensive Wistar Kyoto rats (WKY, n=10).

Results: SHR heart tissue displayed a greater amount of ECM deposition particularly in the perivascular region. Integrin αvβ5 (Figure 1a-c) and LTBP-1 expression (Figure 1g-i) were also significantly increased in the SHR heart (p<0.05, Figure 1e,m). Moreover, isolated SHR cardiac fibroblasts (± recombinant TGF-β1) were more prone to switch to α-SMA expressing cells in vitro, compared to normotensive cardiac fibroblasts, and had a statistically significant higher expression of integrin αvβ5 and LTBP-1 (p<0.05, Figure 1f,n).

Conclusions: Hypertension stimulated the upregulation of integrin αvβ5, LTBP-1, α-SMA and TGF-β1. It also promoted ECM deposition, the main defining feature of cardiac fibrosis. These results open future studies on molecular targets and integrins in cardiac fibroblasts as a strategy to selectively block integrin-mediated TGF-β1 activation and reduce the progression of the cardiac fibrosis process.

P4735 | BEDSIDE
IL-6 signaling in patients with chronic heart failure treated with cardiac resynchronization therapy

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Increased IL-6 concentration has been described in ventricular dysfunction and chronic heart failure (CHF). Apart from the direct effect on membrane bound IL-6 receptor, IL-6 activity (trans-signaling) is mediated by the soluble IL-6 receptor (sIL-6R) and balanced by soluble gp130 (sgp130). Cardiac resynchronization therapy (CRT) is a unique treatment method dedicated for CHF patients, that may reverse the course of the disease.

We evaluated IL-6 signalling, including sIL-6R and sgp130 concentrations, in patients with CHF taking into account the effect of CRT treatment.

Methods: The study enrolled 88 CHF patients (age=64±11, 10 females, BMI=29±4 kg/m²), with stable CHF, NYHA class II or III, EF=35–39%, confirmed by echocardiography and 35 healthy age- and sex-matched controls (age=63±10, 8 females, BMI=28±4 kg/m²). 45 CHF patients underwent CRT device implantation and were controlled after 6 months. All patients underwent transcutaneous echocardiography, cardiopulmonary exercise test (CPET) and venous blood tests. Concentrations of IL-6, sIL-6R and sgp130 were determined using ELISA kits.

Results: The CHF patients were characterized by significantly higher IL-6 (median 2.6 IQR: 1.6–3.8 vs 2.1 IQR: 1.4–3.1 pg/ml, p=0.03) and lower sIL-6R serum concentrations comparing to control subjects (median IQR: 37.64–53 IQR: 45–76 pg/ml, p=0.008). There was no significant difference between sgp130 concentrations.

At the baseline in CHF group IL-6 level correlated positively with BNP (r=0.4, p<0.05) and CRP concentration (r=0.32, p<0.05), while concentration of sgp130 correlated only with BNP (r=0.39, p<0.001). Among CPET parameters death/sedentary rate/total distance (DT)/VE/VO2 slope correlated with sIL-6R level (r=0.25, p<0.05; r=0.3, p<0.05, respectively).

After 6 months of CRT significant improvement in NYHA class (2.6±0.4 vs 2.1±0.3, p<0.001) and echocardiographic parameters, e.g. EF (33±6% vs 32±10%, p<0.001) and LVEFS (193±88 vs 143±88%, p<0.001), was observed. Based on clinical and echocardiographical parameters 31 patients were qualified as responders. In this group a more pronounced decrease from baseline of IL-6 (r=-0.18, p=0.01), sIL-6R (r=-0.26, p=0.01) and sgp130 (r=-0.21, p=0.003) serum concentrations was observed. Spearman correlation coefficient between CRT response and IL-6 serum concentration was 0.36 (p=0.01).

Conclusions: Patients with CHF present higher serum IL-6 and lower sIL-6R levels. The positive response to CRT is associated with IL-6 trans-signaling decrease due to lowered sIL-6R concentration. The exact role of IL-6 pathway in the CRT response remains to be established.

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P4736 | BENCH
Wnt-signaling plays a critical role in cardiac hypertrophy and heart failure progression in mice


Purpose: Heart failure (HF) presents the end-stage of many heart diseases and is associated with a high morbidity and mortality. Disease progression is characterized by a transition from normal heart function to compensatory hypertrophy, finally leading to cardiac dilatation and highly reduced contractility. Increasing evidence results Wnt-signaling to play a critical role in cardiac hypertrophy, remodeling and HF.

Methods: C57/BLEn mice underwent either TAC (transverse aortic constriction) or sham surgery. Cardiac MRI based heart function at different time points after surgery was correlated to the regulation of common HF genes (Nppa, Nppb, Myh6, Myh7, Acta1) as well as genes belonging to Wnt-signaling pathways (Strp2, Wisp2). Further, in vitro studies using cardiac murine HL-1 cells were used to examine the influence of Wnt-signaling activating protein Wnt3a on hypertrophy.

Results: In TAC-mice, decline of systolic LV heart function over time showed strong correlation with HF gene expression and in particular, Wnt-signaling associated genes Wisp2 and Strp2 revealed a significant correlation (p<0.0001).
between their expression and the LVEF (r=0.68; 0.64) and LVEDV (r=0.61; 0.76) in TAC-mice. Microarray analysis identified additional 11 genes associated with Wnt-signaling as differentially expressed (TAC vs. Sham, fc ≥ 1.5) over time. First results of in-vitro studies using the activator of canonical Wnt pathway Wnt3a revealed a concentration-dependent induction of hypertrophic HL-1 cell growth (1% for 0.5 nM; 22% for 1 nM and 29% for 2 nM versus control). This regulatory process was comparable to Endothelin-1 (19% for 100 nM ET-1 versus control), which is a stimulus known to be involved in pathological cardiac remodelling. While ET-1 led to a robust increase in HF gene expression (1.86-1.84-fold for Nkx2-5 and ANP expression), Wnt3a expression was unchanged in control and the expression of all those genes after Wnt3a incubation was not regulated.

Conclusion: Gene expression analysis in mice suffering from cardiac hypertrophy and HF show an important participation of Wnt-signaling in disease progression. Sirtuin 3 expression in cardiomyocyte fraction and the expression of Sfrp2 and Wisp2 support this finding. Further, induction of cardiac cell enlargement and HF gene expression by Endothelin-1 demonstrate similar regulation in an in-vitro model, but hypertrophic growth induced by Wnt-activating protein Wnt3a seems to be regulated by different mechanisms.

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P4737 | BENCH
Klotho and FGF receptor are concomitantly expressed in human individuals with heart failure
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Introduction: In clinical studies elevated levels of FGF23 have been linked with the advent and progression of heart failure. Klotho acts as essential coreceptor for FGF23 whereby tissue-specific expression of Klotho determines target organs of FGF23. Moreover, Klotho is an antilaging protein and actively involved in the prevention of angiogenesis. Previous data in mice suggest that FGF23 exerts its effects on LV hypertrophy independently of Klotho due to not detectable expression of the Klotho receptor. Since no information is available on Klotho expression in human individuals with heart failure we aimed to investigate the cardiac expression of Klotho and FGF receptor in patients with heart failure.

Methods: Endomyocardial biopsies from patients with non-ischemic cardiomyopathy (n=6) and patients -4 weeks after successful heart transplantation (n=6) were analyzed for the expression of Klotho and FGF receptor. The latter were considered as health controls after exclusion of graft rejection. Total RNA was isolated and reverse transcribed using QuantiTect RT kit. Exon spanning primers for Klotho mRNA and FGF receptor were detectable in non-ischemic cardiomyopathy and in healthy hearts by RT-PCR and immunohistochemistry. Expression of both Klotho mRNA and FGF receptor mRNA was significantly upregulated in cardiomyopathy derived cell lines suffering from non-ischemic cardiomyopathy as compared to healthy controls by quantitative RT-PCR (2.65±0.70 vs. 1.32±0.43; p<0.002, and 1.65±0.43 vs. 1.08±0.21; p<0.01, respectively). Immunohistochemically, double stained-revealed colocalization of Klotho and FGF receptor in diseased cardiomyocytes.

Summary and conclusion: We show that Klotho and FGF receptor are concomitantly and highly expressed in non-ischemic cardiomyopathy. Whether adverse cardiac effects of FGF23 are mediated by its coreceptor Klotho and/or cardiac expressed Klotho and its soluble ligand exerts independent effects in heart failure has to be addressed in future studies.

P4739 | BEDSIDE
Hepcidin and its regulator molecule hemoglycin in systolic heart failure
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Introduction: Hepcidin (HPC) is a key regulator of iron metabolism. Hemoglycin (HJV) is believed to stimulate hepcidin production. Derangement of iron homeostasis is well described in chronic heart failure (CHF) and confers a poor prognosis in this group of patients. HJV serum concentration was never determined in CHF patients.

Aim of the study: The aim of the study was to assess HJV and HCV serum levels in patients with systolic CHF and in control group and evaluate its potential prognostic value.

Material and methods: The study group consisted of 130 consecutive patients admitted to the hospital with systolic heart failure and LVEF <45%. In 65 patients primary reason for admittance was CHF exacerbation. The control group consisted of 32 healthy adults matched for age and sex. Fasting blood samples were taken from all study participants for HPC and HJV determination. Routine laboratory tests, including natriuretic peptide, were performed in all CHF patients. Telephone follow-up visits were performed every three months for one year. End-points of the study were: death from all causes, and hospitalisation with heart failure exacerbation.

Results: Significantly higher median level of hepcidin was observed in CHF patients than in controls (28.35 vs 13.47 ng/ml, p<0.0001). Unexpectedly, decreased HPC concentration was found in exacerbated patients comparing to stable ones (19.57 vs 37.71 ng/ml; p=0.002). No significant difference between CHF patients and control group was found regarding hemoglycin serum level. HPC and HJV serum levels were not correlated with each other neither in CHF patients nor in the control group. From among iron metabolism markers HPC was only correlated negatively with soluble transferrin receptor. No correlation was found with these parameters and HJV. None of the studied parameters turned out to be a valuable markers of all-cause mortality in CHF patients.

Conclusion: 1. There is no direct association between hepcidin and hemoglycin serum levels. 2. CHF has no clinically evident impact on HJV serum level. 3. HPC may not be strongly related to iron status in heart failure but tissue ischemia preceding from heart failure exacerbation may lead to inhibition of HPC production.

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P4740 | BENCH
Fish oils may promote lusitropy by reducing phospholamban expression in human heart
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Introduction: Fish oils (omega-3 fatty acids, n-3 PUFA) supplementation has been reported to improve outcome in heart failure (GISSI-HF trial) but the mechanism of such benefit is unclear. Myocardial contractility is intricately linked to calcium handling and the action of the contractile proteins. N-3 polyunsaturated fatty acids (n-3 PUFA) may promote lusitropy by reducing phospholamban (PLB) expression.

Purpose: To evaluate the effect of n-3 PUFA supplementation on calcium handling in human heart.

Methods: Patients undergoing coronary artery bypass graft (CABG) surgery received supplements of fish oils (Omcanor, 2g/day) or a matched placebo (as part of clinical trial) prior to surgery and right atrial tissue obtained during CABG. Tissue samples divided into 4 parts and used for qualitative polymerase chain reaction, immunohistochemistry and Western blot for calcium handling proteins and estimation of tissue n-3 PUFA using gas chromatography. Rats fed with diet rich in n-3 PUFA were used to obtain ventricular myocytes and functional studies evaluating calcium transient amplitudes by field stimulation experiments were carried out on these myocytes.

P4741 | BEDSIDE
Hepcidin and its regulator molecule hemoglycin in systolic heart failure
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Results: Supplementation of n-3 PUFAs reliably increased tissue levels in human heart. Expression of phospholamban was reduced in the n-3 PUFAs group. Ryanodine receptor expression, at m-RNA level, appeared to be increased. Other calcium handling proteins were not significantly altered. A positive lusitropic effect (faster rate of decay of systolic calcium transient) was demonstrated in rat ventricular myocytes.

Expression of calcium handling proteins

<table>
<thead>
<tr>
<th></th>
<th>GPCR (n=30 in each group)</th>
<th>Immunofluorescence (n=30)</th>
<th>Western blot (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fish oil</td>
<td>Placebo</td>
<td>Fish oil</td>
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<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NCX</td>
<td>0.26±0.07</td>
<td>0.17±0.05</td>
<td>0.09</td>
</tr>
<tr>
<td>SERCA</td>
<td>0.25±0.05</td>
<td>0.22±0.07</td>
<td>0.83</td>
</tr>
<tr>
<td>RyR2</td>
<td>0.27±0.06</td>
<td>0.11±0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>PLB</td>
<td>0.10±0.02</td>
<td>0.20±0.04</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Conclusion: Fish oil incorporation in human cardiomycocyte membrane reduces the expression of phospholamban. A more rapid relaxation, the positive lusitropic effect, was seen in rat ventricular myocytes. This could be the mechanism by which fish oils improve clinical outcome in patients with heart failure.

**BASIC MECHANISMS VENTRICULAR FUNCTION**

**P4741 | BEDSIDE**

**Left ventricular deformation accurately predicts the extent of myocardial fibrosis in patients with advanced heart failure requiring transplantation**

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**Purpose:** To evaluate potential relationships between left ventricular (LV) longitudinal deformation function and histopathological evidence for myocardial fibrosis in patients undergoing heart transplantation.

**Methods:** The study population included patients with advanced heart failure, referred for an echocardiographic examination before heart transplantation. Traditional LV function measurements and global longitudinal strain (GLS) by speckle tracking echocardiography, averaging all LV segments in 4-, 2- and 3-chamber views were obtained in all subjects. LV tissue samples were obtained from all patients undergone heart transplantation. Myocardial fibrosis was assessed using Masson’s staining.

**Results:** Of 168 patients referred for cardiac transplantation, 47 underwent cardiac transplantation and were enrolled in the study. LV myocardial fibrosis and its grade strongly correlated with GLS (r=0.75, p<0.0001), modesty with global circumferential strain and LV torsion (r=0.61, p<0.001 and r=0.52, p<0.01, respectively) and weakly with mitral S’ wave (r=−0.41, p=0.01) and MAPSE (r=−0.35, p=0.05) but did not correlate with LV ejection fraction (r=−0.12; p=NS). GLS had the strongest accuracy for detecting LV fibrosis (AUC=0.92). None of the echo parameters correlated with patient’s exercise capacity.

**P4742 | BEDSIDE**

**Ventricular-vascular coupling is altered in marfan syndrome but preserved in TAAD**

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**Background:** Marfan syndrome (MFS) and familial non-syndromal thoracic aortic aneurysm (TAAD) are associated with aortic dilation and increased aortic stiffness. Impairments of both ventricular and vascular function in Marfan syndrome may reflect increased afterload.

**Purpose:** This study examined load-independent measures of left ventricular function in MFS and TAAD, in order to determine whether ventricular-vascular coupling was altered.

**Methods:** Patients with MFS (n=67, 34F, 34±15 yrs) and TAAD (n=70, 33F, 47±15 yrs family history, mutation) were studied by echocardiography and compared with matched controls (n=89, 45F, 37±18 yrs). No patient was taking beta-blockers. Aortic stiffness and arterial elastance (Ees mmHg.ml⁻¹) were measured as indices of ventricular afterload; ventricular function was measured by tissue Doppler and calculation of the end-systolic elastance (Ees mmHg.ml⁻¹). Ventricular function indices were compared between groups by ANOVA.

**Results:** Dilatation of the sinuses of Valsalva was similar in MFS and TAAD, with dilatation of the ascending aorta in TAAD but not MFS. Aortic stiffness index was increased in MFS (16.2±11 and in TAAD 11.6 vs controls 11.3±1.4, p<0.01). Mean blood pressure was increased in TAAD (96±10 mmHg vs 90±10 mmHg), but not MFS (89±9 mmHg and 87±9 mmHg). Left ventricle stroke work was increased in TAAD (p=0.01 vs controls), but not in MFS. The Ees in Marfan was reduced (1.9±0.7 vs controls 2.49±0.8 vs 0.01, but not in TAAD (2.19±0.6). The ratio Ees/Ees was 0.75±0.2 in MFS (p<0.01) vs 0.65±0.10 in controls and 0.68±0.2 in TAAD.

**Conclusions:** Ventricular-vascular coupling differs between MFS and TAAD, with MFS characterized by reduced contractility and altered ventricular-vascular coupling and TAAD by normal contractility and preserved ventricular-vascular coupling but increased stroke work.

**P4743 | BEDSIDE**

**Clinical features of microvascular dysfunction and the relation to exercise hemodynamics in heart transplanted patients**

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**Background:** Microvascular dysfunction, reduced exercise capacity and restrictive left ventricular (LV) filling are common findings in heart transplanted (HTx) patients with preserved LV ejection fraction and no coronary allograft vasculopathy (CAV).

**Purpose:** The aim of the study was to evaluate determinants of microvascular dysfunction and to estimate the influence of microvascular function on LV filling, cardiac output, and exercise capacity.

**Methods:** Fifty HTx patients underwent coronary angiography in order to establish macrovascular CAV status according to ISHLT classification. We measured myocardial blood flow (MBF) by 15O-H2O-PET at rest and during adenosine induced hyperemia. We divided MBF into three segments, with respect to coronary vessels anatomy, and calculated the coronary flow reserve (CFR) as the average of segments with no significant coronary stenosis (microCFR). We calculated refection score based on previous acute cellular rejections and assessed antibody-mediated rejection by luminex analysis. Patients underwent comprehensive assessment of graft function during symptom-limited semi-supine exercise test with simultaneous right heart catheterization.

**Results:** We found no significant correlation between microCFR and diabetes (p=0.47), hypertension (p=0.98), rejection-score (p=0.52), or time since transplantation (p=0.12). Even though segments with severe coronary stenosis were not included in the microCFR, the angiographic CAV-class strongly correlated to microCFR (r=−0.6, p<0.0001). There was a significant correlation between NYHA functional class and microCFR (r=−0.61, p<0.001), and pulmonary artery wedge pressure: r=−0.43, p<0.01), whereas only the correlation to RAP remained significant at peak exercise (r=−0.46, p<0.01). Interestingly, we found microCFR significantly correlated to peak exercise cardiac output (r=−0.44, p<0.01) and pulmonary arterial compliance both at rest (r=0.42, p<0.01), and at peak exercise (r=0.48, p<0.01).

**Conclusion:** The presence and degree of macrovascular CAV strongly correlates with microvascular function. Additionally, microCFR significantly correlated to exercise capacity, NYHA functional class and maximal cardiac output. Finally, a significant correlation between microCFR and pulmonary arterial compliance was seen, indicating remodeling of pulmonary arteries in HTx patients with microvascular dysfunction.
Background: In heart failure (HF) the mitral regurgitation (MR) is clinical and prognostic relevant. Cardiopulmonary exercise testing (CPET) allows evaluating functional capacity and provides indexes for HF risk stratification such as peak oxygen consumption (VO2). Since MR determines a severity-related backward flow to left atrium, it may result in an unfavorable central blood flow exercise redistribution that is physiologically relevant to VO2 increase. Aim: To evaluate the cardiac output (CO) and VO2 exercise-response in HF reduced ejection fraction (HFrEF) patients according to MR severity to dissect what mechanism may be predominant in the VO2 increase.

Methods: HFrEF patients (mean age 64±11 y, male 72%, ischemic etiology 68%, mean LVEF 34±9%) underwent a maximal CPET (incremental ramp protocol) combined with exercise-echo. CO was non-invasively estimated by echo.

Results: Population was divided into 2 groups according to the rest MR: group A (n=80) non-severe MR and B (N=24) severe MR. Despite the groups did not differ in rest CO, VO2 vs B 3.4±1.8 vs 3.4±1.8 L/min, p=ns and VO2 (0.27±0.06 vs 0.28±0.09 L/min, p=ns) group B showed higher peripheral extraction (C(a-v)O2 8±2 vs 9±4 mL/100 mL, p=0.036) already at rest (Figure). At peak exercise group B had an impaired increase both in CO (7.0±2.0 vs 5±2.3, L/min) and VO2 (1.0±0.3 vs 8±3.3 L/min, p=0.001) partially compensated by a greater C(a-v)O2 contribution (15±5 vs 18±5 for A vs B, p=0.047).

Figure 1. LVdp/dtmax (panel A) and QRS narrowing (panel B) at baseline, conventional BiV (BiV) and multipoint pacing (MPP) respectively.

Conclusions: Severe MR and consequent partial abnormal CO redistribution to the pulmonary circulation seems a relevant and pathophysiological mechanisms that limit overall exercise performance in HFrEF. In this high risk subset of patients peripheral extraction compensates for the reduced CO and makes the basis for novel perspectives in these patients.

P4745 | BEDSIDE
Multipoint pacing acutely induces better hemodynamics and QRS narrowing compared to conventional biventricular pacing

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Background: Response to CRT is still challenging. Pacing from multiple sites of the LV has shown promising results. The aim of this study was to systematically compare the acute hemodynamic effects of MPP by means of a quadrupolar lead with conventional BiV pacing.

Methods: 36 pts (29 male, mean age 72±12 years, LVEF 30±7%, 19 with ICM, 20 with LBBB, mean QRS 185±25ms) underwent CRT implantation. Per patient, 3.2±0.7 different MPP measurements were collected per patient. On considering all sites, LVdp/dtmax increased from 962±194 mmHg/s at the baseline to 1157±252 mmHg/s and 1194±253 mmHg/s on BiV and MPP, respectively (panel A). On considering the best site, LVdp/dtmax increased from baseline values of 964±207 mmHg/s to 1230±260 mmHg/s (BiV) and to 1262±258 mmHg/s (MPP). The mean values of QRS duration at any site during MPP and conventional CRT were 171±18ms and 177±20 (p<0.0002), respectively (panel B).

Conclusion: In comparison with BiV pacing at any LV site, MPP yielded a small but consistent increase in hemodynamic response. A correlation between the increase in hemodynamics and Q-LV on MPP was observed for all measurements, including those taken at the best and worst site. The MPP-induced improvement in contractility was associated with significantly greater narrowing of the QRS complex than conventional BiV pacing.

P4746 | BEDSIDE
Strain pressure product- an afterload corrected myocardial strain measure and its association with features of preclinical heart failure and outcomes

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Background: Left ventricular global longitudinal strain (GLS) is a marker for subclinical myocardial dysfunction in early stages of heart failure (HF). However, it is sensitive to hemodynamic conditions, particularly afterload. We propose a new GLS measure with blood pressure and heart rate correction, named Strain Pressure Product (SPP) and assess its association with HF risks, exercise capacity, quality of life and outcome in a non-ischemic Stage A Heart Failure (SAHF) population.

Methods: Asymptomatic subjects ≥ 65 yo with SAHF ≥ 1 HF were recruited from the community. All subjects underwent standard Patient report outcome measures, a 6-minute walk test (6MW) and a comprehensive echocardiogram including QLS. SPP was calculated as the product of GLS and SBP divided by heart rate (HR). New HF symptoms including shortness of breath on exertion or at rest, orthopnea and leg edema were assessed at 1 year follow-up.

Results: Total 521 subjects (age 71±5 y; 49% men) were recruited. 19% had one; 40% had two and 41% had ≥ three risk factors. At baseline, mean LVEF and GLS were 63±5% and −18±3%. Mean SPP was 0.39±0.09. SPP was significantly associated with HF risks, diastolic parameters and PROMs measures independent of age and gender (Table). After an average follow-up time of 10±3 months, 308 subjects underwent assessment of early HF symptoms. 63 developed early HF symptoms. SWP was associated with new HF symptoms (p<0.05) and composite cardiovascular outcome (p<0.043) table.

Conclusion: Strain pressure product, which is a blood pressure and heart rate corrected GLS measure, showed significant association with HF risk, exercise capacity, PROMs measure and diastolic function. It is also associated with early HF symptoms. SPP may be an effective means of addressing the load-dependence of strain.

Acknowledgement/Funding: HY is supported by a Health Professional Scholarship from the National Heart Foundation of Australia (100307).
P4747 | BEDSIDE
A novel and practical method to quantify mitral annulus motion and tricuspid annulus motion from cardiac magnetic resonance
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Background: We have developed a new tracking method to track the mitral annulus motion (MAM) and tricuspid annulus motion (TAM) from cardiac magnetic resonance (CMR). In this study, we compared myocardial velocities (Sm, Em and Am) - calculated at systolic and early and late diastolic filling periods, respectively - with myocardial velocities from tissue Doppler imaging (TDI). We also examined the correlation of E/e' and VAS score.

Methods: We prospectively performed CMR and echo TDI scans on the same day in 20 normal healthy volunteers (age range: 23 to 70 years) and consecutive 104 patients. MAM and TAM motions were tracked automatically using in-house customized algorithm. Velocities (Sm, Em and Am) of the MAM and TAM were calculated as first time-derivatives of the displacement. For TAM assessment, only 4-chamber right ventricular lateral side was used. TDI was performed following by the standard protocol based on ASE recommendation.

Results: See table. There were significant good correlations in myocardial velocities between CMR and TDI methods for both MAM and TAM (all p<0.001).

Conclusions: Myocardial velocities of MAM and TAM calculated from CMR images correlated well with TDI method. CMR method is independent of angle position and imaging reference frames, and thereby computationally light-weight. They can be derived by post-processing of routine CMR images without additional image acquisition. This shall potentially extend routine CMR's capability for LV and RV systolic and diastolic function assessment.

P4748 | BEDSIDE
Rapid improvement of symptoms, filling pressures and pulmonary congestion estimated by combined echo and lung ultrasound protocol during early course of AHF treatment
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Introduction: Rapid decline in left side filling pressures (LSFP) during early course of acute heart failure (AHF) treatment could result in rapid improvement of symptoms and pulmonary congestion.

Objectives: To examine the time course of response to treatment in pulmonary congestive AHF patients using a thoracic FAST ultrasound protocol including echo derived left side filling pressures (medial E/e') combined with lung ultrasound (LUS), and simultaneous symptom assessment.

Methods: We included 70 adult dyspneic patients with a positive thoracic FAST lines (BL) or pleural fluid (PF) right sided or bilaterally. Patients were classified as “responders” if they became asymptomatic at rest and capable of walking > 20 meters. LUS was considered normalized when absent of PF and bilateral BL.

Results: 39/70 (56%) of the FAST - positive patients were responders. Responders had a bigger mean change of E/e' (4.44 vs. 1.0, p=0.004) and VAS scores (6.28 vs. 1.9, p=0.002) than non-responders during the total hospital course. The fastest change among responders occurred during the first 12 hours of treatment (mean Δ E/e' 2.34 (SD 3.31) and mean Δ VAS 3.74 (SD 3.13)) compared with a mean Δ E/e' of 1.77 (SD 2.90) and a mean Δ VAS of 2.47 (SD 2.58) during the rest of total hospital stay (p<0.001 for mean Δ LUS). The time mean until normalization of LUS was 47.3 hours. Among non-responders, VAS score changed slowly and linearly, and E/e' very little at all during hospital stay.

Conclusions: Both symptoms and echo derived LSFP improve rapidly among AHF patients. These changes foresee decongestion as measured by normalization of LUS.

P4749 | BEDSIDE
Microvascular function as a link to left ventricular longitudinal deformation capacity in heart transplanted patients
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Background: Microvascular dysfunction and reduced left ventricular (LV) longitudinal myocardial function is common in heart transplanted (HTx) patients and associated with coronary allograft vasculopathy and high rejection burden.

Methods: The aim of the study was to evaluate the influence of microvascular function on LV longitudinal deformation capacity during exercise in stable HTx patients.

Results: Fifty-four HTx patients underwent coronary angiography. We excluded 16 patients due to significant CAV. The remaining 38 HTx patients were age-matched controls underwent comprehensive assessment of microvascular function during rest and symptom-limited semi-supine exercise test with measure of LV longitudinal deformation by 2D speckle tracking echocardiography. We assessed microvascular function by non-invasive Doppler coronary flow velocity reserve (CFVR) and divided patients into two groups: Group A: reduced CFVR < median CFVR and group B: preserved CFVR > median CFVR.

Conclusions: The HTx patients with reduced CFVR were in significantly higher NYHA functional class compared to the group with preserved CFVR (p=0.02). During exercise, the HTx-group had significantly reduced exercise capacity compared to healthy controls (102±39 watt versus 179±43 watt, p<0.0001). At peak exercise, HTx patients showed significantly lower LV longitudinal myocardial deformation compared to controls, with global longitudinal strain (GLS) of −20±4% versus −25±2%, p=0.001. Diastolic parameter revealed sign of restrictive LV filling in HTX patients with higher E/A-ratio (p=0.01), higher E'/e'-ratio (p=0.10), and shorter E-deceleration time (p=0.03) compared to controls. The HTx patients with reduced CFVR were in significantly higher NYHA functional class compared to the group with preserved CFVR (p=0.02). During exercise, the HTx-group had significantly reduced LV longitudinal myocardial deformation compared to HTx patients with preserved CFVR (p=0.02). At peak exercise, HTx patients showed significantly lower LV longitudinal myocardial deformation compared to controls, with global longitudinal strain (GLS) of −20±4% versus −25±2%, p=0.001. We found a strong correlation between CFVR and peak exercise LV deformation in HTX patients (r=0.55, p=0.0001). The HTx patients with reduced CFVR had significantly reduced CFVR and LV longitudinal deformation capacity measured by peak exercise LV deformation in HTX patients compared to healthy controls. LV longitudinal deformation capacity in addition to NYHA functional class is highly dependent on preserved microvascular function in HTX patients.

P4750 | BEDSIDE
Right to left ventricular interdependence evaluated by the ratio between pulmonary systolic to diastolic time at rest and during exercise in heart failure reduced ejection fraction: clinical insights
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Background: The ratio between the duration of right ventricular (RV) systole and diastole (S.D ratio) has been proposed as an index of RV performance in a pediatric population with pulmonary arterial hypertension in whom it may predict prognosis and functional capacity. In heart failure (HF) S.D may provide relevant insights in the exercise response.

Aim: To analyze the correlation between rest and peak exercise S.D and functional and cardiac parameters in HF/EF.

Methods: 94 HF/EF patients (median age 66±11 y, male 70%, ischemic etiology 71%, mean LVEF 34±9%) underwent a symptom-limited cardiopulmonary exercise testing (incremental ramp protocol) combined with exercise-echo. RV S.D was assessed by echo at rest and peak exercise.

Results: A good correlation was found between rest and peak S.D and CPET indexes of exercise capacity, such as peak oxygen consumption (VO2) (Spearman's rho −0.40 and 0.38 respectively, p=0.02 and 0.023) and maximal workload (rho= −0.42 and −0.45, p=0.031 and 0.034). An higher S.D also correlated with more impaired ventilatory efficiency or higher VE/VCO2 slope (rho 0.49 and 0.32,

Correlation of E/e' and VAS score.
p<0.019 and 0.024). Looking at echo phenotype, interestingly S-D is associated with parameters of mitral regurgitation (MR) severity, such as effective regurgitant orifice (rH rest 0.63, peak 0.35, p<0.01) and pulmonary artery systolic pressure (PASP, rH rest 0.53, peak 0.35, p<0.01) particularly at rest. S-D also correlated with right RV fractional area change at rest and peak exercise (rH 0.39 and 0.39, p=0.035 and 0.04).

Conclusions: In HFpEF population the assessment of S-D at rest and peak exercise predicts functional status and is related to more advanced hemodynamic impairment. Including S-D (PASP and MR) as expression of more unfavorable ventricular interdependence.

P4751 | BEDSIDE
Impact of persistent pulmonary hypertension on patients with severe aortic valve stenosis following TAVI
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Background: Severe aortic stenosis leads to augmented afterload, changes in cardiac function and often increased systolic pulmonary arterial pressure. The persistence of these changes after surgical aortic valve replacement has been linked to unfavorable outcome. There is a controversy regarding the impact of persistent pulmonary hypertension (PHT) on prognosis of patients undergoing transcatheter aortic valve implantation (TAVI).

Purpose: We sought to investigate the impact of persistent PHT on 3-year all-cause mortality of patients with severe aortic stenosis following TAVI.

Methods: Points with severe and symptomatic aortic stenosis (effective orifice area <1cm²) who were scheduled for TAVI with a self-expanding valve at our institution were prospectively enrolled. Prospectively collected echocardiographic data before and after TAVI were retrospectively analyzed in all patients. Systolic pulmonary arterial pressure was estimated as the sum of the right ventricular afterload at the right atrial gradient during systole and the right atrial pressure. PHT flow was classified as absent if <35mmHg and persistent if ≥35mmHg. Primary clinical endpoint was all-3 year all-cause mortality defined according to the criteria proposed by the Valve Academic Research Consortium-2 criteria.

Results: Hundred and thirty-three patients (mean age, 80±7 years) were included in the study. The primary clinical end point occurred in 22 patients (17%) during a median follow-up period of 3 years. Mean systolic pulmonary arterial pressure was reduced in all patients following TAVI (43±11 versus 40±8mmHg, p<0.001). Mortality was higher in patients with persistent PHT compared to patients with normal systolic pulmonary arterial pressure following TAVI (32% versus 10%, p=0.002). Patients that reached the primary clinical end point had a higher post-procedural mean systolic pulmonary pressure (44±8 versus 40±8mmHg, p=0.02). In multivariate regression analysis, persistence of PHT (OR: 3.310, 95% CI: 1.182–9.224, p=0.02) and logEuroSCORE (OR: 1.051, 95% CI: 1.006–1.098, p=0.026) were independent predictors of mortality.

Conclusions: The persistence of pulmonary hypertension post TAVI is associated independently with long term mortality. Further investigation is warranted for the early identification of this population with severe aortic stenosis.

P4752 | BEDSIDE
Statin effects on clinical outcomes in patients with acute myocardial infarction with acute severe systolic heart failure
W. Kim1, J.H. Cho2, J.Y. Rhew3, J.S. Woo1 on behalf of Korea Working Group Cardiovascular Disease in Acute Myocardial Infarction (KorMI) Registry.

W. Kim1, J.H. Cho2, J.Y. Rhew3, J.S. Woo1 on behalf of Korea Working Group

Background: Myocardial infarction and revascularization or myocardial infarction and revascularization was similar between 2 groups (1-year MACE-free survival rate (SR) of treated with statin group: 87.1%, 1-year MACE-free SR of treated without statin group: 86.2%, p=0.78). Likewise, 1-year all-cause mortality was not significantly different between 2 groups (1-year SR of treated with statin group: 93.8%; 1-year SR of treated without statin group: 90.8%, p<0.42). Propensity-score matching yielded 158 pairs, and in that cohorts, we could obtained comparable results in terms of MACE (1-year MACE-free SR of treated with statin group: 87.2%, 1-year MACE-free survival rate of treated without statin group: 86.2%, p=0.85) and mortality (1-year SR of treated with statin group: 94.0%; 1-year SR of treated without statin group: 90.8%, p=0.51). And Cox regression analysis showed that statin therapy was not an independent predictor for MACE (Hazard ratio (HR) 1.06, 95% CI 0.56–2.03, p=0.85) or all-cause mortality (HR 1.34, 95% CI 0.56–3.17, p=0.42).

Conclusions: Statin did not reduce the MACE or deaths from any cause in AMI patients with acute severe systolic HF.

BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS I

P4753 | BEDSIDE
Preserved ventricular-arterial coupling but more myocardial oxygen consumption and less mechanical efficiency in haemodialysis patients
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Purpose: Exercise fraction is limited to assess contractility in haemodialysis (HD) patients due to its preload dependency. This study aimed to elucidate whether there are any differences in load independent cardiovascular parameters among the HD patients and others.

Methods: Echocardiography was performed in patients receiving maintenance HD (HD group, n=210, age 65 yrs, 147 males), hypertension controls (HT group, n=162, age 69 yrs, 114 males) and normotensive controls (NT group, n=126, age 61 yrs, 85 males). End-systolic elastance (Ees) and arterial elastance (Ea) were measured using a noninvasive single beat technique. Ventricular-arterial coupling was calculated as Ea/Ees. Stroke work (SW) and pressure-volume area (PVA) were estimated, and LV mechanical efficiency was expressed as SW/PVA x 100.

Results: HD group had significantly larger EDV index and LV mass index than either HT or NHT group. Ea tended to be higher, but Ees was significantly higher, in HD than NT controls. These abnormalities led to significantly greater PVA in HD patients, suggesting elevated myocardial oxygen consumption. Although ventricular-arterial coupling did not differ among groups, LV efficiency was significantly reduced in the HD patients among groups. In HD patients, age, diabetic nephropathy, EDV index, Ea, and Ees were independent determinants of worsening LV efficiency after adjusting for confounders (sex, BMI, HD duration, inter-dialytic weight gain, and Kt/V).

Comparisons of cardiovascular function

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Non-HT controls</th>
<th>HT patients</th>
<th>HD patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass index, g/m²</td>
<td>85±20</td>
<td>95±24*</td>
<td>120±29†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Characteristic pressure-index, ml</td>
<td>48±16</td>
<td>47±16</td>
<td>51±17*</td>
<td>0.004</td>
</tr>
<tr>
<td>Ea, mm Hg/ml</td>
<td>2.69±0.93</td>
<td>2.78±0.84</td>
<td>2.85±0.96</td>
<td>0.106</td>
</tr>
<tr>
<td>Arterial compliance</td>
<td>0.93±0.49</td>
<td>0.96±0.45</td>
<td>0.95±0.44†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ees, mm Hg/ml</td>
<td>4.44±1.83</td>
<td>4.74±1.61</td>
<td>4.98±2.54*</td>
<td>0.035</td>
</tr>
<tr>
<td>Ea/Ees ratio</td>
<td>0.63±0.16</td>
<td>0.61±0.15</td>
<td>0.62±0.21</td>
<td>0.060</td>
</tr>
<tr>
<td>PVA, mm Hg ml</td>
<td>7931±2536</td>
<td>8134±2674</td>
<td>10710±4037*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SW/PVA efficiency, %</td>
<td>60±6</td>
<td>60±6</td>
<td>55±6*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Final column reflects overall p, *p<0.05 versus Non-HT controls; †p<0.05 versus HT controls.

Conclusions: HD patients had higher myocardial oxygen consumption and less LV mechanical efficiency than hypertensive or normotensive controls, although ventricular-arterial coupling was preserved.

P4754 | BENCH
Left bundle branch block and resynchronisation therapy have major effects on right ventricular work load
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Background: Left bundle branch block (LBBB) results in abnormal motion of the septum and reduces left ventricular (LV) stroke work. Little is known about the effect of LBBB on right ventricular (RV) work and how this is modified by cardiac resynchronisation therapy (CRT).

Conclusions: In HFpEF population the assessment of S-D at rest and peak exercise predicts functional status and is related to more advanced hemodynamic impairment. Including S-D (PASP and MR) as expression of more unfavorable ventricular interdependence.

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**Purpose:** To determine how LBBB and CRT modifies RV work.

**Methods:** In 8 anaesthetised dogs, LBBB was induced by radiofrequency ablation, and CRT was applied by pacing the septum and the LV lateral wall. Pressures were measured by micromanometers. LV and RV short-axis diameters and septal and free wall longitudinal segment lengths were measured by sonomicrometry enabling estimation of work as the area of pressure–dimension loops.

**Results:** LBBB caused marked septal preejection shortening with subsequent rebound stretch (Arrow,Fig.A). Therefore, septal longitudinal work was reduced from 97±49 to 7±60 mmHg*mm (p < 0.01). This was accompanied by an increase of work in the LV lateral wall from 126±97 to 198±113 mmHg*mm, (p < 0.05). CRT essentially normalized the abnormal septal contraction patterns and restored work in both ventricles (Fig.B). LV and RV dP/dtmax were increased by CRT (p < 0.05).

**Conclusions:** Induction of LBBB caused opposite effects on RV and LV short-axis work due to altered septal motion. There were compensatory changes in work in the free wall of both ventricles. CRT restored LV work, but reduced RV short-axis work. It should be explored if the marked changes in RV work have impact on the effect of CRT in patients with RV failure.
LVESV, increase in TAPSE and lowest RAp) (Table 1), and clinical outcomes were most favourable in these patients (Fig. 1).

Conclusion: LBBB and reversal of activation vector post-Biv (evidenced by RV1) are associated with changes in left and right heart function. The latter is associated with better clinical outcomes.

P4758 | BEDSIDE
Acute hemodynamic comparison of biventricular, LV only and multipoint pacing in CRT patients

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Background: In CRT, the comparison of the benefits derived from conventional biventricular vs LV only pacing is still under investigation.

Purpose: Aim of the study was to evaluate the acute effects of different pacing configurations, with and without the additive contribution of Multipoint pacing (MPP), on LV dP/dtmax and QRS narrowing.

Methods: In 31 patients (22 male, 20 LBBB, 18 ICM) 98 measurements (3.2±0.8 pacing sites per patients) were analyzed. The hemodynamic effects of pacing at different sites were evaluated by invasive measurement of LV dP/dtmax at baseline and during different pacing protocol. “LV only MPP” pacing protocol refers to dual bipolar LV pacing. One-way analysis of variance (ANOVA) with repeated measures and with Bonferroni post-hoc testing was applied to evaluate differences in pacing protocols.

Results: Baseline LVdP/dtmax was 985±189 mmHg/s. During the various pacing protocols (LV only, Biventricular, MPP LV only, and MPP BiV) LVdP/dtmax steadily increased, values during LV-MPP being higher than LV-only and values during BiV-MPP being higher than during BiV (panel A). While QRS duration was considerably higher during LV than during BiV pacing, MPP reduced QRS duration during both LV and BiV pacing (panel B).

Conclusions: MPP increased the hemodynamic benefit during both LV only and BiV pacing. This improvement is associated with a reduction in QRS duration.

P4759 | BEDSIDE
Increased galectin-3 was closely associated with arterial wave reflections and provided incremental prognostic value upon natriuretic peptide in patients with acute heart failure

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Background: Galectin-3, a marker of cardiac fibrosis, is an emergent prognostic biomarker in heart failure. However, its associations with hemodynamic parameters and whether it has an incremental prognostic value upon natriuretic peptide in acute heart failure syndrome (AHFS) remained unclear.

Methods and results: Galectin-3 and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were measured in 125 participants hospitalized due to AHFS (mean age 70.4 years; 82% women). We assessed determinants of increased Galectin-3 using logistic regression model and the relation of Galectin-3 to adverse cardiovascular (CV) outcomes by proportional hazards regression. Measures of hemodynamic parameters by tonometry and thoracic fluid content (TFC) by impedance cardiography were obtained within 24 hours of admission. During a median follow-up of 601 days, 66 adverse events developed. In multivariate model, increased Galectin-3 (>25.9 ng/ml) was significantly associated with estimated creatinine clearance with odd ratio (OR) 0.194 (95% confidence interval [CI] 0.101–0.373; p<0.0001) and backward arterial wave reflections (Pb; OR 2.11; 95% CI 1.20–3.71; p=0.0096). Elevated Galectin-3 was associated with risk for adverse outcomes after adjustment for clinical variables and NT-proBNP (HR: 3.49; 95% CI 1.20–11.22; p=0.02). Elevated Galectin-3 was associated with Pb linked increased Galectin-3 with small arteriolar pathology in AHFS. The independent and incremental prognostic value of Galectin-3 upon NT-proBNP lend support to the clinical application of Galectin-3 in the management of AHFS.

Conclusion: The association of Galectin-3 with Pb linked increased Galectin-3 with small arteriolar pathology in AHFS. The independent and incremental prognostic value of Galectin-3 upon NT-proBNP lend support to the clinical application of Galectin-3 in the management of AHFS.

P4760 | BEDSIDE
Model of end-stage liver Disease excluding INR (MELD-XI) scoring system provides the additional prognostic information to hyponatremia in patients admitted with acute decompensated heart failure

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Background: Liver dysfunction has a prognostic impact on the outcome of patients (pts) with advanced heart failure. A model of end-stage liver disease excluding INR (MELD-XI), a robust scoring system of liver dysfunction, has been shown to provide prognostic information in heart failure pts. Hyponatremia is also a prognostic marker in heart failure pts. However, there is no information available on the long-term prognostic significance of MELD-XI score in pts admitted with acute decompensated heart failure (ADHF), relating to hyponatremia.

Methods and results: We studied 125 consecutive ADHF pts discharged with survival. MELD-XI score was calculated by the following formula: 5.11 ln(bilirubin) + 11.79 ln(creatinine) + 9.44. During a follow-up period of 5.0±4.3 yrs, 75 pts had cardiovascular death (CVD). At multivariate Cox analysis, MELD-XI score
min (P<0.0005) and serum sodium level (P<0.02) were significantly independently associated with CVD. ROC analysis revealed that MELD-XI score of 12 was a fair discriminator for CVD (AUC 0.70 [0.64–0.77]). In a group with hypotension (serum sodium <135mEq/L), pts with high MELD-XI score (≥12) had a higher risk of CVD than those with low MELD score (68% vs 29%, p<0.04, HR 2.56 [1.01–6.53]). In a group without hypotension, pts with high MELD-XI score also had a higher risk of CVD (42% vs 15%, p<0.0005, HR 2.56 [1.48–4.43]).

Results: During a mean period of 282 days, adverse event occurred in 27 patients (82% of all events, 107 days in 11 patients). All patients died during follow-up. Obese patients had lower levels of BNP (511.9±81.9 vs. 917.5±57.9 ng/L, p<0.0001) than non-obese subjects (BMI <30) but similar levels of GDF-15 (1855.5±94.7 vs. 1792.6±139.0 ng/L, p=n.s.). In Cox univariate analysis, systolic blood pressure (SBP), LV EF, furosemide daily dose, NYHA class, sodium level, age, diabetes, resting heart rate, estimated glomerular filtration rate, BNP, and GDF-15 were significant predictors of death. In a multivariate analysis encompassing all these variables, only BNP (HR 1.04 per each 100 ng/L, p<0.003), GDF-15 (100 ng/L) 0.49 0.79 0.96 0.007 and GDF-15 (100 ng/L) 0.49 0.79 0.96 0.007 were independent predictors of mortality. When this multivariate model was applied to obese patients only, BNP and SBP were no longer significant parameters; only sodium (HR 0.87 per 1mmol/L, p=0.007) and GDF-15 (HR 1.04 per 100 ng/L, p=0.008) had significant predictive power.

Conclusions: A MELD-XI scoring system could provide the additional long-term prognostic information to hypotension in ADHF pts.

P4761  BEDSIDE
Prognostic impact of plasma phospholipid fatty acid composition and dihomo-gamma-linoleic acid level in patients with acute heart failure

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Background: Malnutrition is an important determinant of poor clinical outcomes in patients with heart failure (HF). Recently, plasma phospholipid fatty acid (PPFA) composition was reported to be altered and especially, the dihomo-gamma-linoleic acid (DHGL) was decreased accompanied with reduced delta-6-desaturase activity in lean HF patients.

Purpose: To investigate the PPFA composition and its impact on clinical outcome in HF.

Methods: 477 consecutive patients with acute HF (AHF) in our prospective registry were examined. Those without accessible PPFA data on admission were excluded. Finally, 454 patients were examined with median follow-up of 205 (IQR 26–455) days.

Results: In multivariate Cox proportional hazard model, DHGL was the strongest predictor for mortality [hazard ratio (HR) 0.87 per 1mmol/L, p=0.007] and GDF-15 (HR 1.04 per 100 ng/L, p=0.008) among other PPFAs. Patients with lower DHGL (<24 μg/ml, the median) had higher mortality than those with higher DHGL (Figure). After adjustment for potential confounders based on the comparison between lower and higher DHGL, including age, serum albumin, creatinine and plasma brain natriuretic peptide levels, and prevalence of statin use, the HR for DHGL was 0.94 (95% CI 0.88–0.98, p<0.01). Furthermore, patients with lower DHGL had higher prevalence of jugular vein distention (p<0.02) and edema of the lower extremities (p<0.01), higher serum bilirubin level (p<0.01), lower serum total cholesterol (p<0.001) and albumin (p<0.01) levels, and lower body mass index (p<0.01) and nutritional risk index (p<0.01) than those with higher DHGL.

Methods: The prognostic power of BNP, GDF-15 and other parameters, such as routine laboratory test results and echocardiographic and clinical findings was analyzed in a cohort of 290 HF patients (61±10 yrs, LVEF 25±5%, 58% with CAD, 92% on beta-blockers, 97 obese). Patients scheduled for heart transplantation were excluded.

Results: All HF patients were prospective followed for 1283±567 days. A total of 137 patients died during follow-up. Obese patients had lower levels of BNP (511.9±81.9 vs. 917.5±57.9 ng/L, p<0.0001) but similar levels of GDF-15 (1855.5±94.7 vs. 1792.6±139.0 ng/L, p=n.s.). In Cox univariate analysis, systolic blood pressure (SBP), LV EF, furosemide daily dose, NYHA class, sodium level, age, diabetes, resting heart rate, estimated glomerular filtration rate, BNP and GDF-15 were significant predictors of death. In a multivariate analysis encompassing all these variables, only BNP (HR 1.04 per each 100 ng/L, p<0.003), GDF-15 (100 ng/L) 0.49 0.79 0.96 0.007 and GDF-15 (100 ng/L) 0.49 0.79 0.96 0.007 were independent predictors of mortality. When this multivariate model was applied to obese patients only, BNP and SBP were no longer significant parameters; only sodium (HR 0.87 per 1mmol/L, p=0.007) and GDF-15 (HR 1.04 per 100 ng/L, p=0.008) had significant predictive power.

Conclusions: Lower plasma DHGL was an independent determinant of mortality in association with right HF sign and malnutrition, suggesting plasma DHGL could be a novel biomarker for risk stratification in AHF patients.

P4767 | BEDSIDE
Impact of elevated end-diastolic pulmonary regurgitation gradient on worse clinical outcome in patients with acute heart failure

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Background: Echo-Doppler end-diastolic pulmonary regurgitation (EDPR) gradient associated with right atrial pressure has been reported to correlate well with catheter-derived pulmonary artery diastolic pressure (PADP). Generally, PADP also well correlates left ventricular (LV) filling pressure and elevated PADP is associated with poor clinical outcomes in patients with acute heart failure (AHF). However, the prognostic significance of EDPR gradient in HF patients has not been elucidated.

Purpose: To evaluate the prognostic impact of EDPR gradient in HF.

Methods: 477 consecutive patients with AHF in our prospective registry were examined. Those without accessible EDPR data on discharge were excluded. Finally, 104 patients were examined and divided into two groups according to EDPR gradient: elevated EDPR gradient group (≥8mmHg, by ROC cut-off) and non-elevated EDPR gradient group (<8mmHg). Adverse events were defined as worsening HF and death.

Results: During a mean period of 282 days, adverse event occurred in 27 patients (26%). Patients with elevated EDPR gradient had higher systolic blood pressure (SBP) (p<0.01), lower LV ejection fraction (LVEF) (p<0.01) and larger LV diastolic diameter (LVDD) (p<0.01) on discharge than those with non-elevated EDPR gradient. The incidence of adverse events was significantly higher in elevated EDPR gradient group than non-elevated EDPR gradient group (Figure). In multivariate analyses, elevated EDPR gradient was an independent determinant of adverse events (HR 1.186, 95% CI 1.02–1.42, P=0.026) among variables including age, sex, chronic kidney disease, SBP, LVDD, LVEF, and tricuspid regurgitation pressure gradient.

Conclusions: Echo-Doppler EDPR gradient might be a noninvasive predictor for clinical outcomes in patients with AHF.

Reference:

P4762 | BEDSIDE
Prognostic role of growth differentiation factor 15 (GDF-15) in obese patients with systolic heart failure (HF)

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Background: BNP is an established biomarker in patients with HF with excellent predictive power for outcomes. However, obese individuals have generally lower levels of BNP and this may limit its performance. GDF-15 is a new biomarker in HF and its prognostic utility is being investigated. The purpose of this study was to analyze predictive power of BNP and GDF-15 for total mortality in a cohort of HF patients and separately in obese (BMI≥30) individuals.
Defining prognosis in patients with advanced heart failure

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Introduction: Patients (pts) with advanced heart failure (AHF) constitute a specific population of cardiac failure pts, with very specific issues and a particular worrisome prognosis.

Aim: Define electrocardiographic predictors in the particular case of AHF.

Methods: Retrospective, observational study of pts with AHF with post-capillary reactive group 2 Pulmonary Hypertension (PH), on optimal medical therapy (including sildenafil 20 mg tid), referred for heart transplant (HTX) between 2004 and 2014. Clinical, laboratory and hemodynamic data were evaluated. Endpoint was survival to all-cause death, HTX and hospitalization for AHF after refer- ence to HTX. Composite endpoints included: death or hospitalization, death or HTX and triple endpoint.

Results: A population of 107 pts were studied, with mean age of 55±11 years, 73% were male. Fifty-six of the patients were in NYHA class IV, with median BNP 605 (IQR 665) pg/dl, and median peak VO2 15.6 (IQR 15) ml/kg/min. Hemodynamicbaseline parameters: mean pulmonary artery pressure (mPAP) 45 (IQR 14) mmHg, pulmonary capillary wedge pressure (PCWP) 27 (IQR 13) mmHg, CI 1.8 (IQR 0.7) ml/min/m², PVR 5.5 (IQR 3.8) Wood units, TPG 17 (IQR 8) mmHg. During follow-up, half of the group had at least one hospitalization during this period, 33.6% underwent HTX and 22.4% died (median days to follow-up: 1658). NYHA functional class didn’t impact on the prognosis of these pts. However, after beginning of sildenafil therapy this predictor predicted the occurrence of hospi-talization (p<0.001). In this specific population of HF pts, BNP was predictor of the composite endpoint death or HTX (p=0.002, HR 1.0; IC 95% 1–1.001). Improvement in functional capacity as predictor by increase in maxVO2 reduced the proportion of hospitalization for HF decompensation (p=0.04, HR=0.88; IC 95% 0.78–0.99). With respect to hemodynamic parameters (using univariate Cox Regression analysis) systolic diastolic arterial pressure predicted all-cause death (p=0.035, HR 0.96; IC 95% 0.92–0.99). Cardiac index predicted evolution for HTX (p=0.023, HR 0.96; IC 95% 0.92–0.99). Regarding composite endpoint of death or HTX, systemic hemodynamic profile was determinant: mean systemic arterial pressure (p=0.001, HR=0.96; IC 95% 0.94–0.98), systemic systolic arterial pressure (p=0.006, HR=0.98; IC 95% 0.96–0.99) and systemic diastolic arterial pressure (p=0.001, HR=0.96; IC 95% 0.94–0.98).

Conclusion: AHF is a terminal morbidity condition with high index of adverse events. However, there are prognostic predictors which might help improving management of these pts and to increase their survival.

Elderly heart failure with preserved ejection fraction patients showed different predictors for cardiovascular mortality than younger counterparts

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Background and purpose: Heart failure with preserved ejection fraction (HFPEF) has been shown to be more common among the elderly population. Never- theless, little is known about the clinical characteristics and outcomes specific for this population.

Methods: We retrospectively reviewed 1,940 patients who had their first heart failure admission to our institution between January 2005 and April 2012. Clinical characteristics and outcomes of patients who were ≥ 70 years of age and had HFPEF, as defined by left ventricular ejection fraction (LVEF) ≥ 40%, were compared to those who were <70 years old. Parameters predictive of cardiovascular mortality were studied in a Cox-regression model.

Results: Among the 569 patients with HFPEF, 109 (19.2%) were ≥ 70 and 460 (80.8%) were ≥ 70 years old. Compared with those who were ≥70, patients who were ≥70 were more likely to be female (60.9% vs 48.6%; p=0.009) and have hypertension (75.4% vs 56.9%; p=0.001), but less likely to have diabetes (35.9% vs 49.5%; p=0.01). At a mean follow-up of 35.8±30.2 months, 175 (38.0%) of those who ≥70 years old and 44 (40.4%) of those who were <70 years old died, of whom 121 (24.3%) and 20 (18.3%) of them died of cardiovascular cause, respectively (log rank test p=0.046, HR 0.47; IC 95% 0.23–0.99). Regarding composite endpoint of death or HTX, systemic haemodynamic profile was determinant: mean systemic arterial pressure (p=0.001, HR =0.96; IC 95% 0.94–0.98), systemic systolic arterial pressure (p=0.006, HR =0.98; IC 95% 0.96–0.99) and systemic diastolic arterial pressure (p=0.001, HR=0.96; IC 95% 0.94–0.98).

Conclusion: Soluble ST2 predicts cardiovascular events, infectious and all-cause mortality in diabetic hemodialysis patients

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Background: Soluble suppression of tumorigenicity 2 (sST2) has emerged as a strong prognostic biomarker in patients with underlying cardiovascular (CV) disease. End-stage kidney disease patients are at high mortality risk due to CV events and infections but the predictive value of sST2 in these patients is unknown.

Objective: The aim of the present study was to investigate the effect of plasma concentrations of sST2 on CV events, all-cause death and death due to infections in diabetic hemodialysis patients.

Methods: We analyzed sST2 concentrations in plasma samples of 1196 diab- etic hemodialysis patients who participated in the German Diabetes and Dialysis Study (4D Study). Hazard ratios (HR) for pre-specified, adjudicated endpoints sudden cardiac death, non-fatal and fatal myocardial infarction (fatal and non-fatal), stroke (fatal and non-fatal), combined cardiovascular events (CV death, stroke, myocardial infarction) and non-cardiovascular mortality were calculated and determined according to sST2 levels at baseline by Cox proportional hazards regression analysis. The Presage ST2 assay was used for measurement of sST2 concentrations.

Results: Patients (mean±SD; age: 66±8.3 years, 54% male) had a median sST2 of 25 ng/ml (interquartile range, 20.1–32.6) and were followed up for 4 years. After adjustment for possible confounders, patients with sST2 concentrations in the highest quartile compared to the lowest showed a more than two fold increased risk of sudden cardiac death (hazard ratio (HR): 2.24 (95% confidence interval (CI): 1.33–3.77), a more than 3 fold increased risk of death due to heart failure
sex, age, history of myocardial infarction, history of coronary artery bypass graft, higher 90-day mortality also in multivariate Cox regression analysis adjusted for between all groups log rank p < 0.05) (Figure 1). Low P-Alb remained predictive of low P-Alb levels (34 g/l) at admission was observed in 134/178 patients (75%) and was more frequent in patients with lower body weight, history of ischemic heart disease or left ventricular ejection fraction <40%. Patients with low P-Alb more often presented with pulmonary oedema on chest X-ray. Low P-Alb was associated with higher 90-day mortality (48.1% vs. 23.3%, p < 0.001). A stepwise increase in 90-day mortality also in multivariant Cox regression analysis adjusted for sex, age, history of myocardial infarction, history of coronary artery bypass graft, ejection fraction, lactate and estimated glomerular filtration rate (hazard ratio 2.2 (95% CI 1.10–4.42, p = 0.025).

P4768 | BEDSIDE

Low plasma albumin at admission is associated with worse outcomes in cardiogenic shock

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Purpose: To assess the prevalence of low plasma albumin levels and the associated clinical profile and outcome(s) in cardiogenic shock patients.

Methods: Albumin levels were determined at enrollment in 178 patients with cardiogenic shock in the prospective multicenter CardShock study. All samples were analysed in a central laboratory. Albumin levels, clinical data and outcomes were analysed using SPSS statistics software.

Results: The 90-day mortality in the cohort was 42.0%. Low plasma albumin (P-Alb <34 g/l) at admission was observed in 134/178 patients (75%) and was more frequent in patients with lower body weight, history of ischemic heart disease or left ventricular ejection fraction <40%. Patients with low P-Alb more often presented with pulmonary oedema on chest X-ray. Low P-Alb was associated with higher 90-day mortality (48.1% vs. 23.3%, p < 0.001). A stepwise increase in 90-day mortality also in multivariable Cox regression analysis adjusted for sex, age, history of myocardial infarction, history of coronary artery bypass graft, ejection fraction, lactate and estimated glomerular filtration rate (hazard ratio 2.2 (95% CI 1.10–4.42, p = 0.025).

P4769 | BEDSIDE

Is the combination BNP- Six-minute walking test a simple and reliable strategy to define prognosis of patients with chronic heart failure?

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Background: Prognostic stratification in chronic heart failure (CHF) is a complex task. BNP and the six-minute walking test (6MWT) proved to be valid prognostic markers that may help to guide therapeutic decision making.

Aims: In our study we sought to investigate the prognostic value of exercise tolerance as assessed by 6MWT in patients (pts) with both reduced (CHFpEF) and preserved (CHFpEF) left ventricular ejection fraction (LVEF). To gain information in the outcome prediction pts were further characterized according to their BNP levels.

Materials and methods: We analysed 616 pts with stable CHF (mean LVEF 42%, 221/616 with CHFpEF). During the same day were performed: physical examination; laboratory tests including BNP, EKG, echocardiography; and finally 6MWT. Pts were observed for a mean period of 60 months for the end point of all cause mortality. The cut - off levels of 6MWT and BNP were determined by ROC analysis. Survival rates were analysed by Kaplan Meier method.

Conclusion: A low albumin (<34g/l) at presentation is independently associated with a worse outcome in a setting of cardiogenic shock with 90-day mortality increasing with lower albumin levels. In this cohort with severe acute illness, low plasma albumin was highly prevalent already at presentation. These findings merit further attention.

P4770 | BEDSIDE

Slovak acute heart failure survey II - predictors of in-hospital mortality

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Purpose: To identify predictors of in-hospital mortality in a non-selected population of pts hospitalised with AHF.

Methods and results: In a community-wide survey of pts with AHF admitted to 49 Slovak hospitals in 2011, we enrolled 4228 pts. We performed univariant and multivariant Cox regression analysis. Low P-Alb levels (34 g/l) at admission was observed in 134/178 patients (75%) and was more frequent in patients with lower body weight, history of ischemic heart disease or left ventricular ejection fraction <40%. Patients with low P-Alb more often presented with pulmonary oedema on chest X-ray. Low P-Alb was associated with higher 90-day mortality (48.1% vs. 23.3%, p < 0.001). A stepwise increase in 90-day mortality also in multivariable Cox regression analysis adjusted for sex, age, history of myocardial infarction, history of coronary artery bypass graft, ejection fraction, lactate and estimated glomerular filtration rate (hazard ratio 2.2 (95% CI 1.10–4.42, p = 0.025).

Conclusion: Among CHF pts with a reduced exercise tolerance (6MWT <330 pg/ml) those with higher levels of BNP (>330 pg/ml) have the worst prognosis. An integrated approach based on the combination of 6MWT - BNP results can provide feasible, reliable and low-cost prognostic information in pts with both CHFpEF and CHFpEF.

P4771 | BEDSIDE

Comparison of characteristics and outcomes in patients with HFrEF and HfPEF: result from KorAHF registry

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Purpose: The aim of the study is to investigate the differences in short-term outcomes and predictors of in-hospital mortality between HFrEF and HfPEF in Asian population.

Methods: We analyzed data from the Korean Acute Heart Failure (KorAHF) which is a nationwide prospective registry of patients hospitalized for acute heart failure syndrome in 10 regionally-representative tertiary university hospitals in Korea. Clinical characteristics, all cause in-hospital mortality and predictors of mortality were compared between patients with HFrEF (LVEF<50%) and HfPEF (LVEF<40%). Patients with borderline LVEF (40–50%) were excluded from the analysis because of heterogeneity of LVEF definition.

Results: 5,627 patients have been consecutively enrolled between March 2011 and March 2014, 24% of these patients had HfPEF and 57% had HFrEF. The median age of patients tend to be older in HfPEF than in HFrEF (72 vs 67 years). A larger proportion of patients were female in HfPEF (81% vs 39%). Valvular heart disease was the most common cause of heart failure in HfPEF (31%), whereas ischemic etiology was the most common cause in HFrEF (43%). The prevalence of hypertension (64% vs 56%) and atrial fibrillation (36% vs 23%) was higher in HfPEF compared to HFrEF. The in-hospital mortality was 72% for the group with CHFpEF and 69% for the group with CHFpEF.

Results: During a mean follow up of 60 months occurred 76 deaths. According to the results of the 6MWT there was a significant difference in the survival of pts with a 6MWT lower than a cut-off of 323 meters (rate of survival = 84%) compared to the pts above the cut-off (rate of survival = 87%) (Chi-square log rank test = 24.4, P < 0.0001). Adding the values of BNP the pts were stratified into four groups. The survival rates at 60 months were: 31% for the group with BNP >330 pg/ml and 6MWT<323 meters, 68% for the group with BNP >330 pg/ml and 6MWT > 323 meters, 82% the group with BNP <330 pg/ml and 6MWT <323 meters and 92% for the group with BNP <330 pg/ml e 6MWT >323 meters. (Chi-square logrank 103 P < 0.0001).

Conclusion: Among CHF pts with a reduced exercise tolerance (6MWT <330 pg/ml) those with higher levels of BNP (>330 pg/ml) have the worst prognosis. An integrated approach based on the combination of 6MWT - BNP results can provide feasible, reliable and low-cost prognostic information in pts with both CHFpEF and CHFpEF.
influence of old age (>70 years), pulmonary congestion, poor functional capacity (NYHA functional class III or IV) and Q wave in electrocardiogram on the risk of mortality was significantly greater in HFpEF than HFrEF. In contrast, the influence of lower BMI (<25 kg/m²) on the risk of mortality was significantly greater in HFrEF than HFpEF.

Conclusions: Compared with HFrEF, HFpEF showed better in-hospital outcome and different predictors of mortality.

P4772 | BEDSIDE
Hepatic dysfunction - an important prognostic indicator for mortality in heart failure; a population based study
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Introduction: Hepatic dysfunction has always been considered as a sequel of chronic heart failure (CHF), however there has been recent interest in it being used as a marker of disease severity in CHF. Previous studies have demonstrated this among patients in clinical trial settings but no population based studies have been conducted thus far. We aim to determine the impact of hepatic dysfunction on a composite of cardiovascular (CV) mortality and heart failure hospitalization in patients treated for CHF.

Methods: We analysed data from the Systems Biology Study to Tailored Treat- ment in Chronic Heart Failure (BIOSTAT-CHF) database which prospectively tracks treatment, comorbidity, blood investigations, hospitalization and death infor- mation of patients with heart failure from a single region in Scotland. Cox pro- portional hazard models were used to assess the prognostic impact of liver dys- function on heart failure outcomes, while controlling for covariates like treatment regimen, previous history of myocardial infarctions, atrial fibrillation, renal disease and CHF duration.

Results: Out of a total 1805 patients, there were 1200 (66.5%) males, with a mean age of 73.6 (± 10.7) years, and mean duration of HF 39.9 (± 54.1) months with a total of 414 CV death or heart failure hospitalization. We found low serum albumin levels (less than 30 g/L) to be an independent predictor of CV death or hospitalization among ambulatory CHF patients.

Acknowledgement/Funding: European commission Seventh Framework Pro- gramme (FP7)

P4773 | BEDSIDE
Pre-operative serum sodium and atrial fibrillation predict improvement in cognitive function following left ventricular assist device implantation
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Cognitive impairment is common in heart failure patients and can negatively im- pact quality of life, functional capacity, and survival. Though the effects of heart transplant support on cognitive function (CF) remain poorly investigated, a recent pilot study with cardiovascular magnetic resonance (CMR) in patients with reperfused acute MI found to be independent predictors for improvement in MoCA score after LVAD implantation.

The Montreal Cognitive Assessment (MoCA) was used to evaluate CF in 56 pa- tients prior to and 8 months after LVAD implantation. Demographic, hemody- namic, echocardiographic, and laboratory data were collected concurrently. Pa- tients were divided into two groups- those with improved and non-improved MoCA scores.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Non-improved MoCA</th>
<th>Improved MoCA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=20)</td>
<td>(n=36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-Implant MoCA</td>
<td>25.0±2.7</td>
<td>22.8±3.7</td>
<td>0.049</td>
</tr>
<tr>
<td>Post-Implant MoCA</td>
<td>23.5±3.0</td>
<td>25.0±6.3</td>
<td>0.008</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.0±12.0</td>
<td>56.7±14.0</td>
<td>0.850</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.6±16.8</td>
<td>27.6±7.5</td>
<td>0.099</td>
</tr>
<tr>
<td>Mean p.m. artery pressure (mmHg)</td>
<td>29.9±10.4</td>
<td>37.9±10.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Sodium (mg/dL)</td>
<td>135.7±3.2</td>
<td>133.2±4.5</td>
<td>0.011</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.2±0.5</td>
<td>3.9±0.4</td>
<td>0.040</td>
</tr>
<tr>
<td>BNP (pg/dL)</td>
<td>350.55±15.32</td>
<td>854.7±480.23</td>
<td>0.020</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (20%)</td>
<td>16 (41%)</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Conclusion: The current results demonstrated that myocardial salvage was at- tenuated in acute reperfused patients with acute MI and inversely related with LVMi. Thus, cardioprotective effects may be impaired in patients with hypertension through increased LV mass.

P4774 | BEDSIDE
Impact of hypertension on myocardial salvage assessed by cardiac magnetic resonance in patients with reperfused acute myocardial infarction
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Introduction: Controversy exists on whether hypertension has a cardioprotective effect in patients with acute myocardial infarction (MI). We sought to assess the influence of hypertension on cardioprotective effects, measured as myocardial salvage index (MSI), by using cardiac magnetic resonance (CMR), in patients with reperfused acute MI.

Methods: A total of 31 patients with acutely reperfused first ST-segment elevation MI caused by proximal coronary culprit lesions and pre-procedural Thrombolysis in Myocardial Infarction (TIMI) flow 0/1 underwent CMR within 2 weeks. Area at Risk (AAR), MI size and MSI were determined by 1.5T and late gadolinium enhanced CMR.

Results: AAR, MI size normalized by LV mass was 36±14% and 27±15%, re- spectively (P<0.05), yielding a mean MSI of 28±20% (range 0–69%). Seventeen patients (55%) had hypertension. Hypertensive patients had significantly lower MSI than non-hypertensive patients (20±16% vs 38±20%, p<0.05). However, there was no significant differences in AAR and MI size between both groups (37±15% vs 35±15%, p=0.7, 30±15% vs 23±14%, p=0.2). Univariate analysis demonstrated that MSI was associated with MI size. TIMI flow, LV mass in- dex (LVMi) and peak CKP level (r=−0.38, 0.40, −0.46, respectively, all p<0.05). The presence of hypertension was a significant predictor of lower MSI (p coefficient=−0.34, p=0.05).

Conclusion: The current results demonstrated that myocardial salvage was at- tenuated in patients with hypertension, which was significantly associated with hypertensive patients compared to non-hypertensive patients. This trend was also observed in acute MI patients with hypertension compared to non-hypertensive patients with acute MI. Thus, cardioprotective effects may be impaired in patients with hypertension through increased LV mass.

P4775 | BEDSIDE
Association between diffuse myocardial fibrosis and decreased myocardial strain in hypertensives with preserved ejection fraction. A pilot study with cardiovascular magnetic resonance
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New cardiovascular magnetic resonance (CMR) T1 mapping sequences have been developed that can be applied to quantify diffuse myocardial fibrosis. Novel analysis softwares allow for the accurate and reproducible measurement of myo- cardial strain. We aimed to use these two new developments in a pilot study in order to assess the association between presence of diffuse fibrosis and changes in myocardial strain.

Methods: 15 hypertensive patients (HT, 51±7yrs, 12 males) with preserved ejec- tion fraction and 15 controls (NT, 49±13yrs, 9 males) underwent a CMR protocol at 3T that included black blood sequences, cine sequences in the 2,3,4-chamber views and short axis series with typically 40 phases for each acquisition, T1- mapping of a bolus of gadolinium-DTPA (0.1mM/kg), and late gadolinium sequences. All the scans were eventually analysed with a dedicated software to obtain left ventricular volumes and mass, precontrast myocardial T1 values, gadolinium par- tition coefficient (GPC) and extracellular volume fraction (ECV), a measure of
diffuse myocardial fibrosis. Also, longitudinal and radial global myocardial systolic strain and strain rate, as well as epicardium-endocardium strain gradient were measured.

**Results:** All subjects had preserved systolic function. Global longitudinal and radial strain (GLS, GRS), longitudinal strain rate (GLSR) and precontrast T1 were all lower in HT, while radial strain gradient between subendocardium and subepicardium (GRS endo-epi) was increased in HT and there was a trend towards increased ECV in HT. There was a significant inverse correlation of GLS and GRS with ECV, and of radial strain gradient (GRSR) with ECV (p < 0.001).

**Conclusions:** In this pilot study we have found that there is an inverse correlation between global strain, a sensitive indicator of regional contractility, and myocardial extracellular volume fraction, a marker of diffuse fibrosis. The finding may have implications for early diagnosis of target organ damage in hypertensive patients.

**P4777 | BEDSIDE**

**COMPARISON OF METHODOLOGY TO EVALUATE ARTERIAL STIFFNESS IN ELDERLY MALES**

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**Background:** The Sphygmocor device (S) is the established method for evaluating arterial stiffness in determining the amplitude of the aortic pressure waveform. Findings support previous data suggesting a relatively minor role for wave reflection in determining distal conduit arterial pressures. The decrease in Ks with distal progression is consistent with gradually rising impedance whilst the increase in Kd is suggestive of progressively decreasing compliance. These findings support previous data suggesting a relatively minor role for wave reflection in determining the amplitude of the aortic pressure waveform.

**Results:** Systolic blood pressure increased from the ascending aorta to the bifurcation, whilst diastolic blood pressure remained constant (see Table). The systolic rate constant Ks (relating to characteristic impedance) increased whilst the diastolic rate constant Kd decreased with distal progression. Peak excess pressure increased with distal progression (P < 0.001) and accounted for the rise in systolic blood pressure whereas the maximum reservoir pressure decreased. Peak reservoir pressure timing decreased along the aorta (P < 0.001).

**Conclusions:** The increase in peak excess pressure along the aorta and the constant time to peak excess pressure suggest that wave transmission is relatively more important in determining distal conduit arterial pressures. The decrease in Ks with distal progression is consistent with gradually rising impedance whilst the increase in Kd is suggestive of progressively decreasing compliance. These findings support previous data suggesting a relatively minor role for wave reflection in determining the amplitude of the aortic pressure waveform.

**Abstract P4777**

**Table 1. Reservoir pressure parameters**

<table>
<thead>
<tr>
<th>Aortic position</th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Reservoir pressure integral (mmHg s)</th>
<th>Maximum reservoir pressure (mmHg)</th>
<th>Reservoir pressure (mmHg)</th>
<th>Excess reservoir pressure (mmHg)</th>
<th>Peak reservoir pressure time (ms)</th>
<th>k_L (Mean SD)</th>
<th>k_D (Mean SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>131.6 (27.4)</td>
<td>65.5 (11.5)</td>
<td>20 (6.2)</td>
<td>49.2 (14.5)</td>
<td>5.9 (2.8)</td>
<td>25.6 (9.9)</td>
<td>59.6 (8.1)</td>
<td>15.5 (4.7)</td>
<td>2.6 (0.9)</td>
</tr>
<tr>
<td>Aortic arch</td>
<td>130.8 (25.4)</td>
<td>65.4 (10.9)</td>
<td>19.6 (6.3)</td>
<td>47.8 (13.7)</td>
<td>6.0 (2.8)</td>
<td>27.9 (9.9)</td>
<td>57 (7.5)</td>
<td>13.9 (3.8)</td>
<td>2.6 (0.8)</td>
</tr>
<tr>
<td>DIAPIHRAP</td>
<td>140.4 (28.7)</td>
<td>69.9 (18.7)</td>
<td>19.7 (6.5)</td>
<td>48.9 (11.6)</td>
<td>7.0 (2.8)</td>
<td>32.3 (10.3)</td>
<td>56.0 (6.5)</td>
<td>12.1 (2.3)</td>
<td>2.8 (0.7)</td>
</tr>
<tr>
<td>Renal arteries</td>
<td>138.7 (23.2)</td>
<td>62.7 (9.7)</td>
<td>18.5 (5.7)</td>
<td>46.9 (12.2)</td>
<td>8.2 (2.8)</td>
<td>40.3 (9.5)</td>
<td>54 (6.2)</td>
<td>9.7 (1.4)</td>
<td>3.0 (0.7)*</td>
</tr>
</tbody>
</table>

k_L, systolic rate constant; k_D, diastolic rate constant. *P < 0.01, **P < 0.001.
tolic strain rate was increased in subjects with concentric and dilated-concentric LVH in comparison with normal LV geometry patients (Table). Nevertheless, statistically significant importance was found only in comparison between normal LV geometry subjects and concentric LVH individuals.

**Conclusion:** RV myocardial deformation in hypertensive patients is significantly impaired compared with healthy controls. Concentric and eccentric LVH patterns have the greatest unfavorable effect on LV mechanics. The new classification of LV geometry provides valuable and comprehensive information about RV mechanical function in hypertensive population.

**P4779 | BEDSIDE**

**Relationship between left ventricular systolic stress and systolic strain on strain rate and pressure examination assessed by one-beat 3-dimensional speckle tracking echocardiography with high volume rate**

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**Purpose:** Left ventricular hypertrophy (LVH) is known as a compensatory mechanism of LV against pressure overload to reduce LV stress and maintain systolic performance even end-diastolic. LVH is associated with increased LV stress without further reduction in longitudinal and radial strain, suggesting that LV longitudinal and radial strain had been already deteriorated and the beginning of reduction in circumferential strain after deterioration of longitudinal and radial contractility may be responsible for HHF.

**Methods:** A total of 168 subjects (114 patients with HTN and 54 controls (age 70±9) were enrolled. Patients with HTN were divided into 3 groups: 50 HTN patients without LVH (age 70±9), 40 HTN patients with LVH (age 69±6) and 24 HTN patients without LVH. LV systolic stress was calculated as LV end systolic radius x systolic blood pressure over volume rates and sought to evaluate the impact of LV systolic stress on contractility in HTN.

**Results:** LV systolic stress in 3 directions and SR at endocardium were reduced in HTN and further reduced in HHF (longitudinal strain; control: −19±4, HTN without LVH: −18±3, HHF: −15±4, p<0.05 vs control). There was a significant correlation between LV systolic stress and longitudinal and circumferential peak strain (r=0.17, p=0.031 and r=0.19, p=0.014, respectively) and between LV stress and LV radial SR during systole at both endocardium and epicardium by the novel 3D-STE with 60–80 vps. LV systolic stress was calculated as LV end systolic radius x systolic blood pressure/LV end systolic thickness.

**Conclusion:** LV contractility assessed by LV strain and SR was reduced associating increased LV stress without further reduction in longitudinal and radial strain, suggesting that LV longitudinal and radial strain had been already deteriorated and the beginning of reduction in circumferential strain after deterioration of longitudinal and radial contractility may be responsible for HHF.

**P4780 | BEDSIDE**

**Myocardial fibrosis correlated with sub-endocardial but not global circumferential strain in hypertension**

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**Background:** Hypertension causes myocardial fibrosis. However, effects of myocardial fibrosis on circumferential deformation of myocardium have not been well elucidated.

**Methods:** This study included 90 patients (34 female, age 65±12 years) with uncomplicated hypertension who have been regularly treated for more than 1 year. Degree of myocardial fibrosis was assessed by microhardness measurements of serum carboxy-terminal propeptide of procollagen type I (PICP). Circumferential and longitudinal deformations of left ventricle were measured by speckle tracking echocardiography.

**Results:** Levels of PICP were not correlated with global longitudinal strain (r=−0.178, p=0.144) and global circumferential strain (CS) (r=−0.169, p=0.118). We further divided CS into sub-endocardial and sub-epicardial CS. Only sub-endocardial CS was significantly correlated with PICP (r=−0.225, p=0.036) but not with epicardial CS (r=−0.055, p=0.613). Multivariate analysis showed sub-endocardial CS was still significantly correlated with PICP (B = −0.464, p=0.022) after controlling age, systolic blood pressure, and left ventricular mass index. Sub-endocardial CS was significantly correlated with early mitral velocity to lateral annulus velocity ratio (E’/E) (r=−0.299, p=0.034).

**Conclusion:** Serum PICP was correlated with only sub-endocardial CS. Myocardial fibrosis occurred majorly sub-endocardial in myocardium in hypertension.

**P4781 | BEDSIDE**

**Effects of iron overload on sympathetic nervous system in essential hypertensive patients**

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**Background and aims:** A recent hypothesis claims that iron metabolism directly or indirectly, i.e. through metabolic (insulin resistance) or inflammatory/autoimmune mechanisms, is linked to the sympathetic nervous system. We tested this hypothesis by recording central sympathetic neural outflow in hypertensive patients with normal or elevated circulating plasma levels of ferritin (FE), i.e. a marker of iron load.

**Methods:** In 8 untreated male essential hypertensives with elevated plasma iron (HFE+) and 9 controls (HC), we assessed central sympathetic neural activity (MSNA) and para-sympathetic activity (HVR) by a green laser Doppler technique.

**Results:** There was no difference in HRR between men (32±13 beats/min) and women (31±12 bpm; p=0.012). There was no difference in HRR between patients without hypertension (31±11 vs. 34±11 bpm; p=0.012). In the group as a whole there was a significant relationship between MSNA and FE (r=−0.4, P<0.01), whose level of statistical significance was greater than the one related to the relationship MSNA and HOMA index (r=0.53, P<0.05). Homa index and FE were also significantly and directly related each other (r=0.56, P<0.05).

**Conclusions:** These data provide the first evidence that in hypertensive males iron overload exerts marked sympathoexcitatory effects associated with a decrease in insulin sensitivity. It is likely that the iron overload directly or through the concomitant hyperinsulinemia may be responsible for this neuroadrenergic response.

**P4782 | BEDSIDE**

**Prolonged heart rate recovery as predictor of incidental hypertension and survival**

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**Background:** Heart rate recovery (HRR), defined as the decline in heart rate immediately following cessation of exercise, is influenced by autonomic function. Prolonged HRR has been associated with poor survival, typically in patients with heart failure or diabetes mellitus, but less is known about its relation to hypertension.

**Purpose:** To study the relation between HHR and ongoing and incidental hypertension as well as the association of HHR with long-term survival.

**Methods:** 1047 consecutive patients (mean age 56±14 years, 43% women) were referred for an exercise ergometry test at a university hospital between May 1996 and December 1997. N=708 patients (68%) remained after excluding patients on beta-blockers, or with a pacemaker, established cardiac morbidity, stroke, and diabetes. N=95 patients had ongoing hypertension (defined as diagnosis of hypertension identified in a medical board’s patient register or as use of antihypertensive medication). HRR was defined as the decrease in HR during the first minute after peak exercise.

**Results:** Information about incidental cardiovascular morbidity and mortality, as well as all-cause mortality, was collected during a mean follow-up of 15±4 years. N=157 patients with incidental hypertension were identified at follow-up.

**Results:** There was no difference in HRR between men (32±13 beats/min) and women (31±12 bpm; p=0.104). The mean HRR was significantly less in patients with ongoing hypertension (30±14 bp; p<0.001). The patients who eventually developed hypertension also had significantly lower HRR than those without hypertension (31±11 vs. 34±11 bpm; p<0.012).

In a survival analysis by Cox proportional model of the whole cohort, the HRR was an independent predictor of survival (HR 0.97; 0.96–0.98; p<0.001) after adjusting for relevant covariates (age, gender, smoking, previous cardiovascular morbidity, and diabetes).

**Conclusion:** Heart rate recovery after an exercise test is associated with both ongoing and incidental hypertension. Thus, this exercise parameter might be useful for predicting both survival and the risk of hypertension.

**Acknowledgement/Funding:** Svenska Läkareförbundet
P4783 | BEDSIDE
Reduced baseline heart rate and increased exercise-induced heart rate response as characteristic features in patients with orthostatic hypotension
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Background: The orthostatic hypotension (OH) is a rare but not so uncommon disease in elderly individuals. Recent attention has been paid to the increase in serious cardiovascular risk in pts with OH and extreme diapper. However, underlying baro-reflex dysregulation and clinical features are still unknown during exercise (Ex).

Purpose and methods: To examine the vital and clinical features, consecutive 802 patients (pts) requiring treadmill Ex-test (Bruce protocol, symptom-limited) were examined and 15 OH (a fall in systolic blood pressure [sBP] at least 15mmHg; [ΔsBP, -17±5 mmHg]) pts and 94 control (no medication/no organic heart disease) were selected. Pts with neurogenic disease, diabetes mellitus, Parkinson disease and current oral medication were excluded. Heart rate (HR; bpm), HR-variability (HRV) [MemCalc™(maximum entropy) method] and baseline heart disease) were selected. Pts with neurogenic disease, diabetes mellitus, 15 OH (a fall in sBP at least 15 OH) were examined and 15 OH (a fall in sBP at least 15 mmHg) were compared to that of HR in each Ex period (rest, Ex, peak-Ex and recovery) by regression analysis.

Results and conclusion: Clinical (BMI, LDL-C, LVDd, LVEF) and autonomic features (HR and high frequency component [log HF; msec²] in each Ex period) were similar in 2 groups but exaggerated HR response during Ex was observed only in pts with reduced baseline HR in a dose-response manner. Therefore, not reduced but exaggerated HR response may be a common autonomic feature in OH pts.

P4784 | BENCH
High sodium enhances non-neuronal acetylcholine release in the renal cortex

Background: In the renal arteries, acetylcholine (ACh) activates endothelial nitric oxide synthesis and causes endothelium-dependent vasorelaxation, resulting in an increased renal blood flow. In the kidney of salt-sensitive hypertensive subjects, exogenous ACh-induced vasodilatation is reported to be impaired. Therefore, there may be a close relationship between the onset of salt-sensitive hypertension and endogenous ACh release in the kidney. However, the mechanism of endogenous ACh release in the kidney remains unclear.

Purpose: To clarify the mechanism of endogenous ACh release in the kidney, we introduced a microdialysis technique to the kidney.

Methods: A microdialysis probe was implanted into the renal cortex of the chloralose-urethane anesthetized rabbits. (1) High potassium (200 mM), (2) high sodium (500 or 900 mM), (3) Na+/K+-ATPase inhibitor, ouabain (100 μM), and (4) epithelial Na+ channel blocker, benzamil (300 μM) were locally administered through the microdialysis probe and dialysate samples were collected. Dialysate ACh concentrations were analyzed using high-performance liquid chromatography.

Results: (1) High potassium did not affect dialysate ACh concentration (1.0±0.2 to 1.0±0.3 nM, not significant). (2) Both doses of high sodium significantly increased dialysate ACh concentrations (500 mM: 1.2±0.4 to 2.4±0.4 nM, P<0.05; 900 mM: 1.1±0.3 to 5.0±1.1 nM, P<0.01). (3) Ouabain significantly increased dialysate ACh concentration (1.2±0.2 to 2.2±0.3 nM, P<0.01). (4) Benzamil significantly decreased dialysate ACh concentrations in both baseline and high sodium (900 mM) conditions. Benzamil, P<0.01; high sodium, P<0.01; interaction, P<0.01 by two-way ANOVA.

Conclusions: High potassium-induced depolarization did not affect endogenous ACh release. This result suggests that renal ACh release is mainly dependent on non-neuronal mechanism. High sodium and Na+/K+-ATPase inhibitor significantly increased endogenous ACh release, but epithelial Na+ channel blocker significantly decreased ACh release. These results suggest that an increase in intracellular sodium level enhances non-neuronal ACh release in the renal cortex. Endogenous ACh in the kidney may increase renal blood flow against high sodium and act as a renoprotective agent.

P4785 | BEDSIDE
Blood pressure and sympathetic activity markers are associated with monocyte chemoattractant protein 1 (MCP1) levels
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Introduction: The monocyte chemoattractant protein 1 (MCP1) is important in various inflammatory and atherosclerotic processes. This protein release is related to several stimuli.

Purpose: The aim of this study was to evaluate the association between MCP1 and anthropometric, hemodynamic, metabolic data, and norepinephrine and adipocytokines in subjects with metabolic syndrome.

Methods: Seventy four consecutive subjects with metabolic syndrome were evaluated [age 41 (18–64) years, 53 females, 54 caucasian and 20 non caucasians]. Anthropometric data (weight, height, body mass index, abdominal circumference), blood pressure, heart rate, heart rate variability, biochemistry data, including norepinephrine and adipocytokines were evaluated.

Results: An association between MCP1 and adipokines was observed (r=0.294, p<0.001), interleukine 6=IL6 (r=0.270, p=0.020), interleukine 6=IL6 (r=0.330, p=0.004), plasminogen activator inhibitor 1=PAI1 (r=0.441, p<0.001), interleukine 6=IL6 (r=0.270, p=0.020), and tumoral necrosis factor alpha=TNFa (r=0.435, p<0.001) was observed. We did not find association between MCP1 and body mass index, blood pressure, heart rate, HDL-cholesterol, triglycerides, uric acid, adiponectine, retinol, and retinol binding protein 4 (RBPA4). In a multiple linear regression stepwise diastolic blood pressure, LF/HF ratio, LDL-cholesterol, PA11, TNFa, and IL6 were independent predictors of MCP1 (r²=0.240–0.593, p<0.001). MCP1 median was 140 pg/mL. Subjects with MCP1 values over the median showed significantly (p<0.05) higher values of MCP1, LDL, TNFa, and PA11 levels than those with lower values than median. Also, the group with MCP1 over the median had higher values of LF component, lower value of HF component and higher LF/HF ratio values in spectral analysis.

Conclusions: In subjects with metabolic syndrome MCP1 is associated with higher blood pressure, LDL-cholesterol, adipocytokines levels, and higher sympathetic activity evaluated by no norepinephrine and spectral analysis.