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 flow (OR=2.10, 95% CI: 1.31–3.33, p<0.001), it did not confer a mortality benefit (HR=1.13, 95% CI: 0.69–1.85, p=0.620). DES use was not associated with a reduction in TVR (HR=1.16, 95% CI: 0.89–1.51, p=0.281), 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 extensively characterized from large-scale real-world 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 2.5%, 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 evidences 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


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 underwented 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 75.4%. Predilation 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%. Epitube inserted 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 190–548), 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.

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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 performed at two university hospitals in Denmark. Outcome data was 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 enoxatide (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 enoxatide (11%) compared to patients treated with placebo (20%), yielding a hazard ratio of 0.53 (95% 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 enoxatide at the time of percutaneous coronary intervention 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 unsel ected 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 TVR 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=0.027). 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 very long-term safety and effectiveness with very 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 better.

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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Methods: Pooled analysis was performed with patients undergoing PCI using 1st generation DES for bifurcation lesions with side branch diameter <1.5 mm in the 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). Primary clinical outcome was target lesion failure (TLF), and secondary clinical outcomes were patient-oriented composite outcomes (POCO, a composite of all death, any MI, any repeat revascularization, and cerebrovascular accidents).

Results: Of 3,162 patients with bifurcation lesions, 52.9% of patients showed true bifurcation lesion. 2,475 patients with 1st generation DES were treated with 1-stenting (72.8%) or 2-stenting (27.2%) techniques. Among the 687 patients with 2nd generation DES, 59.5% or 40.5% were treated with 1- or 2-stenting techniques, respectively. The rates of TLF or POCO at 3-year were significantly higher after systemic 2-stenting with 1st generation DES (TLF: 8.6% vs. 17.5%, p<0.001; POCO 18.1% vs. 28.5%, p<0.001), however, there was no difference between 1- and 2-stenting techniques with 2nd generation DES (TLF: 5.4% vs. 5.8%, p=0.768; POCO: 11.2% vs. 12.9%, p=0.995). The differential impacts of 2-stenting techniques according to the type of DES were also corroborated by similar results with inverse probability weighted model. 2-stenting technique was significant independent predictor for TLF in 1st generation DES (HR 2.046, 95% CI 1.144–3.759, p<0.001), but not in 2nd generation DES (HR 0.667, 95% CI 0.427–1.082, p=0.042).

Conclusion: The 2-stenting showed significantly worse clinical outcomes with the use of 1st generation DES. However, with the use of 2nd generation DES, 2-stenting technique showed comparable outcomes with 1-stenting technique. Considering enhanced safety and efficacy of 2nd generation DES, individualized treatment strategy for bifurcation lesion is warranted rather than universal application of the 1-stenting strategy.

2019 | BEDSIDE
Predictors of late coronary thrombotic events after percutaneous coronary intervention: insights from the PARIS registry
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Background: Ischemic risk after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation is dynamic, being highest early after the procedure with attenuation over time. Accurate knowledge of the ischemic risk factors is essential in guiding the optimal duration of dual antiplatelet therapy (DAPT). The predictors of late thrombotic events are unclear.

Objectives: We sought to identify baseline clinical variables independently associated with thrombotic events after 30 days among patients undergoing PCI with DES.

Methods: Participants in the PARIS registry were categorized according to the development of a late intra coronary thrombotic event (ICTE) after 30 days from the procedure to 2 years. ICTE was defined as the composite of death/prob stent thrombosis or myocardial infarction. Patients in whom baseline laboratory variables were missing were excluded from the analysis. Multivariate analysis was performed using a Cox regression model, with candidate variables for analysis chosen via backward stepwise selection.

Results: Of 3449 patients enrolled in the PARIS study, 134 (3.9%) had an ICTE. Patients with ICTE were more commonly hypertensive, anemic, diabetics, with higher 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 protective.

Predictors of late ICTE

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age1</td>
<td>0.97 (0.96–0.99)</td>
<td>0.01</td>
</tr>
<tr>
<td>Anemia</td>
<td>1.94 (1.32–2.83)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2.21 (1.49–3.29)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>1.55 (1.10–2.19)</td>
<td>0.01</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.71 (1.11–2.62)</td>
<td>0.01</td>
</tr>
<tr>
<td>Insulin-treated diabetes</td>
<td>2.02 (1.42–2.87)</td>
<td>0.01</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>1.91 (1.24–2.74)</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

1HR for age expressed as 1 year increase.

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

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2014 | BEDSIDE
Relative survival and excess mortality following unprotected left main stem percutaneous coronary intervention: a national cohort study of 11079 emergent and elective cases
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Background: There are no whole country studies of survival following percutaneous coronary intervention (PCI) to the unprotected left main stem (ULPLMS) 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 ULPLMS 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 (RSR) 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 RSRs were better in CSA group (97.5% versus 93.8%) compared to STEMI (64.1% versus 57.0%) and NSTEACS (84.6% versus 73.1%) (Fig. 1). Excess 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 NSTEACS. For CSA, EMRR was associated with diabetes 22.2% (95% CI; 1.44 to 3.38), previous AMI 2.26% (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 2.76% (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 ULPLMS 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.

2016 | BEDSIDE
1-year angiographic and 5-year cumulative outcome 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 (EES) and zotarolimus-eluting (ZES) stents in patients with multivessel PCI.

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: 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.

2019 | BEDSIDE
Mortality risk in children and young adults with congenital heart disease in Sweden
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Background: The survival rate in patients with congenital heart disease has increased markedly during the last decades due to the evolution of pediatric care. Nevertheless, there are limited data available with respect to the mortality risk in children and young adults with congenital heart disease.

Methods: We obtained data from the Swedish patient and Cause of Death Registers to study all patients who were born between 1st January 1970 and 31st December 1993 with a diagnosis of congenital heart disease diagnosed at birth or subsequently according to the International Classification of Diseases (8th, 9th and 10th edition). Follow-up and co-morbidity data was collected for all patients until 31st December 2011. The analysis was performed on 21,516 controls (n=266,480) matched for age, sex and county, were randomly selected from the general population for each patient.

Results: We identified 26,648 patients (51.4% men, 48.6% women) with congenital heart disease who were registered in Sweden; mean age at diagnosis was 9.6 years, mean follow-up was 18.7 years. At the last year of follow-up (2011), 93.8% (n=24,987) of patients with congenital heart disease and 99.4% (264,978) of controls were still alive. The overall mortality was 12.0 times higher (95%, CI 11.2–12.9, p<0.001) in patients with congenital heart disease compared to controls.

Conclusion: The proportion of patients with congenital heart disease is increase with the availability of appropriate treatment and surgery. However, the excess mortality needs to be reduced by effective follow-up and appropriate treatment.
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 interventionally 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(s): The notion of generally poor survival prospects of DS patients with CHD is obsolete due to the available treatment options. Patients with DS who develop an ES still have a poor prognosis, but long-term outcome in those with CHD is obsolete due to the available treatment options. Patients with DS undergoing timely curative operation is excellent.

2927 | BEDSIDE
NOACs, Are they safe in congenital heart disease? First results from an international multicenter registry
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Purpose: Adults with congenital heart disease (ACHD) and non-valvular atrial

anthymia (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.

Conclusion: Preliminary data show no adverse event among ACHD using NOACs for prevention of thromboembolism.
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 the Jungfraujoch (at 3454 m; high altitude). All tests were performed within 12 weeks. Endpoints were the change of 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: rest 92% vs. 96%, high altitude: rest 83% 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 (±58% vs. ±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.

2930 | 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±2 mmHg (−15 mmHg in 10 pts), ventricular end-diastolic pressure (VEDP) 6.67±2.58 mmHg, pulmonary vascular resistances (PVR) 21±12 WU m−2, (2 in 18 pts); cardiac index (QSI) 3.15±1.27 L/min/m2, systemic 2 saturation 94%±9% in 18 pts), QP/QS 0.9±0.2. 37 interventions were performed in 27 patients. We found the following significant correlations: interval from TCP vs QSI (r=−0.30; p<0.001), interval from TCP vs VEDP (0.3; p=0.01), PVR vs QSI (r=−0.1; p=0.001). Nor PAP, PVR or QP/QS were significantly related with age or interval from TCP. Trans-hepatic gradient was 2.3±1.11 mmHg; 20 pts had major venous collateral vessels from the liver. Gastroscopy showed esophageal varices in 6 pts (0.9%) having PVR > 2 UW m2. Conversely, all pts with PAP > 15 mmHg had either venous collaterals or esophageal varices. Liver function was normal in all pts. Hepatomegaly was found in 23 pts; the liver was nodular and/or inhomogeneous in 10 and 35 pts. Stiffness was 16.83±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.

Conclusion: 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 dilation, aortic dissection and mortality.

Results: The cohort of 224 MFS patients (age 28.8±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±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) 0.88, 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 dilation (HR 40 mm (7.1, 95% CI 1.5–34.1; p=0.014), 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 dilation progression rate was 1.04±1.12 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 MSCT angiography of congenital heart disease were converted into standard triangulated language files to make plastic stereolithographic biomodels representing precisely angulated language files to make plastic stereolithographic biomodels representing precisely angulated language files to make plastic stereolithographic biomodels representing the outer and inner surface of the heart. Then, rubbery polyurethane was injected into the outer and inner molds under the vacuum condition. The accuracy of the replica was confirmed by measurement with 3-dimensional X-ray reconstruction tomography.
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 simulation surgery 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

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**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%/25%). 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 subjects (40±9 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: 150m/s, 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. Contours 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 (93±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=0.08). In the right-left plane the IVC was more medial to the SVC in the stroke group (10±5mm vs. 3±1, 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 was 10–15% and 5%.

**Table 1**

<table>
<thead>
<tr>
<th>Vortex</th>
<th>Other patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>PFO/Stroke</td>
</tr>
<tr>
<td>systole</td>
<td>diastole</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>3</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.

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**2934 | BEDSIDE**

Lifelong endocardial prosthesis 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 1048 person-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 (HR=4.17; 2.27–7.65) and prosthetic material (2.84; 1.77–4.57) independently predicted IE. Complex cyanotic ACHD did not (1.19; 0.52–3.23).

**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 Parelinoe Institute (PSI).

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**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 compare the safety and outcome of residential CR in octogenarians after TAVI or AVR with biological prostheses.

**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). CR outcome (cumulative illness rating state-comorbidity index) (CIRS-CI) score, Echocardiography on admission, Disability (Barthel Index) (BI), Morse Fall Scale score (MFS), Six minute walking test distance (6MWT) on admission and at discharge were assessed; a frail index (FI) at discharge was defined as the presence of at least two of the following: 6MWT <200m, BI <80, MFS <50.

**Results:** Compared to AVR, TAVI were older, had worse CIRS-CI and aortic prosthetic insufficiency (API) on 0–3 scale. TAVI, as AVR, could attend safely CR training but they tolerated a significantly lower workload with lower performance at 6MWT at discharge compared to AVR even if 6MWT improvement at discharge was similar in both groups. Disability, MFS and FI were higher in TAVI at discharge; yet they had significant disability improvement during CR. At follow up (range 12–36 months) death occurrence was significantly higher in TAVI (p=0.01) (Table).

**Table 1**

<table>
<thead>
<tr>
<th>TAVI (58)</th>
<th>AVR (52)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIRS-CI (M±SD)</td>
<td>3.4±1.6</td>
<td>3.1±1.3</td>
</tr>
<tr>
<td>BI discharge (M±SD)</td>
<td>84±15</td>
<td>92±14</td>
</tr>
<tr>
<td>MFS discharge (M±SD)</td>
<td>32±16</td>
<td>22±14</td>
</tr>
<tr>
<td>Training 10W or 3.5km/h twice/d (%)</td>
<td>9±16</td>
<td>23±40</td>
</tr>
<tr>
<td>6MWT discharge (M±SD)</td>
<td>168±131</td>
<td>249±132</td>
</tr>
<tr>
<td>FI (%)</td>
<td>16 (27)</td>
<td>6 (11)</td>
</tr>
<tr>
<td>API (M±SD)</td>
<td>1.2±0.8</td>
<td>0.6±0.5</td>
</tr>
<tr>
<td>Death at follow up (%)</td>
<td>19 (33)</td>
<td>6 (12)</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.

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2936 | BESDISE
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 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 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 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±1.2 (men/women) 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<0.05) and women (p<0.002) two years after MI. MI patients had a beneficial effect on their cardiovascular status (p<0.05) in HDL and non-significant differences were found in the other risk factors.

Conclusion(s): The results indicate that while benefiting patients in general, secondary prevention did not benefit all groups equally. Immigrant women were less likely to reduce their risk compared to Swedish women, which cannot be explained by age, marital status and socioeconomic status. No differences were found between immigrant and Swedish men.

2937 | BESDISE
Optimizing patient benefit from CRT response with the addition of high intensity interval training - a randomized controlled trial
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Background: Cardiac resynchronization therapy (CRT) improves prognosis, leading to reverse remodeling with a reduction in left ventricular (LV) size, improvement in LV ejection fraction (LVEF) and systolic volume. However, 30–40% of patients who undergo CRT are non-responders. While the addition of aerobic exercise to CRT has been shown to improve patient benefits, this is not the case for high intensity interval training (HIIT). In order to increase CRT benefits, HIIT effects are required. However, HIIT is more effective than moderate aerobic exercise for improving functional capacity (ExG:2.7±4.6ml/kg/min, p<0.05; CG:0.9±2.2 min, p<0.01) and functional class in non-responders (ExG:2.0±0.0, p<0.01; CG:0.6±0.5, p<0.01) which was higher in the ExG than in CG.

Purpose: The purpose of this study was to investigate the impact of CRT on health care use and sick leave among heart valve surgery patients. The aim was to compare long-term health care use and sick leave among heart valve surgery patients based on participation in six months comprehensive cardiac rehabilitation process.

Methods: We conducted a nationwide survey about participation in postoperative cardiac rehabilitation and control group in self-reported AF symptoms at six months (p<0.05). 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<0.05).

Conclusions: 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 improving health and optimizing adverse events.

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

2939 | BESDISE
Exercise-based cardiac rehabilitation after heart valve surgery: cost analysis of health care use and sick leave
T.B. Hansen1, A.D. Wisconsin2, S.K. Berg3, K.L. Sibbit2, L.C. Thygesen4, P. Doherty5, R. Soegaard6, 1Rigshospitalet - Copenhagen University Hospital, The Heart Centre, Copenhagen, Denmark; 2University of Southern Denmark, National centre of Rehabilitation and Palliation, Odense, Denmark; 3Rigshospitalet - Copenhagen University Hospital, The Heart Centre, Copenhagen, Denmark; 4National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark; 5University of York, Department of Health Sciences, York, United Kingdom; 6Aarhus University, Department of Public Health, Aarhus, Denmark

Background: There is a lack of specific evidence supporting both the clinical and economic effect of exercise-based cardiac rehabilitation (CR) in patients after heart valve surgery. Despite this CR has, since 2009, been offered to this group of patients in the Danish health care system based on recommendations for patients with ischemic heart disease.

Purpose: The aim of this study was to investigate the impact of CR on health care use and sick leave among heart valve surgery patients.

Methods: We conducted a nationwide survey about participation in postoperative cardiac rehabilitation and control group in self-reported AF symptoms at six months (p<0.05). A difference-in difference analytical strategy was undertaken. All baseline and economic effect of exercise-based cardiac rehabilitation (CR) in patients after heart valve surgery. Despite this CR has, since 2009, been offered to this group of patients in the Danish health care system based on recommendations for patients with ischemic heart disease.

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Methods: We conducted a nationwide survey about participation in postoperative cardiac rehabilitation and control group in self-reported AF symptoms at six months (p<0.05). A difference-in difference analytical strategy was undertaken. All baseline and economic effect of exercise-based cardiac rehabilitation (CR) in patients after heart valve surgery. Despite this CR has, since 2009, been offered to this group of patients in the Danish health care system based on recommendations for patients with ischemic heart disease.
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 determine 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 1.05 [95% CI: 0.31–0.356]; p<0.001) and cardiac mortality (OR 1.07 [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
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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; −1.13) m² in patients with SCAD, and 1.03 (−2.93;7.11) m² 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 (\Delta VO2/\Delta Watt) in this patients.
**Purpose:** The aim of this study was to evaluate the effect of exercise training on: 1) oxygen consumption (VO2peak); 2) VO2peak/HR, Watts; 3) oxygen pulse (VO2peak/HR); and 4) quality of life in patients with EMF.

**Methods:** 19 patients were allocated: sedentary EMF (n=11) and training EMF (n=8). VO2peak, VO2peak/HR, Watts and VO2peak/HR by cardiopulmonary exercise testing, and quality of life by Minnesota Living with Heart Failure Questionnaire were evaluated. Left ventricle ejection fraction (LVEF) and VO2peak were evaluated by echocardiography (Simpson). Exercise training was performed for 4 months, 3 times/wk, 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=7male=1 vs. female=9male=2, p=0.50, 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±3±3.1 vs. 15.5±0.8 to 15.4±0.7 ml/min/kg; p=0.38, respectively). VO2peak/HR increased in Tr-EMF (9.20±0.79 to 10.71±0.84 vs. 8.9±0.73±3.14/heart beats; p=0.04, respectively). Peak heart rate did not change (128±5 to 114±7 vs. 122±5 to 129±5beats; 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). VO2peak/ΔWatts decreased in Tr-EMF (12.47±0.85 to 9.98±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±0.55ml/min/Watts; p=0.04, respectively). VO2peak/ΔWatts improved the oxygen consumption distribution in the exercised muscle (oxygen uptake kinetics) with increased power output. This result suggests improved tissue perfusion and additional information to the VO2peak, suggesting that other variables of cardiopulmonary exercise testing should be evaluated in restrictive cardiomyopathy patients.

**Conclusions:** Exercise training in patients with EMF improved the oxygen consumption distribution in the exercised muscle (oxygen uptake kinetics) with improved VO2peak/ΔWatts and oxygen pulse of exercise in Tr-EMF compared to Sed-EMF. In contrast, a greater proportion of female compared to male athletes competing in dynamic sport exhibited eccentric hypertrophy. Only 4% of females compared to 15% of males demonstrated concentric hypertrophy/remodelling (p=0.002).

**Acknowledgement/Funding:** Female athletes participating in dynamic sport exhibit predominantly eccentric hypertrophy. Our results indicate that although the presence of concentric remodelling or hypertrophy in male athletes engaged in dynamic sport is a common phenotype, it should raise suspicion of underlying cardiomyopathy in female athletes.

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**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 dose-effect relationship over 44 years 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 which 665 (83%) performed maximum exercise. Predicted VO2max was based on measured heart rate and blood pressure, smoking, alcohol intake and serum cholesterol.

**Results:** 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<0.0001) for VO2max, HR 1.01 (1.002–1.02), (p<0.001) 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<0.0001) for smoking. The variable impact (Wald’s c2) of maximum VO2 tertiles (15.3) was second only to that of smoking habits (31.4). The benefit of high VO2max was confirmed throughout 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:** This study was supported by the Swedish Research Council. The Stockholm Heart Laser Study (SHLS) is supported by grants from the Swedish Research Council and The County Council in Stockholm.

**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=55.8±1.6) and 18 healthy aged matched sedentary controls (M=10, F=8). The lowest inci-
cidence 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 3:30–3:30h for females (see diagram). Run-
ing more or less than those mileages and running slower or faster than these marathon times conferred unfavourable CAC. Male athletes who run faster and lon-
ger than those ranges had a 2–3 fold increase in CAC. 70th centile (39% vs 13%, p=0.003 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 ath-
letes. Running at modest duration and intensity is more beneficial than no exer-
cise but higher doses of exercise may accelerate atherosclerosis.

GENETICS ASPECTS OF ARRHYTHMIAS

2887 | BEDSIDE
Role of electrophysiological study for risk stratification of asymptomatic patients with Brugada syndrome: a meta-analysis
S. Stavrakis, R. Lazzara. University of Oklahoma Health Sciences Center, Oklahoma City, United States of America

Introduction: Brugada syndrome (BrS) is an inherited channelopathy associated with an increased risk of sudden cardiac death. An implantable cardioverter defibrillator is recommended for patients with aborted cardiac arrest or syncpe. Howev-
er, controversy still exists regarding the risk stratification scheme for asymp-
tomatic patients with BrS. We reviewed the predictive accuracy of EPS in asymptomatic patients with BrS. We performed a meta-analysis of published trials to ex-
amine the role of electrophysiological study (EPS) for risk stratification of asympto-
matic patients with BrS.

Methods: We searched MEDLINE and EMBASE databases for studies evaluat-
ing 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 fol-
low up of 34 months, 38 (3%) asymptomatic patients had an arrhythmic event. Based on the pooled estimate across the 16 studies, inducibility of ventricular tachyarrhythmia (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 sup-
port a significant role of EPS for risk stratification of asymptomatic patients with BrS.

2898 | BEDSIDE
Worldwide experience with the S-ICD in patients with congenital long QT
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Background: Tiagarcel (Ticag) has a faster onset of antiplatelet activity than clopidogrel (Clo). Early use of more potent antiplatelet therapy would be expected to have benefit, although the use of another potent antiplatelet prior to angiog-
raphy was seen to have no benefit and increased bleeding.

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

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

Results: Median time to DA was 2.7h (0.6–21.5h IQR). 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 significant interactions 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). Conclusion: In pts with NNTSE-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.

Abstract 3030 – Table 1

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Overall event rate for DA &lt;3h</th>
<th>Adjusted HR (95% CI) for ticagrelor vs clopidogrel for DA &lt;3h</th>
<th>Overall event rate for DA ≥3h</th>
<th>Adjusted HR (95% CI) for ticagrelor vs clopidogrel for DA ≥3h</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>Primary outcome (CV death / MI / stroke)</td>
<td>8.0%</td>
<td>0.82 (0.64–1.04)</td>
<td>9.0%</td>
<td>0.83 (0.67–1.03)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>2.6%</td>
<td>0.81 (0.53–2.16)</td>
<td>4.1%</td>
<td>0.83 (0.58–1.18)</td>
<td>0.95</td>
</tr>
<tr>
<td>Cardiovascular CV death</td>
<td>2.1%</td>
<td>0.81 (0.50–1.30)</td>
<td>3.5%</td>
<td>0.89 (0.60–1.30)</td>
<td>0.79</td>
</tr>
<tr>
<td>Safety</td>
<td>Major bleeding at 7 days</td>
<td>5.9%</td>
<td>0.70 (0.60–1.05)</td>
<td>5.6%</td>
<td>1.51 (1.12–2.04)</td>
</tr>
<tr>
<td>Major bleeding at 30 days</td>
<td>8.3%</td>
<td>0.88 (0.70–1.11)</td>
<td>12.4%</td>
<td>1.22 (1.00–1.49)</td>
<td>0.037</td>
</tr>
<tr>
<td>Major bleeding at 360 days</td>
<td>11.4%</td>
<td>0.88 (0.72–1.08)</td>
<td>15.7%</td>
<td>1.33 (1.11–1.58)</td>
<td>0.000</td>
</tr>
</tbody>
</table>
at 7 days. These data suggest that early use of Ticagrelor provides benefit without increased bleeding in pts referred for early DA.

Acknowledgement/Funding: AstraZeneca

3031 | BEDSIDE

Treatment and long-term results of acute coronary syndrome (ACS) in patients on chronic oral anticoagulants (OAC): data from the EPICOR (NCT01171404) study

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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; repertoire therapy is indicated in all pts <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 pCI and 51 (28.2%) UA/NSTEMI patients had pCI. Two-year mortality in the total OAC group was 45/345 (13.0%).

<table>
<thead>
<tr>
<th>Patients on OAC (n=345)</th>
<th>STEMI</th>
<th>UA/NSTEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>74.0</td>
<td>63.8</td>
</tr>
<tr>
<td>Age, years; mean (SD)</td>
<td>70.3 (15.4)</td>
<td>71.4 (10.5)</td>
</tr>
<tr>
<td>Time from symptom onset to first medical contact, h; mean (SD)</td>
<td>3.5 (5.4)</td>
<td>3.3 (3.8)</td>
</tr>
<tr>
<td>Total length of hospital stay, days; mean (SD)</td>
<td>28.0 (64.2)/33.3</td>
<td>87.7 (94.0)/48.0</td>
</tr>
<tr>
<td>Outcomes 2 years post-discharge, %</td>
<td>9.6 (6.8)</td>
<td>8.9 (6.0)</td>
</tr>
<tr>
<td>Composite of death, MI and stroke</td>
<td>23.4</td>
<td>16.8</td>
</tr>
<tr>
<td>Death</td>
<td>15.6</td>
<td>12.3</td>
</tr>
<tr>
<td>MI</td>
<td>5.2</td>
<td>6.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Bleeding leading to hospitalisation</td>
<td>6.5</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Conclusions: Interventions in ACS patients receiving chronic OAC are rarely performed. PCI in patients with STEMI on OAC is delayed. A high incidence of death, MI and stroke was observed at 2 years post-discharge.

3032 | BEDSIDE

Efficacy and Safety of Ticagrelor for Long-Term Secondary Prevention of Atherothrombotic Events in Relation to Renal Function: Insights from the PEGASUS-TIMI 54 trial

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Background: The PEGASUS-TIMI 54 trial showed that ticagrelor (T), reduces cardiovascular death (CVD), myocardial infarction (MI) or stroke in patients (pts) with prior MI (full details at ACC 2015). Pts with reduced renal function (RF) have been shown to be at increased ischemic and bleeding risk, raising the question of the risk-benefit ratio with antithrombotic therapy in these pts. We evaluated the risk of ischemic events and bleeding in PEGASUS-TIMI 54 by RF and whether T profile was modified by RF.

Methods: PEGASUS TIMI-54 randomized 21,162 pts with a history of MI 1–3 years prior to T 90mg BID, T 60mg BID, or placebo. Pts requiring dialysis were excluded. Serum creatinine was available in 20,898 (99%) pts at baseline.

Results: Overall, 4,849 pts had an eGFR < 60 mL/min (MDRD). Pooling all arms there was an inverse relationship between eGFR and risk of CVD, MI or stroke, with pts with severe renal dysfunction having a 5-fold risk compared to pts with normal renal RF (HR 5.14, 95% CI 1.97–12.66, P-trend = 0.0001, Figure 1A). The relative risk reduction in ischemic events with T was similar by category of eGFR (P-int=NS). The relative risk of TIMI Major bleeding was similar across categories of RF (P-trend=−0.4, Figure 1B) however, minor bleeding increased with worsening RF (P-trend=0.007). There was no heterogeneity in bleeding risk with T by RF (P-int=NS). Full details by T dose at ESC.

Conclusions: In pts with a history of MI in the PEGASUS-TIMI 54 trial, worsening RF was associated with an increased risk of ischemic events but with similar TIMI Major bleeding risk. Pts with non-end stage renal dysfunction may enjoy a favorable benefit-risk profile with long-term T treatment, with greater absolute risk reduction for ischemic events, but a similar absolute risk increase for TIMI Major bleeding.

Acknowledgement/Funding: The PEGASUS-TIMI 54 Study was funded through a grant from AstraZeneca

BICUSPID AORTIC VALVE DISEASE – NEW KNOWLEDGE AND OPEN QUESTIONS

3049 | BEDSIDE

Gender differences in the clinical history of adult patients with bicuspid aortic valves

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Background: Bicuspid aortic valve (BAV), the most common congenital heart defect, affects men more than women, but long-term assessment of gender-specific outcomes is lacking.

Purpose: To determine gender-specific outcome differences in BAV adults within a community cohort, and verify gender-patterns of morbidity and mortality in large tertiary-referral groups.

Methods: Retrospective analysis of long-term outcomes in a community-cohort of 416 patients diagnosed with BAV from 1980 to 1999 (age 35±21 years, follow-up 15±7 years), and in a tertiary-referral cohort of 2824 adult patients diagnosed with BAV from 2010 to 2011 (age 51±16 years, follow-up 9±6 years). Cross-sectional analysis of a third group of 2242 adult BAV patients referred for aortic valve replacement from 1995 to 2010 (age 62±14 years).

Results: Community-cohort analysis showed no gender difference in 25-year survival (p = 0.41), however, 20-year risk of BAV-related morbidity was higher in men (52±24% vs 35±6%, p = 0.01), as was the 20-year risk of developing >moderate aortic regurgitation (36±5% vs 14±5%, p = 0.01). Overall incidence of Infectious endocarditis was 13.94 (95% CI 7.25–28.79) per 10,000 patient-years (age-adjusted relative risk 11.39 [95% CI 4.74–27.36] compared to the general population, p = 0.001) with 25-year rate of ≤2% for men versus 0% for women (p = 0.046). Tertiary-referral group analysis showed no gender difference in 20-year survival (p = 0.79), but overall 20-year survival rate was lower than expected compared to the general population (64±2% vs 72%, p = 0.0001), with age-adjusted relative death risk of 1.16 (95% CI 1.05–1.29) for men and 1.67 (95% CI 1.38–2.03) for women, p = 0.001. Independent predictors of mortality were age >50 years and Charlson comorbidity index for both genders (all p < 0.009), and ejection fraction for men only (p = 0.004). Surgical-referral group supported observed morbidity gender-patterns.

Conclusions: The long-term outcome of adults with BAV is not benign as both men and women incur excess mortality. Risk of significant aortic regurgitation and BAV-related complications is higher in men compared to women. Infectious endocarditis incidence is higher in BAV patients compared to the general population, and affects men more frequently. Paradoxically, when compared to the general population, women exhibit higher long-term risk of death than men. These observations warrant due attention from the clinical and research communities.
**3050 | BEDSIDE**

**Bicuspid aortic valve disease – New knowledge and open questions / Detect to repair deficient cardiac genes**

**Objective:** 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. The team applied a targeted screening of 10 exons and the adjoining introns of NOTCH1, previously described in association with LVOT malformations and BAV.

**Results:** In 12 of 34 patients with a combination of COA and BAV observed AR and BAV.

**Conclusion:** Stricly bicuspid aortic valves, especially with left-right cusp orientation, more often have a left dominant coronary artery system and are most 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.

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**3065 | BENCH**

**Proximal titin A-band truncation causes dilated cardiomyopathy in response to increased afterload in mice**

**Objectives:** To determine the influence of titin truncation on cardiac function and identify potential therapeutic targets.

**Methods:** The study investigated the effects of titin truncation on cardiac structure and function in mice with and without stress.

**Results:** Mice with titin truncation exhibited increased afterload and a decrease in cardiac output. The team identified potential therapeutic targets for treating dilated cardiomyopathy.

**Conclusion:** Titin truncation is a significant contributor to dilated cardiomyopathy, and potential therapeutic targets have been identified.

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**3066 | BENCH**

**AAV9-mediated gene transfer of desmin restores cytoskeletal integrity and attenuates development of cardiomyopathy in desmin-deficient mice**

**Objectives:** To investigate the effect of AAV9-mediated gene transfer of desmin on cardiomyocyte function.

**Methods:** The team used AAV9-mediated gene transfer of desmin to assess its effects on cytoskeletal integrity and cardiomyocyte function.

**Results:** Mice with AAV9-mediated gene transfer of desmin exhibited improved cytoskeletal integrity and attenuated cardiomyopathy development.

**Conclusion:** AAV9-mediated gene transfer of desmin is a promising therapeutic approach for treating desmin-deficient cardiomyopathy.

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**I.G. Lunde 1, H. Wakimoto 1, M.A. Burke 1, V. Soukoulis 1, W.A. Linke 2, J. Gorham 1, D. Conner 1, G. Christensen 1, J.G. Seidman 1, C.E. Seidman 1, 1 Harvard Medical School, Department of Genetics, Boston, United States of America; 2 Ruhr University Bochum (RUB), Bochum, Germany; 3 Institute for Experimental Medical Research, Uelleval University Hospital, Oslo, Norway.

**Purpose:** To determine the influence of titin truncation on cardiac function and identify potential therapeutic targets.

**Methods:** The study investigated the effects of titin truncation on cardiac structure and function in mice with and without stress.

**Results:** Mice with titin truncation exhibited increased afterload and a decrease in cardiac output. The team identified potential therapeutic targets for treating dilated cardiomyopathy.

**Conclusion:** Titin truncation is a significant contributor to dilated cardiomyopathy, and potential therapeutic targets have been identified.

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**M.B. Heckmann 1, R. Bauer 1, L. Winter 2, K.H. Strucksberg 2, A. Jungmann 1, R. Schroeder 2, H.A. Katus 1, O.J. Mueller 1, 1 University Hospital of Heidelberg, Cardiology Department, Heidelberg, Germany; 2 University Hospital Erlangen, Institute of Neuropathology, Erlangen, Germany.

**Desmin is a type III intermediate filament, which is mainly expressed in cardiac muscles comprising 2% of the muscle’s total protein mass. Its ability to form a filamentous network is crucial for maintaining the structural integrity of skeletal and heart muscle cells.**

**Aim of this study was to investigate the effect of adenovirus-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 randomy assigned 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. Ventricular function was assessed using transthoracic echocardiography before vector application and every three months following 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 attenuated diastolic dysfunction observed in DKO mice.**
22.2±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 syncollin 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 a feasible method to restore desmin filaments in desmin deficient mice. Reconstitution of syncollin filaments, reduced fibrosis and hypertrophy as well as ameliorated contractile 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

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 89% 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 mutations. One CNV was found 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 aortic disease probands.

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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¹Department of Internal Medicine I, Molecular Cardiology, Wurzburg, Germany; ²University of Wurzburg, Department of Internal Medicine I, Comprehensive Heart Failure Center, Wurzburg, Germany

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 regulates among others, regulates the expression of p27kip1 (p27), a known inhibitor of hypertrophy 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 the truncated Eya4 isoform E193. As judged by MRI, hemodynamic and morphometric analysis both transgenic mouse models developed cardiac phenotypes compared to age-matched wildtype littermates already at basal conditions in an age dependent manner. p27 expression and downstream factors were also altered in both transgenic lines as a result of Eya4, and accordingly, E193 overexpression.

Conclusion: In summary, we provide evidence that the Eya4/Six1 signalling cascade is not only relevant in a rare version of heritable DCM but also in more common forms of acquired heart disease such as Myocardial infarction and/or pressure overload. Eya4/Six1 seem to be important regulator of cardiac physiology in postmitotic cardiomyocytes.

3069 | BENCH
Immunomodulatory microRNAs expressed in the myocardium predict individual antiviral capacity in human enterooviral 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 of heart function and aortic disease.

Methods and results: Transcriptome mapping of CVB3 cardiomyopathy patients revealed cardiac miR patterns associated with differential clinical courses. Profiling of 754 miRs in endomyocardial 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 underexpressed 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 antisense therapeutics drugs aiming at suppression of miRs associated with virus persistence and adverse clinical outcome.

To further assess therapeutic potential we used locked nucleic acid (LNA) antisense oligonucleotide (ASO)-mediated ablation of miRs 135b, 190, 422a and 590 in monocytes and macrophages. Strongest immunomodulating effects were observed upon RNAi mediated macrophage depletion 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 cytotoxicity against FAS 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 sequenced and analysed 64 cardiomyopathy genes in 332 Caucasian DCM patients and in 319 ethnically matched healthy volunteers who underwent cardiac magnetic resonance imaging. Targeted next generation sequencing of DCM genes was performed, and variants were called after mapping the data to the Hg19 human genome reference. Burden testing for rare (minor allele frequency <0.1%), coding variants was performed for each gene, and regression 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, 36 of the 64 genes were enriched for variations in DCM patients. At the gene level, only variants causing a truncation of titin (TTNtv) remained significant after correction for multiple testing (12.7% DCM, 1.9% controls, p=2.5E-6). Rare coding variants in MYH6, previously reported to play an important role in DCM, were not enriched in patients at all by burden testing (1.2% 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 basis 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 TTNtv and variants in MYH7 being the strongest contributors.

**Conclusions:** Our data show that, of all DCM genes and variant classes, TTNtv alone are 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.

**ACKNOWLEDGEMENTS/FUNDING:** 1. National Institute for Health Research & Heart & Stroke NHS Foundation Trust and Imperial College London; 2. EU FP7/2007-2013 Grant Agreement 289600.
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/LMNA neg 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/LMNA neg DCM patients.

Strikingly, an LVEF increase of at least 10% occurred in 50.0% of the TTN sub-

ers but also when compared to TTN/LMNA neg 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/LMNA neg DCM patients.

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

3074 | BEDSIDE

Genetics of noncompaction cardiomyopathy (NCCM)

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Introduction: Noncompaction cardiomyopathy (NCCM) is a genetic cardiomy-
opathy, characterized by hypertrabeculations with deep recesses of the left ventric-

tular wall. We present the results of genetic analysis of a large NCCM cohort.

Methods: All NCCM index patients fulfilling the diagnostic criteria for NCCM diag-
nosis at any of our medical centers were included. Molecular testing was performed using next generation sequencing of a panel of 48 cardiology 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 MIB1 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/Funding: Jaap Schouten Foundation

DIFFERENT ASPECTS IN MANAGEMENT OF ATRIAL FIBRILLATION

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) < 95 mL/min.

Purpose: We evaluated the frequency and characteristics of those with normal and abnormal 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 70 mL/min (25th, 75th; 50, 97), while 26% had an eCrCl > 95 mL/min (Figure). Patients with eCrCl > 95 mL/min were younger (median 64 vs 78 years, p < 0.0001), 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 > 95 mL/min was 3 (25th, 75th; 2, 4), and 94% of these patients had a CHA2DS2-VASc score ≥ 1 and 77% ≥ 2.

Conclusion: Pulmonary vein PTA seems to be a feasible method to treat iatro-
genic PVS, however even in high volume centers with experienced operators the risk of specific complications is the occurrence of restenosis after balloon dilation alone or BMS stent implantation remains high. In the presence of veri-
fied PVS self expanding DES implantation seems to be the most effective method of treatment.
Ancona, Italy; 2 Maastricht University Medical Centre (MUMC), Department of Areas with reduced atrial electrogram amplitude (“low voltage areas”, LVAs) are considered to represent fibrotic remodeling. We assessed the in-reduced atrial function and 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 those with normal LA function (LA strain >18%).

Results: In the whole group, mean percentage of LVAs was 4% ± (min/max: 0/34%) and mean LA strain was 24% ± 6 (min/max: 12/28%). 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% ± 2 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 &gt;18%</th>
<th>p valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=36</td>
<td>63 (10)</td>
<td>62 (8)</td>
<td>70 (16)</td>
</tr>
<tr>
<td>Mean age in years (SD)</td>
<td>63 (10)</td>
<td>62 (8)</td>
<td>70 (16)</td>
</tr>
<tr>
<td>Male (% SD)</td>
<td>19 (53)</td>
<td>17 (55)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>CAD (group %)</td>
<td>6 (17)</td>
<td>4 (13)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Art. HTN (group %)</td>
<td>26 (72)</td>
<td>23 (74)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>LVEF, % (SD)</td>
<td>58 (9)</td>
<td>59 (5)</td>
<td>48 (22)</td>
</tr>
<tr>
<td>LA-diameter mm (SD)</td>
<td>41 (5)</td>
<td>41 (5)</td>
<td>41 (1)</td>
</tr>
<tr>
<td>Baseline LA strain % (SD)</td>
<td>24 (6)</td>
<td>26 (5)</td>
<td>15 (3)</td>
</tr>
<tr>
<td>Low voltage area, % (SD)</td>
<td>4 (8)</td>
<td>2 (5)</td>
<td>15 (7)</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.

P3080 | BEDSIDE
CHA2DS2-VASc score predicts in-hospital mortality beyond GRACE score after acute myocardial infarction

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Background and aims: CHA2DS2-VASc score have recently been suggested to predict death in patients with Atrial Fibrillation (AF). In acute myocardial infarction (AMI), silent AF is more common than symptomatic AF and associated with poor prognosis. In patients with AMI, we aimed to assess the distribution of CHA2DS2-VASc score in patients with silent or symptomatic AF and the association of the score with mortality.

Methods: 849 consecutive AMI were prospectively analyzed by continuous ECG monitoring (CEM) -48 hours after admission. Silent AF was defined as asymptomatic episodes lasting >30 sec. Symptomatic AF was defined as any AF occurring on ECG during the hospital stay, resulting in clinical symptoms or need for urgent cardioversion. The population was studied into three groups: No AF, Silent AF, and symptomatic AF. CHA2DS2-VASc and GRACE risk score were calculated for each patient.

Results: One hundred and thirty five patients (16%) developed silent AF and 45 (5%) had symptomatic AF. Compared with the no AF group, patients with silent AF were markedly older 80 (67–85) vs. 62 (53–75) years; p<0.001, more frequently women (58 (43%) vs. 198 (30%); p=0.006), and less smoker (26 (20%) vs. 242 (36%); with 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).

Table 1

<table>
<thead>
<tr>
<th>Patients developing asymptomatic AF</th>
<th>Patients not developing asymptomatic AF</th>
<th>CHA2DS2-VASc</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality</td>
<td>19 (1.2%)</td>
<td>26 (2.9%)</td>
<td>2.41</td>
<td>1.32–4.39</td>
</tr>
<tr>
<td>CV mortality</td>
<td>10 (0.6%)</td>
<td>20 (2.2%)</td>
<td>3.52</td>
<td>1.64–7.57</td>
</tr>
<tr>
<td>CV hospitalization</td>
<td>483 (31.7%)</td>
<td>517 (37.7%)</td>
<td>3.08</td>
<td>2.55–3.73</td>
</tr>
<tr>
<td>Stroke</td>
<td>18 (1.1%)</td>
<td>26 (2.9%)</td>
<td>2.55</td>
<td>1.39–4.68</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>29 (1.9%)</td>
<td>54 (4.0%)</td>
<td>3.37</td>
<td>2.13–5.64</td>
</tr>
<tr>
<td>HF reactivation</td>
<td>141 (9.1%)</td>
<td>212 (23.7%)</td>
<td>3.11</td>
<td>2.46–3.92</td>
</tr>
</tbody>
</table>

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.
EXPERIMENTAL AND CLINICAL RESEARCH IN MYOCARDIAL ISCHAEMIA

P3082 | BENCH
Pharmacological evaluation of novel adenine-hydrogen sulfide slow release hybrids designed as multi-target cardioprotective agents

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Adenosine receptors have a major role in triggering the intracellular signal transduction pathways involved in the prevention of reperfusion (reper) injury. Exogenous administration of hydrogen sulfide (H2S) triggers cardioprotection in animal models of ischemia/reperfusion. However, the exposure of biological systems to inorganic H2S “donors”, such as NaHS, causes a burst of H2S release that does not recapitulate the low level of continuous production of H2S that occurs in vivo.

Purpose: We aimed to evaluate the cardioprotective effect of novel hybrid compounds that simultaneously contain two pharmacophore groups, an adenine and a H2S releasing moiety.

Methods: The slow releasing sulfur containing agent 4-hydroxythiobenzamide (4-OH-TBZ) was coupled either with 9-(4-hydroxybutyl) adenine providing the product S1, or with adenosine providing the product S6. The capability of the new hybrid compounds was assessed in vitro. Anesthetized rabbits 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. S1, treated with the compound S1 at a dose of 1.79 μmol·kg⁻¹·h⁻¹ for the 20th min of isc; 4. S6, treated with the compound S6 at the same mode as S1; 5. S1+SPT, treated as S1 with the addition of the adenosine receptor blocker SPT; 6. S6+SPT treated as S6 with the addition of SPT; 7. 9-(4-hydroxybutyl) adenine at a dose of 1.79 μmol·kg⁻¹·h⁻¹ for the next 120 min. Doses of S1 and S6 were estimated at 20-fold lower dose compared to NaHS. The infarcted (i) to risk (R) areas were estimated as % I/R. The circulating plasma levels of thiocysteine were assessed by the above validated UPLC-UV methodology using a derivatization reaction with the CMQT reagent.

Results: The S1 and S6 compounds reduced the infarct size (17.4±0.7% vs 48.05±2.0% in Control, p<0.05), 1%) and PostC (24.3±0.5%). SPT did not abrogate the benefit of S1 (16.9±1.8%). The S1 and S6 compounds showed a significant reduction of myocardial ROS by DHE fluorescence. Co-administration of L-NAME or Wor along with NTG eliminated the effect of NTG on %I/R (37.9±2.0%, and 38.3±2.6% respectively vs 23.0±3.2%, p<0.05). Inhibition of adenosine and PKG did not affect the protection afforded by S1 or S6, nor did NOS inhibition or Akt inhibition. In conclusion, the novel adenine-H2S hybrid compounds may provide a new strategy for cardioprotection by modulating the intracellular signals involved in the regulation of myocardial ischemia-reperfusion injury.

P3083 | BENCH
Tenascin-C regulates inflammatory response and aggravate ventricular remodeling after myocardial infarction in mice model

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Tenascin-C (TN-C), an extracellular matrix glycoprotein, transiently appeared in myocardial tissue after acute myocardial infarction (AMI). We have previously reported that AMI patients with higher serum TN-C levels had worse long-term prognosis, suggesting TN-C may play important roles during the development of ventricular remodeling. However, the biological function of TN-C in ventricular remodeling is not fully understood. In this study, using TN-C knock-out (KO) mice, 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.

The 8 to 10 weeks old male wild type (WT) and TN-C knock-out (KO) mice were assigned into groups of WT + Sham, KO- Sham, WT + MI and KO + MI. 12 weeks after MI, TN-C KO - MI group had the better cardiac function than WT + MI had (LVEF, 19.02±6.31% vs 10.63±4.43%; p<0.001, LV diastolic diameter 5.45±0.57 mm vs 5.93±0.47 mm). Interstitial fibrosis at border area was significantly increased in TN-C KO - MI group compared to WT - MI. However, the extent of fibrosis in the remote area revealed no significant difference between the two groups. By RT-PCR analysis, WT + MI 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+, Ly6c 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 + MI group. 7 days after MI, RT-PCR analysis showed that the expression of IL (interleukin)-10 in (Mannose receptor, C type) was significantly higher in KO + MI than WT + MI. These findings suggest, TN-C aggravates the deterioration of LV function due to MI partly by regulating inflammation at acute phase.
Transferrase (GET) to incident acute coronary events to which Tissue Factor (TF), the principal initiator of the coagulation process, is known to contribute actively. GGT and TF are also co-expressed by plaques harvested from atherosclerotic patients, thus making it conceivable a direct role of the former on TF expression and activation. The aim of our study was to assess the direct effect of GGT on TF antigen (α), TF mRNA and TF pro-coagulant activity (PCA) in human peripheral blood mononuclear cells. All experiments we run using an enzymatically inactive human recombinant (hr) GGT to exclude confounding from its enzymatic activity. Methods: Human peripheral blood mononuclear cells were obtained from healthy donors through a discontinuous Ficoll/Hypaque density gradient and incubated with hrGGT (0.5ng/ul) either alone or with anti-hrGGT, a specific polyclonal antibody (2.5ug/ml), BAY-11-7082 (10−5M) a selective NF-κB inhibitor, and N-acetylcysteine (10−3M) an antioxidant. TF expression was assessed by ELISA, TF mRNA by real-time PCR and PCA by a 1-stage clotting assay.

Results: hrGGT increased TF expression (from 85.5±9 to 536±317 pg/mL, n=13, p<0.001) and stimulated PCA (from 0.08±0.07 to 0.37±0.3 arbitrary units, n=14, p<0.001) and TF mRNA (from 0.006±0.02 to 0.048±0.04 arbitrary units, n=13, p<0.001). hrGGT-induced TF and PCA was inhibited by anti-hrGGT antibodies (PCA: from 0.70±0.56 to 0.27±0.34 arbitrary units, n=8, p<0.01, −64%; TF: from 489±393 to 193±65pg/mL, n=6, p=0.01) as well as by pre-treatment with BAY-11-7082 (PCA: from 0.21±0.17 to 0.08±0.11 arbitrary units, n=7, p<0.01, −70%; TF: from 410±255 to 146±94 μg/mL, n=7, p<0.01) and N-acetylcysteine (0.38±0.07 to 0.00±0.13 arbitrary units, n=7, p<0.01).

Conclusions: These data represent the first demonstration of a direct effect of GGT on TF expression independent of its own enzymatic activity, a behavior consistent with a cytokine-like mechanism acting through NF-κB stimulation. This mechanism might contribute to promote acute thrombotic events, a possibility in need, however, of further evaluation.

P3088 | BENCH
Andexanet alfa reverses edoxaban-induced anticoagulation in a rabbit liver laceration model of acute bleeding

Background: Edoxaban (edox) is an oral, direct FXa inhibitor recently approved in the US to reduce the risk of stroke in patients with nonvalvular AF. A serious risk with FXa inhibitors is bleeding, and a specific reversal agent is not available. Andexanet alfa (AnXa) is a modified recombinant FXa derivative that forms a 1:1 stoichiometry. Published preclinical studies demonstrated that AnXa effectively reversed rivaroxaban anticoagulation in a rabbit liver laceration model, restored anti-FXa activity, reduced the plasma free fraction of rivaroxaban, and corrected PT and aPTT to pre-anticoagulation levels.

Purpose: Study objective was to evaluate the ability of AnXa to reverse edox anticoagulation in a rabbit liver laceration bleeding model, as assessed by coagulation markers and blood loss (BL).

Methods: Edox treatment increased BL from 9.3±3.0g in vehicle controls (N=10) to 22.±18.9g in rabbits anticoagulated with edox (N=12, p<0.01), while administration of AnXa in edox-treated rabbits decreased BL to 13.8±3.7g (N=10, p<0.05). Mean unbound edox plasma concentration at the beginning of AnXa infusion was 99±5.6 mg/mL, and was reduced 5-fold by the end of the AnXa infusion to 20.9±5.4 mg/mL. Total mean plasma concentration of edox increased 10-fold (from ~350 ng/mL to ~3700 ng/mL, from start of to end of infusion), demonstrating that edox was redistributed rapidly from the extra- to the intra-vascular compartment. Similarly, anti-FXa activity was reduced (446±54.3 vs 99.5±40.9, p<0.001 (N=10), edox alone vs edox + AnXa), as were PT and aPTT (by 66% and 18%, respectively), vs. animals treated with edox alone.

Conclusion: In active visceral bleeding due to edoxaban anticoagulation, AnXa significantly reduced BL, which correlated with a reduction in anti-FXa activity, plasma free fraction of rivaroxaban, and corrected PT and aPTT to pre-anticoagulation levels.

P3087 | BENCH
Gamma-Glutamyltransferase Stimulates Tissue Factor Expression Independent of Its Enzymatic Activity in Human Mononuclear Cells
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Background: A highly consistent association links circulating Gamma-Glutamyl-
P0389 | BEDSIDE
Impact of sleep apnea on severe microvascular dysfunction assessed by cardiovascular magnetic resonance after primary angioplasty in patients with acute myocardial infarction


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 intimal 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 one week after primary PCI. Sleep apnea was classified into 4 categories based on an apnea-hypopnea index (AHI): no (AHI <5), mild (AHI <15), moderate (15 <AHI <30), and severe sleep apnea (AHI ≥30). An AHI of ≥15 was considered diagnostic of OSA. We assessed the association between severe sleep apnea and microvascular dysfunction determined by CMR.

Results: There were 96 (54.1%), 49 (44.1%), 33 (29.7%), and 23 patients (20.7%) with 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=0.0222) and hemorrhagic infarction (OR, 3.84; 95% CI, 1.50–10.7, p<0.0045) compared with OSA.

Conclusion: Undiagnosed OSA was associated with severe microvascular dysfunction after primary PCI in patients with STEMI.
Cardiovascular magnetic resonance – Ischaemic heart disease / New advances in cardiovascular genetics and gene therapy

P3093 | BEDSIDE
Subendocardial stress perfusion defects on cardiovascular magnetic resonance in patients with angina and unobstructed coronaries are frequently related to functional coronary vasomotor abnormalities
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Background: Patients with angina pectoris and unobstructed coronary arteries represent a cure with a new therapeutic challenge. Defects on stress-perfusion cardiovascular magnetic resonance (CMR) may be attributed to functional coronary vasomotor abnormalities (i.e. microvascular dysfunction and/or epicardial spasm). However, this has not been assessed systemically in a large patient cohort.

Methods: Between 2012 and 2014 we consecutively recruited 125 patients (mean age 64±16 years, 64 (51%) male) with angina pectoris who underwent an adenosine-stress perfusion-CMR study (including cine 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 complete coronary spasm (100% spasm) in 29 (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 myocardial infarction (57%) compared to patients with a myocardial perfusion abnormality. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treatment.

P3094 | BEDSIDE
Left ventricular thrombus formation in patients with acute reperfused ST-elevation myocardial infarction: insights from cardiovascular magnetic resonance imaging
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Background: On the exact incidence and predictors of left ventricular (LV) thrombus formation after primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) are scarce. Moreover, data on the prognostic significance of LV thrombus on hard clinical outcome measures are completely lacking.

Non-invasive investigation by gadolinium-enhanced cardiac magnetic resonance (CMR) may be attributed to functional coronary vasomotor abnormalities. Defects on stress-perfusion CMR imaging (CMR) enables the detection of LV thrombi with high spatial resolution and superior diagnostic accuracy as compared to echocardiography. Aim of our study was 1) To assess the incidence, determinants and clinical characteristics of LV thrombi in a large multicenter cohort of high-risk STEMI patients, 2) to assess the prognostic significance of LV thrombi at one-year follow-up.

Methods: We enrolled 746 STEMI patients reperfused by primary angioplasty (≤12 h after symptom onset) in this CMR study at 8 centers. CMR was completed within one week after infarction using a standardized protocol. Central core lab masked analyses for the presence of LV thrombi were performed. The primary clinical endpoint of the study was the occurrence of major adverse cardiac events (MACE) defined as death, reinfarction, readmission for congestive heart failure and stroke at one year follow-up.

Results: LV thrombi were detected in 33 patients (4.4%). The presence of LV thrombi was associated with larger infarcts (p<0.001), less myocardial salvage (p<0.001), lower ejection fraction (p<0.001) and more pronounced reperfusion injury (late microvascular obstruction p<0.004, intramyocardial hemorrhage p=0.02). In multivariable regression analysis infarct size, anterior infarction, age and pain-to-balloon time emerged as significant predictors of LV thrombi. The presence of LV thrombi was not associated with MACE.

Conclusions: In this large multicenter cohort of patients with STEMI, thrombus prevalence was 4.1% by CMR. The presence of LV thrombi is associated with decreased myocardial salvage, larger infarcts, and more pronounced reperfusion injury. However, presence of LV thrombi was no independent predictor of prognosis at one year follow-up.

P3095 | BEDSIDE
Long term effect of pulmonary endarterectomy on right ventricular loading conditions in patients with chronic thromboembolic hypertension by cardiac MRI
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Purpose: To study the natural history of RV adaptation to varying loading conditions in patients with chronic thromboembolic hypertension (CTEPH) from before pulmonary endarterectomy (PEA) to one year follow up.

Background: Nearly 4% of patients with pulmonary embolism develop CTEPH. Between 2012 and 2014 we consecutively recruited 125 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 (EDVI) and end-systolic (ESVI), and stroke (SV) volumes were indexed for body surface area. Ed-pulm_i was calculated as pulmonary artery mean pressure (mPAP_i) / SV and Es-RV_i as mPAP_i / SV.

Results: mPAP decreased from 47±12 to 25±9 mmHg, p=0.001 and PVR decreased from 646±286 to 334±265 dynes*s*5. Ed-pulm_i was increased before PEA and normalized afterwards (2.5±2.2 vs. 0.85±0.4 mmHg/ml/m2, p<0.0001). Es-RV_i was depressed before and after PEA (0.72±0.7 vs. 0.66±0.3 mmHg/ml/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). EDVI and ESVI improved significantly (EDVI 92±32 to 72±23 ml, p=0.0001; ESVI 59±31 to 42±14 ml, p=0.0001; EF 25±12 vs. 37±9%, p<0.0001).

Conclusion: RV function is largely determined by 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
PRKG1 mutations and thoracic aortic disease: another candidate gene under genetic diagnosis 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 syndromes. When they appear isolated the patients are considered affected by non-syndromic aortic disease, a monogenic condition inherited as an autosomal dominant disorder with low penetrance and variable expression. Mutations in ACTA2, TGFBR1 and 2, TGFBR2, SMAD3, MYLK, MYH11 and FBNU genes 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 members.

Methods: Customized targeted-genotyping of aortic disease candidate genes in the proband through 5500 SOLiD System followed by whole-exome sequencing of 4 affected (including the proband) and 2 unaffected family members using HiSeq 2000/2500 sequencing technology. All variants were filtered by location, functional prediction (PMID 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-genotyping assay, the analysis and filtering of whole-exome sequence data, assuming an autosomal dominant inheritance model, brought out the c.575G>A: p.Arg192Gln PRKG1 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 affected and absent in the 2 unaffected family members. No other mutation was found in the remaining aortic disease candidate genes.

Conclusions: This new independent PRKG1-thoracic aortic disease familial case

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Introduction: HLA-DRB1*01 allele of the human leukocyte antigen (HLA) class II major histocompatibility complex (MHC) single nucleotide polymorphisms (SNP) to identify genetic risk loci for acute coronary syndrome with effective clinical implications.

Methods: New pro-angiogenic factors like Thymosin ß4 might be suitable for inducing therapeutic neovascularization.

Diabetes mellitus is one of the major risk factors for developing cardiovascular disease; especially in combination with chronic myocardial ischemia it represents one of the most common causes of disability or death. This might be a reason, why pro-angiogenic factors failed to show clearcut improvement in clinical trials. New pro-angiogenic factors like Thymosin ß4 might be suitable for inducing therapeutic neovascularization in chronic myocardial ischemia a cardiovascular risk factors.

Methods: In wildtype and transgenic pigs displaying diabetes mellitus type I (a C4H4 mutation), vascularization and myocaridal function were analyzed. In a second set of experiments, chronic myocardial ischemia was induced with or without diabetic transgenic pigs via reduction stent graft in the circumflex artery. Retrievalsin of rAAV Tß4 (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 (SES) 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±4 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±5 chpf) and collaterals (9:1±3 vs. 2:1 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% of 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: Thymosin ß4 transduction induces therapeutic neovascularization and thereby improves the myocardial function in the presence of type I diabetes mellitus. Therefore, rAAV.Tß4 appears suitable for treatment of ischemic cardiomyopathy associated with this cardiovascular risk factor.

P3098 | BEDSIDE Major histocompatibility complex risk haplotype predisposes to acute coronary syndrome


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Introduction: HLA-DRB1*01 allele of the human leukocyte antigen (HLA) class II gene on chromosome 6p21.3 has been associated with coronary artery disease (cMRI) have resulted in considerably increased detection rates, enabling a col-

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.
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 genetic testing varies between 20% and 75% in different diseases. These numbers are mainly derived from studies evaluating only the most frequently affected genotypes. 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 retesting was worthwhile in previously negative patients – 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 captured regions of 75 genes validated in PAS and CMP was performed. Variant interpretation and classification was done according a stringent scoring system implementing different in-silico analyses, population frequencies and paralogous and orthologous conservation. Sanger sequencing was performed to confirm the presence of class 3 variant of unknown significance, 4 (probably pathogenic) and 5 (pathogenic) variants. Co-segregation was done when DNA and clinical data of family members was available.

Results: 96 patients were included: 25 with LQTS, 6 with BrS, 4 with CPVT, 1 with SSCS 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 reclassification in 1, heterozygous calling with sequencing failed in 1 and a wrong initial diagnosis in 1.

Conclusion: Genetic retesting in robust PAS and CMP cases, who were genotyped negative with older scanning techniques, resulted in a genetic diagnosis 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 kits. The performance of iteratively improved sequence captures (ICCv1, ICCv2 and ICCv3) and a non-custom WES panel (Nextera Rapid Capture Exome 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 call failure was achieved at 4.5–5M reads/sample. The callability of ICC gene was improved in the ICCv2 panel by reducing the targeted region from 1.47Mb in ICCv1 (comprising exons and UTR) to 0.58Mb in ICCv2 (exons only). Difficult to capture exons are targeted with added sequence captures (ICCv3) that achieved 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 ICCv1-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 ICC genes at low cost, while WES does not yet adequately capture ICC genes for clinical application.

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 (RSIE) occurred in the context of intravenous drugs use. However, due to the widespread indications for device implants in the last decade and the ageing of the population, RSIE 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 devices carriers (9.5%). Of them, 13 were excluded from the analysis due to concomitant involvement of left valves. Therefore, our final study population is 100 patients with isolated right-sided IE (8.5%). An analysis of 65 variables has been performed.

Results: Mean age (±SD) was 67±14 years, 75% were males and 35% health-care related. Local infection (23%) 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. Systemic signs of infection, such as fever (81%) and shivering (54%), were the predominating symptoms 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 6.16 [95% CI, 1.256–30.285]), 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, 3.033–125.704]) 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 enterococci 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
viridians group streptococci, and Group III (n=113), those episodes due to enterococci.

### Results:

The incidence of enterococci IE have significantly increased in the last two decades (6.4% [1996–2004] vs 11.1% [2005–2013]; p=0.005), while the incidence of IE due to S. bovis and viridians 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 Group I and Group III. Chronic renal failure was more prevalent in patients from Group III (4.3% vs 1.5% vs 19%; p<0.001). Prosthetic valve IE was more frequent in enterococcal IE. Infection upon native normal valves 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 enterococcal episodes (Table).

<table>
<thead>
<tr>
<th>Group</th>
<th>S. bovis</th>
<th>Viridans g. streptococci</th>
<th>Enterococci</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital evolution</td>
<td>Group I</td>
<td>Group II</td>
<td>Group III</td>
</tr>
<tr>
<td>CNS embolisms</td>
<td>5 (10.6%)</td>
<td>18 (13.5%)</td>
<td>12 (10.6%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>26 (55.6%)</td>
<td>63 (47.0%)</td>
<td>82 (73.2%)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>18 (38.3%)</td>
<td>39 (29.3%)</td>
<td>60 (53.1%)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>5 (10.9%)</td>
<td>7 (5.3%)</td>
<td>9 (7.9%)</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>
</tr>
</tbody>
</table>

### Conclusions:

S. bovis IE is associated with a high prevalence of colonic tumours, and affects 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 viridians group streptococci. Thus, S. bovis should not be considered a virulent microorganism.

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**P3105 | BEDSIDE**

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

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

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

**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 after 24 hours. These results were compared with a control group, including SAIE treated with standard therapy from 2002 to 2013. The primary endpoint was 30-day mortality.

**Results:** Among 245 definite SAIE, 75 received C+C, 170 standard therapy. C+C treatment showed better results compared with standard therapy (mortality 5 vs. 14% [p=0.04]). C+C was more effective than the vancomycin and gentamicin protocol (p=0.007). Furthermore, 7 additional days of rifampicin and gentamicin resulted in a dramatical reduction of early mortality compared with control group (0 vs. 14% [p=0.02]). The rate of acute renal failure was similar between the two groups (36 vs. 44%, p=0.3). The hospital stay was shorter in the C+C than in the control group (31 [14–32] vs 22 [19–43] days; p=0.007).

**Conclusions:** This new antibiotic protocol, using the association of high doses of cotrimoxazole and clindamycin, appears useful in the treatment of SAIE. A care-ful 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.

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**P3106 | BEDSIDE**

**External validation of a risk score for symptomatic embolisms in infective endocarditis**

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**Aim:** Embolic events are an important cause of morbidity and mortality in infective endocarditis (IE). Recently, an embolic risk calculator (Embolic Risk French Calculator) has been developed. Our aim was to perform an external validation of the Embolic Risk French Calculator in our multicentre cohort of patients with IE.

**Methods:** From 1996 to 2013, 1076 episodes of IE were prospectively recruited at three tertiary referral centres. Episodes that involved only a pacemaker or defibrillator lead, and those without previous information regarding history of atrial fibrillation were excluded. Finally, 759 episodes were included in the analysis. The Embolic Risk French Calculator (age, diabetes mellitus, previous embolism before initiation of antibiotics, history of atrial fibrillation, S. aureus infection, vegetation length) was then applied to our cohort to predict the risk of new symptomatic embolic event after admission.

**Results:** Mean age of our cohort (n=759) was 62 (15) years, and 64% were men. The incidence of new symptomatic embolisms after initiation of antibiotic therapy was 10.1% (n=77). No significant differences were found in the prevalence of diabetes mellitus (15.8% vs 21.0%, p=0.219) or previous history of atrial fibrillation (26.5% vs 28.7%; p=0.723) between patients with and without new embolic events during hospitalization. Mean age (62 [15] vs 61.5 [16]; p=0.702) in patients with and without new embolic episodes was similar between the two groups. Conversely, vegetation size (0 vs. 10 mm; p=0.050) was significantly associated with the rate of new symptomatic embolic events (6% of incidence if absence of vegetation, 20% if vegetation size <10 mm, 74% if vegetation >10 mm; p<0.001). S. aureus infection was also more frequent in patients with new embolic episodes (36.4% vs 17.2%; p=0.050). In-hospital mortality was higher in patients with new embolic events (41.5% vs 29%; p=0.10). No differences were found in the need for cardiac surgery between those with and without new embolisms (55.2% vs 55.8%; p=0.921).

**Embolic Risk French Calculator including the mentioned variables was finally applied to our cohort. The accuracy of this prediction model was moderate, with an area under the ROC curve of 0.63 (95% confidence interval: 0.58 to 0.69).

**Conclusions:** Assessment of embolic risk is decisive in the management of patients with IE. Patients with symptomatic embolisms have a worse prognosis, with higher in-hospital mortality. In our population, the Embolic Risk French Calculator was useful; nevertheless a more accurate tool would be desirable.
Nosocomial infective endocarditis (NIE) is a serious, potentially preventable complication of nosocomial bacteremia that is associated with high mortality rates. 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 cessation on cardiovascular prognosis: myths and reality**

### P3100 | BEDSIDE

Time course changes of atherosclerotic LDL complexes after smoking cessation.

S. Shimada1, M. Komiyama1, H. Wada1, S. Ura1, S. Terasshima1, H. Yamanakage1, M. Akao, A. Shimatsu2, Y. Takahashi3, K. Hasegawa3,1 Kyoto Medical Center, Kyoto, Japan; 2Nara Women’s University, Nara, Japan

**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 alpha1-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 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 (AT-LDL from 2.1 μg/ml to 1.9 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, significantly decreased at 3 months 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 associated with 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 a 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 5702 participants (male 49.7%, 55.1±11.5 years old) were analyzed. MetS was diagnosed according to Japanese...
P3112 | SPOTLIGHT
Exposure to cigarette smoke and the morphology of atherosclerotic plaques in the extracranial arteries assessed by computed tomography angiography in patients with essential hypertension
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1 4th Military Hospital, Warsaw, Poland; 2 Wroclaw Medical University, Wroclaw, Poland

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. This study was designed to fill an existing research gap, which 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 on the 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, in 4.13±1.51 segments 3-4 plaque calcifications, and mixed plaques in 4.56±2.14 segments. The number of segments with the plaques was significantly higher in group A compared to groups B and C (A: 8.88±1.76; B: 7.28±1.41; C: 7.23±1.37, pA-B < 0.01, 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±2.06, B: 5.22±2.02, C: 3.38±1.72, pA-C < 0.001, pB-C < 0.01). 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 | BEDSIDE
Prognostic influence of smoking in patients with an acute myocardial infarction: paradox or confusion? A propensity-score matched analysis

Introduction: Smokers have been shown to have lower mortality after acute myocardial infarction (AMI) than non-smokers. This has been attributed to the younger age, more aggressive treatment and lower risk profile of the smoker. Some studies, however, have used multivariate analyses to show a residual survival benefit for smokers; that is, the “smoker’s paradox.” The aim of our study was, therefore, to perform a propensity score matching to avoid interaction of baseline differences between smokers and non-smoker in order to analyze the real impact of smoking in AMI patients.

Methods: We conducted a retrospective cohort study with 4,420 patients with the primary diagnosis of AMI between 2004 and 2011. We performed a propensity-matched analysis to draw up two groups of 877 patients paired according to their smoking status. Differences between smokers and non-smokers in terms of morality after admission were analyzed using Cox regression, showing Kaplan Meier curves.

Results: Between the 4,420 patients of the prematched cohort, smokers (n=1,128 [25.5%]) were younger, with lower rate of hypertension, dyslipemia, diabetes, and chronic kidney disease, lower GRACE risk score; more ST-elevation AMI but a lower rate of Killip class ≥ II than non-smokers. Smokers underwent more percutaneous coronary intervention, and received a higher rate of optimal drug therapy. During follow-up (4.0±2.9 years), 1,307 patients (29.6%) died. Smokers had lower mortality rate (12.3% vs 31.1%; p<0.001).

In the matched cohort (n=877), we found no difference between smokers and non-smokers (16.1% vs 16.5%; p=0.796) [hazard ratio=1.00; 95% CI: 0.79–1.27; p=0.970].

Conclusions: Our findings indicate that there is no association between smoking habit and lower rate of all-cause mortality in AMI patients.
Impact of smoking cessation on cardiovascular prognosis: myths and reality / Management of procedural risks

P3116 | 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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1 Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece; 2 University of Marburg and Giessen, Cardiology and Cardiac Arrest Unit, Marburg, Germany

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 life style 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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Results: Transradial access (TRA) for PCI has become more common in an effort to minimize procedural related complications such as bleeding. Despite this, significant variation remains in arterial access site used for PCI depending on operator characteristics 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<0.001) during 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<0.001). 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 ischemic preconditioning study (EURO-CRIPS): a randomized controlled trial
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Aims: The potential protective effect of remote ischemic preconditioning (RIPC) on renal function after prolonged 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 analysis.

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 URL; 8.4% vs 16.4%, p=0.07; troponin T more than 5 URL; 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, F. Marino1, H. Suryapranata2, G. De Luca1 on behalf of Novara Atherosclerosis Study Group (NAS), 1Maggiore Della Carita Hospital, Department of Cardiology, Novara, Italy; 2University Hospital Nijmegen, 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 2388 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 diabetes mellitus. Procedural success was low and hospital mortality was very high. Patients at a priori high risk were more likely to be affected by this complication. Hospital mortality rate was very high.

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.

P3120 | 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, F. Marino1, H. Suryapranata2, G. De Luca1 on behalf of Novara Atherosclerosis Study Group (NAS), 1Maggiore Della Carita Hospital, Department of Cardiology, Novara, Italy; 2University Hospital Nijmegen, 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 2388 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 diabetes mellitus. Procedural success was low and hospital mortality was very high. Patients at a priori high risk were more likely to be affected by this complication. Hospital mortality rate was very high.

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.

P3121 | BEDSIDE
Complications of percutaneous thrombin injection in patients with post-catheterization femoral pseudoaneurysm
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Background: Ultrasound-guided percutaneous thrombin injection (UGTI) is safe and feasible method in the management of iatrogenic femoral post-catheterization pseudoaneurysm (pSA). However, UGTTI complications have not been reported.

Purpose: To assess iatrogenic thrombin effects during UGTI.

Methods: A total of 347 patients with pSA underwent UGTI and prospective screening for complications.

Results: Arterial microembolization occurred in 53 patients (15.3%) and pulmonary embolism in 1 patient (0.29%). The risk of embolization was related to the length of channel between pSA and artery with OR 1.16, 95% CI (1.09–1.125, p<0.0001) per 1 mm, similar to the need for repeat procedure (p<0.02). The channel length of 2 mm was the borderline value for odds of having complications (sensitivity 0.6724, AUC=0.72905). Thrombin dose, pSA morphology, and the interval between cannulation and UGTI did not influence the complication rate.

Conclusions: Thrombin dose, pSA morphology, and the interval between cannulation and UGTI did not influence the complication rate.

P3122 | 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 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. Patients at a-priori high risk were more likely to be affected by this complication. Hospital mortality rate was very high.

Conclusions: During UGTI performed for the treatment of pSA the longer the channel the smaller the chances for developing complications. A repeat procedure increases the risk of complications.

P3123 | BEDSIDE
Radiation dose reduction in the cardiac catheterization laboratory utilising a novel protocol
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Introduction: The cardiac catheterization laboratory is an important source of
P3123 | BEDSIDE
On- and off-label use of vascular closure device in Japan


Introduction: To analyze the results of a novel radiation reduction protocol (RRP) implementation consisted in reducing the number of ventriculographies and angiographies for cases with a clean evidence, 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).

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 clean evidence, 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 PCI performed during the 2 periods (56.7% 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).

Conclusions: With the implementation of a RRP, a highly significant 56.7% reduction (PCI). However, limited data is available for Asian patients, who are known to have less evidence for lower radiation. A reduction in radiation doses as low as possible, maintaining the quality of procedures. A RRP should be strongly considered among interventional cardiology practice.

P3124 | BEDSIDE
Differences in prognosis between heart failure with preserved and depressed ejection fraction can be partially explained by differences in renin-angiotensin-aldosterone system (RAAS)


Introduction: Baseline characteristics of heart failure with preserved (HFpEF) and reduced (HFrEF) ejection fraction are different, and prognosis of HFrEF seems to be better than that of HFpEF. Differences in renal function activation and vasodilatory mechanisms (i.e., RAAS activation) are involved in this difference. Recently, a novel renal activation strategy between HFrEF and HFpEF has been described. The aim of this study was to analyze whether renin-angiotensin-aldosterone system (RAAS) activation is different between HFrEF and HFpEF and its relationship with prognosis.

Methods: Post-hoc analysis of a cohort of 1018 chronic ambulatory heart failure patients from a single-center study evaluating RAAS activation by measuring baseline plasma levels of aldosterone (ALD, pg/mL, n=978), plasma renin activity (PRA, ng/mL/h, n=982), plasma angiotensin-converting enzyme activity (PACE, pg/mL, n=993) and NTproBNP (NTproBNP, pg/mL, n=1018). Data are given in median (interquartile range). HFrEF was defined as left ventricular ejection fraction (LVEF) <45%. Multivariate analysis using a General Linear Model (GLM) adjusted for covariates was constructed to analyze de relationship between RAAS markers and HFrEF. Cox regression was constructed to analyze the relationship of HFrEF and cardiovascular (CV) mortality.

Results: Mean LVEF was 60% in HFrEF and 31% in HFpEF. Patients with HFpEF (n=496) were older, more frequently female and hypertensive, with less coronary artery disease as a cause of HF, and higher prevalence of chronic kidney disease, anemia and atrial fibrillation. Functional class was similar (NYHA III-IV in 43% of the cohort). HFrPH patients received less frequently treatment with beta blockers, ACEI/ARB and mineralocorticoid antagonists. Use of diuretics was similar.

There was a negative correlation of NT-proBNP, ALD, PRA and LVEF (p<0.006). NT-proBNP was significantly lower in HFrEF (1277 [474–2873] vs. 1998 [749–4687]), p<0.001 as were ALD and PRA (92 [44–156] vs 104 [58–186], p=0.004 and 2.7 [0.9–8.3] vs 3.5 [1.1–10], p=0.043, respectively). No differences in PACE were seen between HFrEF and HFpEF. In GLM adjusted for covariates, PRA (p=0.021) and NT-proBNP (p=0.001) were significantly lower in HFrEF compared to HFpEF.

During a median follow-up of 12 (6–18) months, CV mortality was higher in HFrEF (11% vs 7%, p=0.021). In multivariate Cox analysis adjusting for demographic and comorbid conditions, cardiovascular death was higher in HFrEF (HR 1.62; 95% CI 1.03–2.53, p=0.036). However, this difference was lost when markers of RAAS activation were taken into account (HR 1.47; 95% CI 0.91–2.35, p=0.11).

Conclusions: RAAS activation is lower in HFrEF, partially explaining the differences in prognosis compared to HFpEF.

P3125 | BEDSIDE
Predictors of development of diastolic dysfunction in the middle-aged subjects: a prospective follow-up study


Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland.

Introduction: Factors in the middle-age associated with the risk for development of diastolic dysfunction in long-term are not fully established.

Methods: The OPERA (Oulu Project Elucidating Risk of Atherosclerosis) study randomly selected middle-aged hypertensive subjects and age- and sex-matched control subjects (n=1,045, age 51±6 years, males 49.8%). ARMS exclusions 1,004 subjects underwent thorough clinical examinations including a standardized blood pressure assessment, laboratory tests, an evaluation of autonomic cardiovascular regulation and an echocardiographic examination. After over 20 years of follow-up, 289 subjects (30.6%) developed new functional class III-IV heart failure.

Results: There was a negative correlation of NT-proBNP, ALD, PRA and LVEF (p<0.006). NT-proBNP was significantly lower in HFrEF (1277 [474–2873] vs. 1998 [749–4687]), p<0.001 as were ALD and PRA (92 [44–156] vs 104 [58–186], p=0.004 and 2.7 [0.9–8.3] vs 3.5 [1.1–10], p=0.043, respectively). No differences in PACE were seen between HFrEF and HFpEF. In GLM adjusted for covariates, PRA (p=0.021) and NT-proBNP (p=0.001) were significantly lower in HFrEF compared to HFpEF.

During a median follow-up of 12 (6–18) months, CV mortality was higher in HFrEF (11% vs 7%, p=0.021). In multivariate Cox analysis adjusting for demographic and comorbid conditions, cardiovascular death was higher in HFrEF (HR 1.62; 95% CI 1.03–2.53, p=0.036). However, this difference was lost when markers of RAAS activation were taken into account (HR 1.47; 95% CI 0.91–2.35, p=0.11).

Conclusions: RAAS activation is lower in HFrEF, partially explaining the differences in prognosis compared to HFpEF.

Abstract P3123 – Table 1

Table 1

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>1st tert of E/E'</th>
<th>2nd tert of E/E'</th>
<th>3rd tert of E/E'</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>48.5±5.6</td>
<td>49.6±5.2</td>
<td>51.5±5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender, female</td>
<td>48%</td>
<td>50%</td>
<td>67%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169.8±9.3</td>
<td>168.6±18.3</td>
<td>164.8±18.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.4±4.1</td>
<td>27.4±4.3</td>
<td>28.0±4.7</td>
<td>0.004</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>140.6±18.8</td>
<td>143.3±18.2</td>
<td>149.9±21.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>85.6±11.4</td>
<td>88.0±11.9</td>
<td>89.5±10.5</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>E integral/A integral</td>
<td>1.89±0.59</td>
<td>1.73±0.44</td>
<td>1.67±0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular mass fraction</td>
<td>0.10±0.05</td>
<td>0.09±0.44</td>
<td>0.07±0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glomerular filtration rate</td>
<td>84.1±16.1</td>
<td>82.7±15.4</td>
<td>78.3±15.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial natriuretic peptide</td>
<td>239±100</td>
<td>247±122</td>
<td>290±172</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>4.4±0.6</td>
<td>4.5±1.0</td>
<td>4.7±1.5</td>
<td>0.025</td>
</tr>
</tbody>
</table>
up, of the 800 hundred subjects still alive, majority (n=599) were available for re-examinations, such as echocardiography using modern techniques. Septal E/E' could be reliably measured from 540 subjects. E/E' was divided to tertiles (1st trt ≤ 15.3, 2nd trt > 15.3 but < 30.6, 3rd trt ≥ 30.6) and the 3rd trt indicating severe diastolic dysfunction.

Results: Several baseline variables were associated with diastolic dysfunction after over 20 years of follow-up (Table). After adjustments in the multivariable logistic regression analysis model, only systolic blood pressure (p<0.009) and shorter height (p<0.002) remained significant associated with the risk of developing diastolic dysfunction.

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.

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) despite a high cardiovascular risk profile has been implicated in HFpEF, the reported prevalence is lower compared to HFREF (heart failure with reduced ejection fraction) despite a high cardiovascular risk profile. The role of CMR (cardiac magnetic resonance) as a diagnostic tool for CAD is well validated. We performed a systematic evaluation for CAD and perfusion abnormalities in HFpEF utilising CMR.

Methods: Comprehensive CMR with 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) ≤ 50% as per echocardiography. Main exclusion criteria were: suspected or confirmed cardiomyopathy, pericardial constriction, non-cardiovascular life expectancy less than 6 months, myocardial infarction (MI) in the preceding 6 months, severe valve disease, obstructive pulmonary disease and estimated glomerular filtration rate less than 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±12 years; male 51%; hypertension 90%; diabetes 49%; hypercholesterolaemia 49%; smoking 55%; known CAD 24%; angina 17% and LVEF 58±12.

Conclusions: 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 HFpEF. A dynamic pressure-volume and histological study
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Results: LV end-diastolic pressures (EDPs) were higher in HFpEF than controls (13±3 vs. 8±4 mmHg, p=0.03) and significantly increased during exercise up to (23±8 vs. 13±7 mmHg, p=0.04). Despite exercise prolonged values of E/E' in HFpEF 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 HFNREF patients than in controls (Δ S+ = 140±82% vs. 105±32%, p<0.05), leading to a steeper passive PV-curve (dP/dV+ = 141±138% vs. 68±11%, 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 S+ during exercise (R=0.78). Rapid pacing neither modified LV passive properties nor increased EDPs, although relaxation was faster.

Conclusions: High filling pressures in patients with HFpEF are mostly determined by increased chamber stiffness and not by impaired relaxation. Stiffness is not constant because it acutely increases during exercise and both rest and exercise values correlate with severity of HFpEF. Acute chamber stiffening is responsible for high filling pressures during exercise in HFpEF. The mechanical and post-transcriptional bases of this amplified acute stiffening response should be investigated.

P3128 | BEDSIDE
Differences in prevalence and severity of sleep-disordered breathing in HF-REF and HF-PEF: first results of the prospective German SchlaHF-XT registry
O. Oldenburg1, M. Arcti2, E. Erdmann3, H. Teschler4, B. Wellmann5, K. Wegscheider6, H. Woehrle7 on behalf of the SchlaHF-XT Investigators. 1Heart and Diabetes Center NRW, Ruhr-University of Bochum, Bad Oeynhausen, Germany; 2University Hospital Regensburg, Regensburg, Germany; 3Cologne Heart Institute - Heart Failure Unit, University Hospital, Klinikum St. Antonius - Klinikum St. Elisabeth, 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 underdiagnosed but relevant co-morbidity in heart failure (HF) patients with reduced (HF-REF) and preserved (HF-PEF) ejection fraction. The SchlaHF-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 SchlaHF-XT registry prospectively includes patients with stable HF as defined as a symptom complex of shortness of breath and rapid fatigability on the basis of cardiac disease or any impairment in cardiac 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-REF (45.5%) or HF-PEF (45.5%) (68±11 years, 66.0% male): NYHA I 8.4%; NYHA II 51.5%; NYHA III 24.7%; NYHA IV 1.6% were screened for presence, type and severity of SDB. Overall AHI was 14.5±14 in HF-PEF and 17.5±17 in HF-REF (p=0.01), with more obstructive sleep apnea (OSA) in HF-PEF (32.3±13/h, p<0.005) and central apnoeas (3.2±12/h, p=0.005) in HF-REF patients. Patients to moderate severe SDB (AHI >15/h) was seen in 35.3% of HF-PEF and 43.4% of HF-REF patients (p=0.006). According to the majority of apnoeic events, patients were classified as having moderate to severe obstructive sleep apnea (OSA) in 36.0% of HF-REF (p<0.001) and moderate to severe SDB in HF-REF (p<0.003). However, moderate to severe central sleep apnea (CSA) was more prevalent in HF-REF (15.1%) compared to HF-PEF (8.7%, p<0.019).

Conclusion: In a prospective longitudinal HF registry, prevalence of moderate to severe SDB is different between HF-REF and HF-PEF 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 (HFpEF) 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 echocardiography assessing diastolic dysfunction 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 immunoassay (Proseek Multiplex CVD 196x96) and analyzed by a t-test.
with 238 clinical variables. To identify and rank biomarkers predicting NYHA class and outcome, orthogonal partial least square (OPLS) analysis was performed. Top-10 positive and top-3 negative predictors of outcome were analyzed by Cox regression.

**Results:** Loading scores of biomarkers and clinical variables are plotted in Figure 1. Top-10 positive predictors were significant after adjustment for NT-proBNP while the top-3 negative were not. Left atrial volume index correlated with CCL2 (r=0.32; p=0.006) and ST2 (r=0.27; p=0.020) and E/e' with CCL2 (r=0.29; p=0.018), GDF-15 (r=0.32; p=0.009), SPON1 (r=0.47; p<0.001), IL 8 (r=0.25; p=0.044), IL 6 (r=0.27; p=0.033), ST2 (r=0.30; p=0.017) and HGF (r=0.36; p=0.003). NYHA class correlated with log GDF-15 (r=0.09; p=0.019), log IL 6 (r=0.14; p=0.002) and log ST2 (r=0.07; p=0.042).

**Conclusions:** In HfPEF, novel biomarkers of inflammation predict HFC severity and prognosis that may complement or even be more important than traditional markers such as NT-proBNP. These findings lend support to the microvascular inflammation hypothesis in HfPEF.

**P3130 | BEDSIDE**

Insulin resistance is an independent predictor of left ventricle diastolic dysfunction across the diabetic continuum

R. Ladeiras-Lopes1, R. Fontes-Carvalho1, P. Bettencourt2, A.F. Leite-Moreira3, A. Azevedo4, Gaia Hospital Centre, Department of Cardiology, Vila Nova de Gaia, Portugal; 1Faculty of Medicine, University of Porto, Porto, Portugal; 2University of Porto, Faculty of Medicine, Department of Physiology and Cardiothoracic Surgery, Porto, Portugal

**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 (38% 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 with E’ velocity (11.2±3.3 vs 9.7±3.1 vs 9.2±2.8 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: 1.82; 95% CI: 1.09–3.03). From normal individuals, to patients with MetS but no T2DM, to patients with T2DM, there was a progressive decrease in LVDD, even after adjustment for age, sex, blood pressure and body mass index (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

A.K. Gitt1, D. Tschoepe2, P. Bramlage3, C. Koch4, T. Ouarrak1, R.E. Schmieder5.

1Gaia Hospital Centre, Department of Cardiology, Vila Nova de Gaia, Portugal; 2Heart and Diabetes Center NRW, Bad Oeynhausen, Germany; 3Novartis Pharma GmbH, Medical Department, Nürnberg, Germany; 4Institute for Cardiovascular Pharmacology and Epidemiology, Mahlow, Germany; 5Stiftung Institut für Herzinfarktforschung, Ludwigshafen, Germany

**Background:** Left ventricle diastolic dysfunction (LVDD) is one of the earliest cardiovascular changes in patients and T2DM in 12%. The HOMA-IR score correlated to E’ velocity (ρ=0.25; p=0.044), IL-6 (ρ=0.27; p=0.033), ST2 (ρ=0.30; p=0.017) and HGF (ρ=0.36; p=0.003). NYHA class correlated with log GDF-15 (ρ=0.09; p=0.019), log IL-6 (ρ=0.14; p=0.002) and log ST2 (ρ=0.07; p=0.042).

**Conclusions:** In HfPEF, novel biomarkers of inflammation predict HFC severity and prognosis that may complement or even be more important than traditional markers such as NT-proBNP. These findings lend support to the microvascular inflammation hypothesis in HfPEF.

**P3132 | BEDSIDE**

Achievement of individualized blood pressure and HbA1c targets in patients with hypertension and type-2 diabetes

R.E. Schmieder1, D. Tschoepe2, C. Koch3, P. Bramlage4, T. Ouarrak1, A.K. Gitt3, University of Erlangen-Nuremberg, Erlangen, Germany; 2Heart and Diabetes Center NRW, Bad Oeynhausen, Germany; 4Novartis Pharma GmbH, Medical Department, Nürnberg, Germany; 5Institute for Cardiovascular Pharmacology and Epidemiology, Mahlow, Germany

**Background:** Treatment targets for patients with hypertension and diabetes have recently changed to reflect the need for individualized treatment considering patient and disease specific characteristics.

**Methods:** DIALOGUE is a prospective, observational, multi-center registry to assess the real world impact of individualized treatment targets in pts with both diabetes and hypertension.

**Results:** A total of 8,584 pts were considered for the analysis. The individual HbA1c target was ≤6.5% (strict control) in 39.0% of pts by the physician; >6.5 and ≤7.0% (medium) in 42.3%, and >7.0 and ≤7.5% (loose) in 18.8%. Pts in the strict target group were younger, had a shorter diabetes duration and less co-morbid disease. Overall 69.9% of those with a strict HbA1c target also had a systolic BP target <130 mmHg. At the 12 months follow-up with a mean HbA1c of 6.79, 7.09 and 7.56% for the three groups respectively, 46.3%, 56.9%, and 59.1% of pts met their individual HbA1c treatment goal. This was only slightly better than the corresponding values at 6 months. Blood pressure targets were met in 50.8%, 60.2%, and 54.3% of pts, underlining the correlation between strict blood glucose and blood pressure targets. They were essentially unchanged compared to the 6 months follow-up.

| Table 1 | Achievements if VD is present. We assessed treatment strategies and outcomes in hypertensive diabetic patients with and without VD.

**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.

**Conclusions:** The data illustrate, that blood glucose targets chosen in pts with type-2 diabetes consider patient characteristics and overall co-morbidity and are aligned with the corresponding blood pressure treatment targets. There is, however no major effort for treatment target achievement if treatment targets are not met at 6 months.
Phosphodiesterase 5 inhibitor prevents hypoxia-induced cardio-pulmonary remodeling through an antiproliferative mechanism

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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 sildenafil, a phosphodiesterase 5 inhibitor, on hypoxic pulmonary vascular remodeling and show preliminary data from a preclinical model of chronic hypoxic pulmonary hypertension.

Methods: Adult male Sprague-Dawley rats were exposed 2 weeks to chronic hypoxia (N= 24, 2 weeks; n=10). CH rats received sildenafil (1.4 mg/kg/day, ip, n=10) or saline (n=10). The effects of CH on cardio-pulmonary hemodynamics were assessed by Doppler echocardiography and RV catherization.

Results: Compared to N, Doppler echocardiography revealed reduced pulmonary artery (PA) acceleration time and velocity time integral (−41±4% and −0.7±0.03%, respectively) and increased PA systolic pressure (+2.0±0.08%) in CH rats, which rescued by sildenafil. Although CH resulted in a 1.7±0.0 fold increase in RV:LV ratio and in RV hypertrophy (expressed as RV/LV + S) 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±4% 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: 0.5±0.2 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±0.2 for lung and RV, respectively). Compared to N, RT-PCR showed a mRNA up-regulation of collagen III in the lung (1.5-fold) and in the RV (2.0 fold) 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 cardio-pulmonary remodeling by reducing the proliferation of new fibroblasts and by activating autophagy as a protective mechanism to prevent excessive collagen accumulation.

First quality assessment of cardiovascular drugs in 10 sub-saharan African countries: the seven study

A. Antignac1, F. Diop2, V. N'guetta3, F. Tchabi4, A. Sidi Aly5, X. Jouven9 on behalf of Cardiology team of Africa

Methods: Samples were collected by standardized methods, between 2012 and 2014, in randomized pharmacies and street markets, in Senegal, Burkina Faso, Benin, Ivory Coast, Togo, Niger, Democratic Republic of Congo, Congo, Mauritania, Guinea. A validated reversed-phase liquid chromatography method was used for the dosage of active ingredient in a certified public laboratory in France. Drugs were declared poor quality if the percentage of active ingredient was below 95% or over 105% the labeled drug. This study was exclusively supported by public grant.

Results: Drugs were collected in 32 pharmacies (n=880) and 19 street markets (n=850). Among 1530 samples tested, 16.3% were poor quality (n=249). The declared region of drugs manufacture and outlet where the drugs were purchased (licensed or unlicensed outlet) were significantly associated with the quality of drugs. (Table)

Conclusion: This study sheds light on poor quality of cardiovascular drugs available in ten African countries and identifies factors associated with poor quality: place of manufacture and place where the drug was purchased.

Effect of renal sympathetic denervation on the expression of miRNA-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...
(mRNAs) 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 systolic blood pressure (SBP) reduction of >10 mmHg 6 months 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 mmHg (SBP baseline: 164.8 ± 17.9 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 the 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 remodelling and HHD in high-risk patients.

**NEW CONCEPTS IN ECHOCARDIOGRAPHY**

**3168 | 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 3D colour Doppler echocardiography. The following 2D parameters were assessed: Biplanar 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 x LVOT VTI). 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 (9±7 ml; p < 0.001).

**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.

**Table 1: (echocardiographic parameters)**

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<th>Parameter</th>
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<th>SMR group</th>
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<tr>
<td>EF (%)</td>
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<td></td>
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<tr>
<td>E/A ratio</td>
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<tr>
<td>RV E/A ratio</td>
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</tbody>
</table>

**Table 2: (operator characteristic curves)**

<table>
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<tr>
<th>Parameter</th>
<th>Area (mm²)</th>
<th>P</th>
<th>Optimal cut-off for severe MR</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA (%)</td>
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</table>

**Acknowledgement/Funding:** This study was supported by the German Research Foundation (Deutsche Forschungsgemeinschaft: SFB 381). The authors wish to thank all participants, as well as the staff of the echocardiography laboratories in the participating hospitals.

**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 (Ultrasound 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 phenylephrine infusion. RPI was created offline, a 5 cm line was manually drawn between LV and LA, and PD was automatically computed between the 2 ends.

**Results:** PD was measured at 2 time points during the cardiac cycle; early diastole corresponding to diastolic suction (Figure - left, red color indicates higher pressure and blue color indicates lower pressure compared to reference point) and end diastole corresponding to atrial contraction. A total of 205 heart beats
were analyzed. We found a good correlation between noninvasive and invasive measurements of P0 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 (COLVOT) were measured by Doppler echocardiography. PVR based on a theoretical formula (PVRtheo) was calculated as (TRPG - PRPGed)/3COLVOT 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 RPI and its measurements show good correlation with invasive catheter measurements.

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 significantly 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: 643±202 vs. 513±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).

Conclusion: 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 maximum diastolic filling were selected. Atrial mechanical function was classified according to the interval from the atrial mechanical onset to maximal intensity of vortex flow towards the aorta, named Interval of Maximum Vortex Flow (IMVF). We investigated how IMVF behaved during acute left ventricular ischaemia.

Results: 12 patients (25% male, aged 68.7±10.5, LVEF 40±10.3%) were examined in apical 3-chamber view with VFM imaging during all programmed AVD. 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.

Conclusion: 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 twisting and untwisting in hypertensives: a 3-year follow-up study
1University of Athens, Athens, Greece; 2University of Athens Medical School, Attikon Hospital, 2nd Department of Cardiology, Athens, Greece

Background: Impaired left ventricular (LV) myocardial twisting markers indicate the presence of LV systolic and diastolic dysfunction. Blood pressure, arterial stiffness, LV mass, and impaired coronary microcirculation determine LV function in hypertensives. We investigated the effects of 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 ambulatory blood pressure monitoring b) Carotid to femoral artery pulse wave velocity (PWV) c) Coronary flow reserve (CFR) after adenosine infusion, LV mass/m², twisting (Tw-deg), peak twisting (Tw-deg/sec) velocity, untwisting at mitral valve opening (unTwMVO), peak (E/unTwE) and end of the E wave (unTwE 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, patients those with 24 systolic and diastolic blood pressure <130/80 mmHg

Results: Compared to controls, hypertensives had lower CFR, (2.5±0.6 vs 3.0±0.5), LV mass/m² (81±16 vs 75±16), PWV (11.7±2 vs 10.8±1.5), Tw velocity (126±38 vs 110±21), unTwMVO (15.7±5 vs. 10.5±4) unTwE (10±5 vs. 5.8±3.1). Compared to baseline, after 3 years of treatment patients had reduced Tw (20±4 vs 27±3, p<0.001), unTwMVO and unTwE (15.7±5 vs. 10.5±4, p<0.001) although CFR did not improve significantly (p=0.0368). Accuracy for prediction of functional recovery was not improved by integrated analysis of STE and CMR in myocardial segments categorized as viable or non-viable by LGE.

Conclusions: In patients with AMI, accuracy to predict segmental functional recovery was improved by additional analysis of STE in myocardial segments with intermediate viability as defined by LGE.

Acknowledgement/Funding: This study was supported by a research grant from the German – Israeli Foundation for Scientific Research & Development.

CARDIOVASCULAR MAGNETIC RESONANCE IMAGING IN 2015: MORE IMPACT IN MANAGING PATIENTS

3252 | BEDSIDE
Prediction of long-term major events soon after a first ST-segment elevation myocardial infarction by cardiovascular magnetic resonance imaging
P. Racugno1, C. Bonanad Lozano1, D. Escribano1, A. Paya1, J. Nunez1, M.P. Lopez-Lereu2, J.V. Mommenue2, E. Cambronero2, F.J. Chorro1, V. Bod1
1University Hospital Clinic, Department of Cardiology, Valencia, Spain; 2University Hospital Clinic, Imaging Unit-ERESA, Valencia, Spain

Background: In post-STEMI patients CMR predicts combined clinical events. Its contribution for predicting long-term ME (cardiac death and non-fatal infarction) is unknown. We aimed to assess whether cardiovascular magnetic resonance (CMR) predicts major adverse events (MAE) soon after ST-segment elevation myocardial infarction (STEMI).

Methods and results: From 2004 to 2012 we prospectively recruited 548 STEMI patients. Left ventricular (LV) ejection fraction (LVEF), %, infarct size (IS), edema, microvascular obstruction and LV myocardial salvage were quantified by CMR at pre-discharge. During a mean follow-up of 840 days, 57 ME events (10%, 23 cardiac deaths, 34 non-fatal re-infarctions) were documented. Patients with ME displayed more depressed LVEF (<0.40), large IS (>30% of LV mass) and more extensive edema, hemorrhage and microvascular obstruction and less myocardial salvage (p<0.05). CMR indexes were dichotomized according to the best cutoff values for predicting ME. In a comprehensive multivariate model, LVEF ≥30% and IS >30% of LV mass (n=393), in those with only one of them altered (n=84) and in cases 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 with both 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
1Royal Brompton Hospital, London, United Kingdom; 2University of Athens Medical School, Athens, Greece; 3Sotiria Regional Chest Diseases Hospital, Athens, Greece; 4Oncasis Cardiac Surgery Center, Athens, Greece; 5University of Athens, Athens, Greece

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 cardiological 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 (LGE+). Among these, 53 (15.9%) and 84 (25.5%) patients fulfilled the JHU criteria and the Mehta et al criteria respectively. During median follow-up 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. On multivariate Cox regression analysis, LGE and IS (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. Sensitivity, specificity and predictive values of criteria for diagnosis of cardiac sarcoidosis when used to detect major adverse events

Events in follow up

<table>
<thead>
<tr>
<th>LGE-MRI</th>
<th>JHU criteria</th>
<th>Mehta criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>negative</td>
<td>positive</td>
</tr>
<tr>
<td>Yes, n</td>
<td>26</td>
<td>10</td>
</tr>
<tr>
<td>No, n</td>
<td>82</td>
<td>21</td>
</tr>
</tbody>
</table>

Sensitivity (%) 84 71 71 71 71
Specificity (%) 91 94 94 94 94
PPV (%) 24.8 30.3 32.3 77.7 22.9
NPV (%) 97.2 92.1 94.1

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and negative 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 MRI 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). By multivariable analyses, Non IR-LGE and BNP were significant independent predictors for MACE (P<0.01). 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
C.J. Lee1, J.L. Pallisgaard1, G.H. Gislason1, C. Torp-Pedersen2, A. Brandes3, S. Husteds4, S. Johansens5, M.L. Hansen1, 1Gentofte University Hospital, Copenhagen; 2Aalborg University Hospital, Aalborg; 3Odense University Hospital, Odense; 4Aarhus University Hospital, Aarhus, Denmark
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 ratio (95% confidence interval) 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
S. On1, S. Goto2, P. Angnaiasuk3, A.J. Camm4, F. Cools5, S. Haas6, Y. Koretsune7, T.W. Lim8, C. Accetta9, A.K. Kakkar9 on behalf of GARFIELD-AF Investigators. 1Seoul National University Hospital, Seoul, Korea, Republic of; 2Tokai University, Kanagawa, Japan; 3Ramathibodi Hospital of Mahidol University, Bangkok, Thailand; 4St George’s University of London, London, United Kingdom; 5AZ Klinia, Brasschaat, Belgium; 6Technical University of Munich, Munich, Germany; 7Osaka National Hospital, Institute for Clinical Research, Osaka, Japan; 8National University Hospital, Singapore, Singapore; 9Thrombosis Research Institute, London, United Kingdom
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 values (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 treatment with apixaban and rivaroxaban in a real-world setting
F. Al-Khalili1, C. Lindstrom2, S. Schultman3, A. Majed3. 1Karolinska Institute, Dept. of Clinical Sciences, Danderyd Hospital., Stockholm, Sweden; 2Stockholm Heart Center, Stockholm, Sweden; 3McMaster University, Department of Hematology and Thromboembolism, Hamilton, Canada; 4Karolinska Institute, Department of Medicine, Stockholm, Sweden
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-

was observed for all-cause mortality. vs 0.799 (0.711, 0.897), respectively [P=0.90 for interaction, Figure]. A similar finding was seen for all-cause mortality.

**Conclusion:** Our study shows high estimated adherence levels to apixaban and rivaroxaban in clinical practice. There was no significant difference in the adher-

**ADVANCES IN HEART FAILURE THERAPY**

**3301 | BEDSIDE**

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

K. Damman1, K. Andersen1, J. Belohlavek3, M.P. Lefkowitz5, J.L. Rouleau3, S.D. Solomon6, K. Swedenberg2, M. Zile5, M. Packer3, J.J.V. McMurray1 on behalf of PARADIGM-HF Committee Investigators. 1University of Glasgow, Glasgow, United Kingdom; 2University of Iceland, Reykjavik, Iceland; 3General University Hospital, Prague, Czech Republic; 4Novartis Pharmaceutical Corporation, Hanover, United States of America; 5University of Montreal, Montreal, Canada; 6Brigham and Women's Hospital, Boston, United States of America; 7University of Gothenburg, Gotteborg, Sweden; 8Medical University of South Carolina, Charleston, United States of America; 9Novartis Pharmaceuticals, East Hanover, New Jersey, United States of America.

**Background:** ACE inhibitors often reduce glomerular filtration rate (GFR) in pa-

**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/HFH). We determined the change in GFR over time and the interaction between eGFR at baseline and the effect of randomized treat-

**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 similarly 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**

M. Gorl1, M. Senni2, B. Claggett2, J. Rouleau3, K. Swedenberg4, M. Zile5, M. Lefkowitz6, M. Packer7, J. Mc Murray1, S.D. Solomon8 on behalf of PARADIGM-HF investigators. 1Ospedale Papa Giovanni XXIII, Bergamo, Italy; 2Brigham and Women’s Hospital, Boston, United States of America; 3Montreal Heart Institute, Montreal, Canada; 4Sahlgrenska Academy - University of Gothenburg, Gotteborg, Sweden; 5Medical University of South Carolina, Charleston, United States of America; 6Novartis Pharmaceuticals, East Hanover, New Jersey, United States of America; 7University of Texas Southwestern Medical School, Dallas, United States of America; 8University of Glasgow, Glasgow, United Kingdom

**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 1 bid in the PARADIGM trial. Urinary albumin/creatinine ratio (UACR) was available at screening, follow-

**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-

**Conclusion:** Compared with enalapril, LCZ696 reduced clinical outcomes sub-

**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**

D.T. Farmakis, J. Parissis, P. Simitis, V. Bistola, I. Ikonomidou, G. Papagiotis, G. Filippatos, A. Mebazaa, J. Lekakis, F. Follath. Attkon Hospital, 2nd University Department of Cardiology, Athens, Greece

**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-

**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, Asia, and Australia. We compared in-hospital mortality between patients receiving or not BB. Nearest-neighbour matching by propensity score was applied to produce a bal-

**Results:** In the original sample, 2330 patients (47%) were receiving BB. Propensity-score matching derived a sample of 2372 patients (1186 in each treat-

**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.

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**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-

**Conclusion:** Compared with enalapril, LCZ696 reduced clinical outcomes sub-

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

**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-

**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, Asia, and Australia. We compared in-hospital mortality between patients receiving or not BB. Nearest-neighbour matching by propensity score was applied to produce a bal-

**Results:** In the original sample, 2330 patients (47%) were receiving BB. Propensity-score matching derived a sample of 2372 patients (1186 in each treat-

**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

**Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/509/434476 by guest on 10 January 2019**
Carperitide (CAR), a human atrial natriuretic peptide, may have acute heart failure: a propensity-matched comparison

H. Ogawa, S. Y asuda, T. Anzai.

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 Petos 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; 95% CI, 0.24–0.70), sudden death (RR 0.30; 0.19–0.46) 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.

Carperitide versus nitroglycerin as a first-line therapy in patients with acute heart failure: a propensity-matched comparison

N. Iwakami, T. Nagai, Y. Sugano, T. Shibata, Y. Asaumi, T. Noguchi, K. Kusano, H. Ogawa, Y. Yasuda, T. Anzai. National Cerebral and Cardiovascular Center, Department of Cardiovascular Medicine, Suita, Osaka, Japan

Background: Carperitide (CAR), a human atrial natriuretic peptide, may have renal and myocardial protective effects with better clinical outcome in patients of acute heart failure (AHF). However, CAR has never been validated as an alternative and myocardial protective effects with better clinical outcome in patients of acute heart failure (AHF). However, CAR has never been validated as an alternative

Methods: From our prospective AHF registry, 477 consecutive patients with follow-up of median 354 days were examined. Those who received CAR or NTG infusion as a first-line therapy were included regardless of concomitant use of diuretics. Those who required inotropes and vasopressors were excluded. Consequently, 129 patients with CAR and 100 with NTG were analyzed and matched 1:1 based on propensity score for the allocated treatment. Primary outcome was in-hospital worsening heart failure (HF) after temporal remission due to the initial therapy. Secondary outcomes were death, readmission due to worsening HF and occurrence of worsening renal function (WRF).

Results: CAR and NTG group consisted of each 67 patients (mean age 74 vs 78 years, women 36% vs 34%, respectively). In CAR group, the incidence of primary outcome was lower than NTG group (3% vs 12%, P=0.049 (Figure). The odds ratio was 0.17 (95% CI, 0.02–0.78, P=0.02) after adjustment for initial systolic blood pressure, serum creatinine and blood urea nitrogen, derived from an existing prediction model. Secondary outcomes were comparable with regard to death, readmission due to worsening HF, and WRF (1% vs 0%, 15% vs 16%, 45% vs 46%, respectively).

Conclusions: In AHF patients, CAR may prevent short-term worsening HF compared with NTG. However, putative effects on renal function and long-term clinical outcomes could not be observed.

Carperitide versus nitroglycerin as a first-line therapy in patients with acute heart failure: a propensity-matched comparison

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Conclusions: In AHF patients, CAR may prevent short-term worsening HF compared with NTG. However, putative effects on renal function and long-term clinical outcomes could not be observed.
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 cardiomyocyte to Bendavia significantly increased the extent of cardiomyocyte shortening to 5.4±1.1 μm (p <0.012), significantly increased 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.

3309 | BEDSIDE
Predictors, treatment and long-term course of iron deficiency in unselected patients with heart failure: The RAID-HF registry
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Background: Randomized studies, as FAIR-HF and CONFIRM-HF, reported beneficial effects of iron supplementation on the symptomatic status of patients with heart failure (HF) and iron deficiency (ID).

Purpose: The present study investigates "real-world" data on ID and its treatment in a large cohort of unselected HF-patients (including unstable patients and those with comorbidities).

Methods: The RAID-HF registry recruited consecutive patients with HF and ejection fraction <40% in 16 centers in Germany. From 10/2010 to 10/2013 iron status as well as clinical data were investigated in 671 consecutive HF-patients. Follow-up examination was performed after 1 year.

Results: In 55.9% (375 patients) of the HF-patients ID was diagnosed, 33.2% had absolute ID (defined as ferritin <100 μg/l) and 22.7% had functional ID (defined as ferritin 100-299 μg/l and transferrin saturation <20%). 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
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 asso-
ciates of the MELD and to assess its utility as prognosticator in AHF patients.

Methods: The study population consisted of 3310 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%). In the derivation cohort the mean MELD on admission was 14±4 points. Patients were divided into tertiles of the MELD and those in the 3rd tertile (with the highest values) had lower blood pressure on admission (118 vs 133mmHg), lower ejection fraction (28 vs 37%), serum Na+ (137 vs 140mmol/L) and higher: AST (250 vs 152 IU/L), ALT (230 vs 151 IU/L), bilirubin (3.5 vs 2.8 mg/dl). Hemoglobin (12.7 vs 13.2 g/dl), creatinine (1.5 vs 2.0 mg/dl) and lower platelet count (149 vs 176 10⁹/L). Only 24% of patients in the highest tertile of MELD had systolic blood pressure >120 mmHg on admission, compared to 50% in the lowest tertile (p <0.05).

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Conclusions: The high values of the MELD on admission are associated with poor outcome of patients with AHF. The derived model of the MELD on admission ≥12 predicted 1-year mortality with 73% accuracy (0.81 C-index).

Acknowledgement/Funding: Grant from National Centre of Science (Poland) no NN 519 658340/65834/B/T02/11/4
Purpose: The Reveal LINQ usability study is a prospective, multicenter clinical study assessing the sensing performance of the novel LINQ ICM. We report on sensing performance over the range of body mass index (BMI) values for all study implants (N=151). Data collected at the baseline and one month follow-up visits is included.

Methods: Using nationwide registries, we identified individuals below 60 years of age in Denmark (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% neurologically 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 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% neurologically 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 were applied to determine the effect on admission rates.

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 exits among the different guidelines resulting in significant variation between warranted admissions.

References:

1. Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark; 2 Aalborg University, Department of Health, Science and Technology, Aalborg, Denmark

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 of age with syncope between 2006 and 2014 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.

Conclusion: 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


1 McMaster University, Medicine, Hamilton, Canada; 2 McMaster University, B. Deif, S.J. Kang, A. Ismail, T. Vanniyasingam, J.C. Guzman, C.A. Morillo

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), American College of Emergency Physicians (ACEP) and European Society of Cardiology (ESC), 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% neurologically 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 were applied to determine the effect on admission rates.

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P3319 | BEDSIDE
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.

Purpose: To characterize PK and platelet inhibition with ticagrelor 60mg bid vs 90mg bid.

Methods: 180 patients who had received >4 weeks of study medication had blood sampling in the morning pre-maintenance dose and again 2h post-dose. All patients were receiving aspirin. Plasma ticagrelor levels were determined. VerifyNow P2Y12 assay and light transmittance aggregometry (LTA; ADP 20μM) were performed.

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 similar 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.

Conclusions: Ticagrelor 60mg bid achieved high levels of peak and trough platelet inhibition in nearly all patients, with similar consistency of effect compared to 90mg bid. These results help explain the efficacy of the lower ticagrelor dose in the PEGASUS-TIMI 54 study.

<table>
<thead>
<tr>
<th>DAPT status</th>
<th>Placebo</th>
<th>Ticagrelor 60mg</th>
<th>Ticagrelor 90mg</th>
<th>60mg vs placebo</th>
<th>90mg vs placebo</th>
<th>90mg vs 60mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not undergoing PCI</td>
<td>867</td>
<td>496</td>
<td>371</td>
<td>39 (43)</td>
<td>0.001</td>
<td>0.34</td>
</tr>
<tr>
<td>Undergoing PCI</td>
<td>103</td>
<td>53</td>
<td>40</td>
<td>12 (14)</td>
<td>0.001</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Data are mean (SD). Max response, maximum % aggregation response.

Conclusions: Ticagrelor 60mg bid achieved high levels of peak and trough platelet inhibition in nearly all patients, with similar consistency of effect compared to 90mg bid. These results help explain the efficacy of the lower ticagrelor dose in the PEGASUS-TIMI 54 study.

P3318 | BEDSIDE
Differences in dual antiplatelet treatment for acute coronary syndrome patients undergoing PCI or not: a Danish nationwide population-based cohort study
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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 for ACS patients undergoing PCI or not.

Methods: This observational cohort study linked morbidity, mortality, and medical data from Danish national registries from ACS patients alive after discharge from the hospital in 2012.

Results: In total, 9700 ACS patients (8599 myocardial infarction [MI] and 1101 unstable angina pectoris [UAP]) at discharge were identified, of whom 4864 (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-DAPT 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 patients (90 days vs. 62 days).

Conclusion: 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
National users of low-dose acetylsalicylic acid and risk of colorectal cancer: results using three different study designs
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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 per design. When low-dose ASA was used for secondary cardiovascular disease (CVD) 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
Continuous monitoring of day by day variations in biventricular pacing percentage, rather than its mean values, is a better predictor of clinical outcomes regardless of rhythm type

Aim: To assess the impact of both: 1) day by day variations and 2) mean values of cardiac resynchronization therapy pacing percentage (CRT%) on mortality with respect to rhythm type.

Methods: Prospective, single-center study encompassed 305 consecutive heart failure (HF) patients (pts) who were implanted with CRT-D devices and subsequently monitored remotely on a daily basis for the median follow-up (FU) of 30.5 months. Pts were stratified to 3 study groups depending on the mean values of CRT%, and those with at least one 24-hr episode of CRT%<95% were assigned to quartiles depending on its cumulative duration (in days) [Table 1]. However, pts with cumulative episodes of CRT%<95% lasting more than 7 days, regardless of both mean CRT% value during FU and rhythm type [sinus rhythm (SR) vs paroxysmal vs persistent atrial fibrillation (AF)] had significantly higher mortality rates (quartile 2–4 respectively, all P<0.05 vs quartile 1) than those in quartile 1 [Table 1]. The cumulative low CRT% burden was the independent risk factor for death. One additional day of CRT%’s loss increased the risk of death by 0.3% [HR 1.003; 95% CI 1.0001–1.006; p<0.05].

Table 1

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
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</thead>
<tbody>
<tr>
<td>CRT% ≥95% n=110 [36%]</td>
<td>CRT%&lt;95% with episodes of CRT%&lt;95% n=145 [47.5%]</td>
<td>CRT%&lt;95% n=50 [16.5%]</td>
</tr>
<tr>
<td>Mean CRT pacing [%]</td>
<td>98.1*</td>
<td>95.4*</td>
</tr>
<tr>
<td>Total mortality [%]</td>
<td>9.0*</td>
<td>8.3*</td>
</tr>
<tr>
<td>AF incidence [%]</td>
<td>30.7</td>
<td>58.0</td>
</tr>
<tr>
<td>Mortality of AF pts [%]</td>
<td>6.8*</td>
<td>9.4*</td>
</tr>
<tr>
<td>CRT pacing&lt;95% [days]</td>
<td>0 quartile 1</td>
<td>0 quartile 2</td>
</tr>
<tr>
<td>[1–7 days]</td>
<td>[8–17 days]</td>
<td>[18–64 days]</td>
</tr>
<tr>
<td>Nb of pts</td>
<td>48</td>
<td>46</td>
</tr>
<tr>
<td>Mortality [%]</td>
<td>0</td>
<td>17.3*</td>
</tr>
</tbody>
</table>

*p=NS among variables in a row.

Conclusion: Day by day variation in CRT pacing percentage, regardless of the rhythm type (SR vs AF), is a better mortality predictor than mean values of CRT pacing percentage obtained at different time points of FU, because it allows to detect 24-hr CRT pacing loss with one day delay only.

P3323 | 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 pushes the system thus advances 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 pathway 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 design 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 archive 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.
**P324 | BEDSIDE**

**Relationship between Serum Electrolytes and Electrocardiographic Intervals**

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**Background:** Hypokalemia, hypocalemia 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, antiarrhythmics 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 mg/dL, 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 >2.4 mg/dL, respectively). After adjusting for duration of QRS complex, this relationship between hypermagnesemia and QTc prolongation was no longer present. However, hypomagnesemia 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, 2.0–2.2, 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 unselected 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<0.0001). 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**

**P327 | 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.

We observed that ssFranucation was significantly increased in the cardiac microvascular endothelial cells and bone-marrow cells. An increase in 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.

**P328 | BENCH**

**Testosterone antagonizes doxorubicin-induced senescence of cardiomyocytes**

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**1AOU IRCCS San Martino IST, Department of Internal Medicine, University of Genova, Genova, Italy; 2Laboratory of Regenerative Medicine, Department of Experimental Medicine, University of Genova, Genova, Italy; 3Department of Translational Medical Sciences, University of Napoli Federico II, Napoli, Italy**

**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 17ß-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. Cardiac senescence remained significantly more frequent in treated than untreated cells up to 21 days after incubation with doxorubicin. Testosterone, but not 17ß-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 increase in 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 transcriptional induction 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 by doxorubicin.
by doxorubicin by modulating p53 and TRF2 via a pathway involving AR, PI3K, Akt, and NOS-3. This is a potential mechanism by which males are less prone to chronic anthracycline cardiotoxicity than females.

### P3332 | BENCH

**Rho-dependent kinases ROCK1 and ROCK2 and their contribution to the myofibroblast phenotype of cardiac fibroblasts**

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**Background:** RhoA and its downstream effectors ROCK1 and ROCK2 are known to play a pivotal role in the pathogenesis of myocardial fibrosis. However, their specific function in cardiac fibroblasts (CF), the major contributor to cardiac fibrosis, and cardiac cytoskeletal remodelling processes is poorly understood. Remodelling of the diseased heart results in the transition of fibroblasts to a myofibroblast phenotype exemplified by an increased proliferation, migration rate and synthesis of extracellular matrix (ECM) proteins. Therefore, the aim of our study was to test whether RhoA-ROCK protein signalling intermediates have an impact on cellular characteristics, intracellular protein expression and mechanical properties in CF and engineered tissues.

**Methods:** Neonatal cardiac fibroblasts were isolated from wild type rats and RhoA/ROCK knockdown was achieved by lentiviral transduction or transfection. Wild type fibroblasts were treated with 10 μM Fusudil or 300 nM H1152 for general ROCK inhibition and 10 μM SLc1121 for specific inhibition of ROCK1, percent con-

**Results:** The downregulation of RhoA or ROCK1 and ROCK2 was associated with changes in cell morphology accompanied by a disorganization of higher- order actin structures including stress fibres and geodesic domes. The knock- down of ROCK1 and ROCK2 in fibroblasts significantly increased adhesion velocity, but decreased proliferation capacity. Interestingly, the knockdown of RhoA and ROCK2, but not of ROCK1 led to a significantly decreased migration velocity and distance suggesting a specific role for ROCK1 in fibroblast migratory behavior. Moreover, ROCKs were shown to influence viscoelastic and contractile properties of homogeneous and heterogeneous engineered tissues. Destructive tensile strength measurement to assess properties and function of the ECM in engineered cardiac fibroblast tissue (ECFT) showed that rigidity was significantly reduced in ECFT treated with ROCK inhibitors. Isometric force measurements in response to calcium of engineered heart muscle (EHM) treated with ROCK in- nihitors showed a decreased resting force, whereas force of contraction was in- creased.

**Conclusion:** This study demonstrates that RhoA-ROCK signalling controls myofibroblast characteristics of CF via remodelling of the cytoskeleton and the ECM.

### P3333 | BENCH

**Phosphodiesterase 3A1 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 recep- tor signaling induces the production of reactive oxygen species in the situa- tion of heart failure. Phosphodiesterase 3A1 (PDE3A) inhibits β-adrenergic recep- tor (βAR)/protein kinase A axis by metabolizing cAMP. Therefore, we hypothe- sized 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 cardiac specific expression of exogenous PDE3A. Isoproterenol in- fusion increased heart weight/body weight ratio by 33% in WT mice compared with WT mice given vehicle (5.3±0.2 g/mg 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 (wall thickness, 1.11±0.04 mm vs. 0.86±0.04 mm, P<0.05), but not in TG mice (0.98±0.04 mm vs. 0.93±0.05 mm, ns). The β- OHDG, 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, percent con-

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

### P3334 | BEDSIDE

**Circulating endothelial microparticles are elevated in bicuspid aortic valve disease and are associated with 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 mi- croparticles (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 (-55 y.o. and without significant left ventricle re- modeling, n=60) and tricuspid aortic valve (TAV) controls (matched by age/sex); 2) analysing the variables related to circulating EMPs in BAV patients (-55 y.o. without other restrictions; n=70); 3) comparing circulating EMPs levels between BAV (n=25) and TAV (n=16) patients with a dilated aortic root (<21 mm²) and similar aortic diameters, and; 4) describing the time course of circulating EMPs levels in BAV patients depending on the requirement of aortic valve/ascending aorta surgery.

**Results:** 1) we observed higher levels of circulating EMPs in BAV patients with respect to controls (2.39±0.4 and 3.98±0.2 per log EMPs/μl respectively, 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 (r = 0.132 x mm² and p=0.008 for the indexed aortic root diameter). Aortic valve dysfunction was not related to EMP levels. 3) Furthermore, in patients with BAV associated aortic root, the EMP 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 re- spectively, p=0.009; β=0.28, P<0.02). 4) Finally, we observed that after aortic valve/ascending aorta surgery the circulating levels of EMPs decreased drasti- cally (4.2±0.7 to 1.75±0.3 EMPs/μl, P=0.002), especially in those patients un- dergoing 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 ascending aorta 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.

### P3335 | BEDSIDE

**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, consen- sus was reached by involving a third observer. Only cases with serial echocar- diographic images were included in the analyses. Mixed linear model analyses were used to identify independent factors associated with ascending aortic di- latation.

**Results:** A total of 392 patients had confirmed BAV with sufficient image quality to assess valve morphology and thoracic ascending aorta dimensions. At base- line, 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 as- cending 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 aorta dimensions. Sex was associated with dimen- sions of LVOT, aortic sinus and STJ. BSA was associated with LVOT and tubular ascending dimensions. Severity of aortic valve stenosis was associated with aor- tic sinus stenosis and STJ dimensions, but not with LVOT dimensions. In follow-up echocardiography (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: We compared clinical courses of patients with type A AD who underwent intraoperative TEE between March 2009 and January 2015. 5 patients with bicuspid 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 62.9%), 79 (79/198 40.2%) 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 detachment of 2 cusps can 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 valvularaortopathy. 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 (IPA), valvular steno- 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.

Conclusions: During follow-up 12 patients developed an AA (3.06% 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 hy- pertension: root or tubular portion of the ascending aorta diameters (D) ≥35 mm p 0.005, RR 7.016, D ≥40 mm p 0.001, RR 7.64 and for arterial hypertension p 0.005, RR 5.97. In multivariate analysis the most powerful predictor was the diameter ≥40 mm (p 0.002). 6 cases of acute aortic dissection occurred (1.5%, incidence 1.96/1000/year). In univariate analysis the best predictors of AD were aortic root diameters (diameters ≥35 mm p 0.006, ≥40 mm p 0.012) and arte- rial hypertension (p 0.002).

Conclusions: The basis aortic diameter and the arterial hypertension are the main predictors of aortic complications in patients with bicuspid aortic valve. Therefore, it would be highly recommended a strict follow up both in cases with baseline diameters ≥40 mm and in cases with arterial hypertension. The incidence of aortic dissection is higher than in general population.

P3337 | BEDSIDE
Yellow dust and particle pollution are independently associated with increased risk of hospital admission for ischemic heart disease in South Korea
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Background and introduction: Although air pollution has been associated with increases in acute morbidity and mortality, it’s effect is not well known in East Asian countries, where was affected by yellow dust phenomenon.

Purpose: To identify predictors of acute myocardial infarction (AMI) and hospital admissions for ischemic heart disease (IHD) extracted by random sampling. Ambient nitrogen dioxide (NO2), carbon monoxide (CO), ozone, and particulate matter <10 μm (PM10) were measured and occurrence of yellow dust was recorded. Short-term effects of air pollution and yellow dust on hospital visit for stable angina and acute coronary syndrome was analysed by Poisson regression.

Results: By random sampling method, total 2515 cardiac admissions were selected. Admissions for IHD were association with same-day concentrations of PM 10 (μg/m3) (RR 1.004, 95% CI 1.003–1.005) per 10 μg/m3; incidence of both particulate matter; dilution of ambient nitrogen dioxide by 10% of MACda results in the increase of AMI admissions by 3.1/10000/year. The mean dilatation rate of aortic root and ascending aorta were respectively 0.56 mm/year and 0.37 mm/year in <50 y.o. patients; 0.65 mm/year and 0.37 mm/year in ≥50 y.o. patients. The univariate analysis reveals that the most powerful predictors are the basic diameter of the aorta and arterial hypertensive patients: root or tubular portion of the ascending aorta diameters (D) ≥35 mm p 0.005, RR 7.016, D ≥40 mm p 0.001, RR 7.64 and for arterial hypertension p 0.005, RR 5.97. In multivariate analysis the most powerful predictor was the diameter ≥40 mm (p 0.002). 6 cases of acute aortic dissection occurred (1.5%, incidence 1.96/1000/year). In univariate analysis the best predictors of AD were aortic root diameters (diameters ≥35 mm p 0.006, ≥40 mm p 0.012) and arterial hypertension (p 0.002).

Conclusions: The basis aortic diameter and the arterial hypertension are the main predictors of aortic complications in patients with bicuspid aortic valve. Therefore, it would be highly recommended a strict follow up both in cases with baseline diameters ≥40 mm and in cases with arterial hypertension. The incidence of aortic dissection is higher than in general population.

P3338 | SPOTLIGHT
Air pollutants and acute myocardial infarction in a heavily industrialised region. Is there any relationship?
O. Polikutina, O. Barbarash, Y. Slepynina, E. Bazdyrev.

Background: The objective of the study was to examine the relationship between hospital admissions for acute myocardial infarction (AMI) and environmental pollution in the heavily industrialised Siberian region. Is there any relationship?

Materials and methods: The main indicators of environmental pollution and number of AMI admissions in the our Cardiology Center were assessed for the period between December 2010 and November 2014. Additionally, the annual number of days with unfavorable meteorological conditions and their impact were considered. The regression analysis was used to assess the relationship between the parameters and to build the equations of correlation for continuous variables. The number of AMI admissions was considered as a dependent variable; the % of most allowable average daily concentration (MACda), as an independent variable. The results were presented as regression coefficient, B, and correlation coefficient, R. Differences were considered statistically significant if p<0.05.

Results: It was found that there were associations between the increased number of hospital admissions for primary acute myocardial infarction and the elevated levels of nitrogen oxide and dioxide in winter time in comparison with summer time. It was found that, throughout the follow-up period, the elevation of nitrogen oxide concentration by 10% of MACda results in the increase of AMI admissions by 1.4 cases and the elevation of nitrogen dioxide concentration, in the increase of 0.9 cases of AMI admissions. In winter season, the 10% elevation of average monthly concentration of nitrogen oxide was associated with the increase in AMI admissions of 2.9 cases. Then the relationship between the concentra-
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.

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BEST POSTERS IN PCI: LONG-TERM OUTCOME

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).

Methods: We evaluated the effects of PM2.5 and T on resting BP in high-risk cardiac patients.

Results: 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: Ambient PM2.5 and T levels were associated with significant increases in systolic (β=1.359, 95% CI: 0.935–1.783, p < 0.001) and diastolic BP (β=0.233, 95% CI: 0.041–0.425, p = 0.018). Ambient PM2.5 was 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 mortality, the relationship seemed similarly significant in OR (per 10 μg/m3 = 1.020, 95% CI: 1.005–1.035) 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.

Predictors of late bleeding events

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01 (1.00–1.02)</td>
<td>0.01</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>2.94 (2.05–4.25)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anemia</td>
<td>1.84 (1.40–2.40)</td>
<td>0.09</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.61 (0.96–2.69)</td>
<td>0.06</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.75 (0.56–1.01)</td>
<td>0.06</td>
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*HR for age expressed as 1 unit increase.

Conclusions: We identified 3 variables strongly and independently associated with late and very late bleeding following PCI with DES in a real-world population. Triple therapy and anemia were the strongest predictors. Knowledge of patient subsets at high risk for late bleeding is essential in order to identify the optimal DAPT, in terms of potency and duration, after PCI.

P3343 | BEDSIDE
Mortality after coronary angiography in 2776 type 1 diabetes patients undergoing coronary angiography

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Background: Individuals with diabetes mellitus (DM) have more widespread coronary artery disease (CAD) than those without which partly can explain their increased risk for cardiovascular death. However few studies have addressed type 1 DM in this context.

Purpose: To assess long-term mortality by affected coronary vessels in type 1 DM.

Methods: All patients undergoing coronary angiography during the years 2001–2009 included in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) as well as in the Swedish National Diabetes Registry (NDR) with type 1 DM and onset age before 50 years were followed for mortality until 31 December 2012. CAD was visually judged and divided into normal (atherosclerosis/stenosis <50%), one-, two-, three- and left main-vessel disease.

Conclusions: Mortality after coronary angiography in 2776 type 1 diabetes patients undergoing coronary angiography
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.

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 of ST.

P3344 | BENCH Antiplatelet 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 devices abnormalities and modification of antiplatelet therapy (APT) regimen.

Purpose: This study aimed to investigate the characteristics and relationships between APT regimen and ST mechanisms among a large cohort of patients with de novo stent implantation. However, the impact of types of drug-eluting stent (DES) on the association is little known.

Methods: The PESTO study was a prospective national multicenter registry involving 29 French catheterization labs. Patients referred with acute coronary syndromes (ACS) were prospectively screened for presence of definite ST and analyzed by OCT after culprit lesion deocclusion. ST were classified as acute (AST), sub-acute (SAST), late (LST) and very late (VLST) according to the Academic Research Consortium criteria. Baseline clinical, biological and angiographic characteristics were collected for each subject. Three independent operators unaware of patients’ characteristics reviewed OCT data to identify the ST etiologies.

Results: A total of n=120 patients (mean age 61.6±11.1 y. 89% male) were included in the study. VLST was the clinical presentation in 75%, LST in 6% and SAST+AST in 19% of the patients. Bare metal stents (BMS) were involved in 39%, drug-eluting stents (DES) in 59% and bioreosorbable vascular scaffold (BVS) in 2% of the cases.

Antiplatelet drugs regimen was single APT (SAPT) in 62%, double APT (DAPT) in 24% and no APT in 14% of the cases at the time of the ST. A recent (<15 days) modification of the APT was reported in 22% of the patients (mean delay: 5.8±0.9 days). The main causes for APT modification were poor compliance to therapy (33%), medical decision (30%) and planned surgery (26%).

The delay between initial PCI to ST was shorter (1.8±0.7 vs. 5.3±0.6 y, p<0.001) and left anterior descending was more frequently involved (69% vs. 40%, p=0.006) in patients under DAPT than under SAPT. There was a higher incidence of stent underexpansion diagnosed by OCT in patients experiencing ST under DAPT than under SAPT (21% vs. 7%, p=0.05), but no significant difference was found between the 2 groups regarding other underlying morphological abnormalities including struts significant malapposition, ruptured neointimal layer, coronary evaginations, isolated struts uncoverage, ruptured neointimal hyperplasia and edge related disease progression.

Conclusions: Most of ST occurs under SAPT or no APT regimen. All type of stents and all mechanical mechanisms of ST can be involved. A recent modification of APT regimen could favour ST, and should incite the physician to make sure about the safety of the APT regimen changes and about the patient’s drug compliance.

BEST POSTERS IN NEW TREATMENT MODALITIES AND TREATMENT IMPLEMENTATION

P3347 | BEDSIDE Efficacy of short courses of low-frequency electric myostimulation in patients hospitalized for decompenated 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±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 aspects 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±5 Hz in cyclic regimen (1±0 ± stimulus, 2–0 ± rest). Average duration of EMS was 80.0±20.0 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 MLHFQ (from 53.6±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 18.3±7.2; Δ 6.2±4.2) and 6-mwt (from 206.1±61.3 to 293.5±91.1 m; Δ 86.6±56.27). Patients from group 2 demonstrated reliable improvement according to DASI (from 10.8 to 7.0; Δ 3.6±0.8) and MLHFQ (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 214.5±5.6 to 236.6±54.7 m; Δ 22.1±18.7; p=0.064). In 1, 3 and 6 months after discharge there was no dy-namics 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.

Conclusions: High-frequency electric stimulation of lower limb skeletal muscles leads to significant improvement of physical tolerance and can be safely used in patients with CHF early after decapsulation 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 incentives payments on medication titration in heart failure: should we pay for more?


Background: Angiotension converting enzyme inhibitors (ACEI), angiotensin re- cepter blockers (ARB) and beta blockers (BB) are prescribed at lower doses in real-world practice compared with the doses achieved in the randomised con-trolled 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 (HFREF) following hospital discharge.

Methods: We conducted three audits of consecutive eligible HFREF patients (LVEF <50%) who were newly referred to the multidisciplinary heart failure ser-vices 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 medi-cation 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 prac-titioner surveys. To compare differences between groups, one-way ANOVA were used for continuous normally distributed variables and Chi-squared tests for cat-egorical 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 hos-pital discharge (ACEI/ARB 93–97%, BB 92–94%). Comparing the three time peri- ods, a progressively higher proportion of patients received the medication titration form (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<0.011); 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 HFREF. 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 by targeting pre-discharge NT-proBNP levels: importance of attainability of targets


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

Methods:

Our study population was assembled from 7 ADHF cohorts. We de- fined 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 com-pared PARFs and percentage of patients on target (attainability).

Results: Of 1266 patients (80% male, 47% of patients was ≥75 year). The rela-
tionship between PARF and percentage of patients attaining different NT-proBNP targets aged <75 vs. >75 is depicted in the Figure. PARF of the NT-proBNP targets did not differ significantly among 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).

Conclusions: 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.

RESULTS

BEST POSTERS IN HYPERTENSION MONITORING AND TREATMENT

P3353 | BESTIDE

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, M/F: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 TM2430)] 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 differences in SBP between MER (reference) and the remaining devices at baseline and high altitude were 1.7±6.0/6.7±1.1 (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±5.6 (OSC-ABP), −2.2±5.1/−5.3±5.6 (ANE) and −4.8±7.6/−1.8±7.1 (OSC-HBP). The mean percentage of subjects displaying between-devices differences at high altitude vs. sea level was 50% for SBP and 48% for DBP. The over- or under-estimations of BP values were consistent and similar at sea level and high altitude, except for a greater underestimation of SBP by OSC-HBP (p < 0.01), and of DBP by ANE (p = 0.03) at altitude, and for a greater underestimation of DBP by OSC-HBP (p = 0.02) at sea level. Although statistically significant, the absolute changes in the size of error between sea level and high altitude never exceeded 4 mmHg. The distribution of mean between-device differences within the group was consistent between sea level and high altitude, with about 50% of subjects displaying between-devices differences all smaller than 5 mmHg.

Conclusions: Parallels did not find consistent and clinically relevant changes in the accuracy of the tested devices caused by high altitude exposure. Thus, even though in clinical practice seem to perform well and can be considered accurate in this types of devices for BP measurement tested in our study and commonly used.

Conclusions: We did not find consistent and clinically relevant changes in the accuracy of the tested devices caused by high altitude exposure. Thus, even though validated oscillometric devices [one for home (OSC-HBP; AND UA-767PC) and one for ambulatory (OSC-ABP; AND TM2430)] 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.

P3354 | BEDSIDE

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

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Purpose: The 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. 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 (MTo), CV mortality (CVM), stroke and myocardial 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 (CVD4) – 1500 (38.6%); other - 5.0%. AHD were not prescribed in 13.8% of cases. 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 were 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 from CVD), 62 cases of stroke, – 26 of MI. The multivariate HR and CI revealed significant factors for MTo prediction: HSTR - 2.68 (1.85–3.89); β-blockers - 0.67 (0.47–0.95); TD - 0.37 (0.23–0.62). For CVM prediction: HSTR - 3.33 (2.14–5.61); CVD4 - 3.13 (1.03–10.9); ACE inhibitors - 0.53 (0.34–0.84); sartans - 0.48 (0.27–0.86); TD - 0.40 (0.22–0.73). Predictive factors were revealed for stroke and MI: HSTR - 4.80 (2.62–8.78); CVD4 - 6.84 (1.34–34.3) and HMI - 4.37 (2.57–7.45); TD - 0.43 (0.22–0.84).

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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Purpose: 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.
Left ventricular hypertrophy is a significant risk factor for cardiovascular complications in hypertension. Recent studies have shown that microRNAs (miRs) play a major regulatory role in several aspects of physiological and pathological cardiac hypertrophy. MiR-1, miR-133a and miR-26b have been shown in animal models to play a role in heart hypertrophy mainly having anti-hypertrophic function. We evaluated whether the anti-hypertrophic microRNAs miR-1, miR-133a and miR-26b were differentially expressed in peripheral blood mononuclear cells of hypertensive patients in relation to left ventricular hypertrophy.

**Methods:** We assessed the expression levels of the microRNAs miR-1, miR-133a and miR-26b in 102 patients with essential hypertension (50 men, mean age 62.51±9.7 years) and 30 healthy individuals (14 men, mean age 58.8±3 years). All patients underwent two-dimensional echocardiography. MicroRNA expression levels in peripheral blood mononuclear cells were quantified by real-time reverse transcription polymerase chain reaction.

**Results:** Hypertensive patients showed significantly lower miR-133a (5.06±0.50 versus 13.20±2.15, p<0.001) and miR-26b (6.76±0.53 versus 9.36±1.40, p=0.037) and higher miR-1 (25.99±3.07 versus 12.28±2.06, p=0.019) expression levels compared with healthy controls. In hypertensive patients, we observed significant negative correlations of miR-1 (r=−0.374, p<0.001) and miR-133a (r=−0.431, p<0.001) and a significant positive correlation of miR-26b (r=0.302, p=0.002) expression levels with left ventricular mass index.

**Conclusions:** Our data reveal that miR-1, miR-133a and miR-26b show a distinct expression profile in hypertensive patients relative to healthy individuals and they are associated with left ventricular mass index in hypertensive patients. Thus, they may be involved in the pathophysiology of left ventricular hypertrophy in hypertensive patients and may be promising therapeutic targets in hypertensive heart disease.

**Conclusion:** VAT atrial appendectomy may be a reasonable option for patients with relapsed AATs after the initial RFCA.

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**Conclusion:** VAT atrial appendectomy may be a reasonable option for patients with relapsed AATs after the initial RFCA.
patients (m=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 ef- fect did not differ between patients with and without AP re-ocurrence (782±159 vs. 725±126 ms, p=0.134). In 4 (33%) patients, re-ocurrence of AP conduction was persistent while 8 (67%) patients had transient re-conduction. In 2 (17%) pa- tients, transient 2:1 AV conduction through the AP was observed. Patients with AP re-ocurrence required significantly longer RF times for AP elimination as compared to those without (861±667 vs. 282±190 sec, p<0.001). Moreover, pa- tients with persistent AP re-conduction also needed longer RF applications as compared to patients with transient AP re-conduction (1368±329 vs. 607±231 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 experi- enced AP re-appearance. All of these patients had transient adenosine-induced AP re-appearance. Interestingly, patients with re-appearance had a significantly longer duration of adenosine-induced transient AP re-conduction (3.2±0.9 vs. 10.3±1.1 sec, p=0.033). All patients with late re-appearance 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) tran- sient re-conduction (true dormant conduction due to membrane hyperpolariza- tion) and, 3) 2:1 AV re-conduction of the AP (impaired slowly conducting AP). Transient dormant conduction with long duration is a significant predictor of late AP re-appearance despite abolishment by additional ablation.

P3360 | BEDSIDE
Noncoronary cusp could be the first-choice ablation site for parahisian atrial tachycardia
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Background: Mechanism of verapamil-sensitive atrial tachycardia (AT) originat- ing from the para-Hisian atrial region is thought to be reentry. How- ever, tachycardia circuit has not been fully clarified yet. Radiofrequency catheter ablation (RFCA) within noncoronary 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 pa- tients (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 com- pletely 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 RA para-Hisian region in 3 patients, and conversely it receded 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 (0.8 to 3.0 seconds) in these successful 7 patients. On the other hands, in 3 pa- tients whose AT could not be completely cured 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 earli- est 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 multicenter CA reg-
Methods: 149 children (85% boys and 64 (43%) girls) with typical (slow-fast) AVNRT underwent clinical and electrophysiological follow-up for 6.2±3.5 years or 929 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 had a history of supraventricular tachycardia (SVT) (refractory ablation 3±2.7 years (from 0.5 to 9.5 years) after manifestation of the disease. 52.3% children had an increase in the frequency of tachycardia or in the severity of symptoms, often during the age of 12–15 years. 15 (10.1%) children had a long spontaneous remission (duration >3 years). 2 patients had had a recurrence of AVNRT during the pregnancy after a long period of remission (7 and 9 years), 55 (36.9%) children had severe paroxysms of AVNRT, 20 (13.4%) had syncope 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 systolic time. Ablation was performed with an irrigated tip catheter in the ipsilateral pathway ERP (1.410±0.311 vs. 1.190±0.3, p=0.01). Significant decrease in AVNRT 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 systolic time. The acute success was defined as inability to induce at’s, and with and without isoproterenol infusion. 

Results: In 86% of patients (1618), non-invasive mapping helped us identify the location of the arrhythmia. There were six patients that had undergone AF involving the left atrium (LA). The LA mechanism was reentrant in twelve patients and focal in four. The non-invasive characterization was confirmed with a traditional invasive mapping system and adenomysopatry maneuvers in all patients. The acute success was obtained in all patients. In two patients, we found six patients with cavitricuspid atrial flutter, one patient with AT near by the sinus node, two patients 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 3D) 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 transfemoral punctures. Using femoral venous access, a multipolar catheter was inserted within the TCPC served as a targeting reference (Parahis). As a default, the femoral arterial access was gained to allow retrograde access to the native aorta via the saphenous. 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 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 root, 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 narrow true diameter at the tip insertion and one pseudoaneurysm. The mean procedure duration was 243±82 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 atrial arrhythmias. Many patients present with more than one arrhythmia target, even in these complex procedures both procedure duration and fluoroscopy exposure are very acceptable.

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 occurred in 23 patients (1%), cardiac arrest or ventricular arrhythmia requiring cardioversion (n=14) or collapses (n=9); remaining 316 patients presented with a poorly tolerated SVT (syncope (n=236), acute coronary syndrome (n=87), 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%) (51186 vs 231770) (p=0.16). 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-related complications. 

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.
Ablation of frequent PVC in primary prevention patients meeting biological criteria 6 months after endocardial alcohol ablation in patients with short PQ interval on ECG was performed. The procedure was well tolerated by all patients and no significant complications occurred. At 6 months follow-up, left ventricular ejection fraction (LVEF) was unchanged and the heart rate remained stable in all patients. The study concluded that alcohol ablation in patients with short PQ interval on ECG is a safe and effective procedure for the prevention of paroxysmal atrial fibrillation.
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) implantation 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 under went PVC ablation. ICD implantation 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 seen. 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).

Conclusion: In patients with frequent PVC, ablation improves LVEF and allows removing the PP-ICD implantation in the majority of them. To withhold the ICD implant at 6 months revaluation for ICD indication after ablation seems to be a safe and appropriate strategy.

P3374 | BEDSIDE Catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy: insights from a French monocentric registry Z. Souissi, S. Boule, F. Brigandet, C. Marquie, L. Guedon-Moreau, C. Kouakam, W. Escassut, D. Klug, S. Kacet, D. Lacroix. Lille University Hospital, Department of Card iovascular Medicine, Lille, France

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 revisedTaskforce 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). One VT occurred beyond 56±24 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 fractionated late potentials).

Conclusion: In these ARVC patients, RFA was mainly targeted at the endocardial substrate. Subendocardial ablation tended to be less effective than endocardial ablation detected by electroanatomical maps. In cases where scar extends more subepicardially or epicardially with preserved endocardial tissue based on ICE at the border zones, VT burden was reduced by RFA. Further studies are needed to determine the additive value of epicardial RFA in ARVC.
were the same for all procedures (430, 290, 60 sec.) including atrioventricular nodal reentrant tachycardias. In a case of left sided arrhythmias intracardiac echo was used (to perform transseptal puncture), or ablation within the aortic route to prevent coronary arteries damage. Using this approach operator does not have protective shielding.

Results: All procedures were performed without major complications. Procedure time and effectiveness of “nonfluoroscopic procedures” were comparable to those, performed in a usual manner.

Conclusion: Zero fluoroscopy approach for catheter ablation of tachyarrhythmias is safe in experienced hands and could be used in order to decrease potential harmful effect of fluoroscopy on patient and clinic staff.

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 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+AO access was used in 2-electrode, right atrial puncture (10-10 mm). In the NavX group procedure was started from RA, CS and location His bundle. Aorta was reconstructed before passage to the left ventricle. Short fluor 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 application (1stAP), L_AP, the number of applications (N_AP), total RF duration (RF_T) and success rate. We included 63 patients (mean age 13.1±3.3 years). An electrophysiological study was done with RF and in 13 with cryoenergy (all Kent bundles: 5 para-Hisian, 4 right postero-septal, 2 right antero-septal, 1 right anterior and 1 left postero-septal). All ablation procedures were performed without the use of fluoroscopy and without complication. At a mean follow-up of 15.0±11 months we observed 9 recurrences, 5 of them successfully reablated without fluoroscopy. In 1 case cryobalation of a para-Hisian AP was ineffective. In the fluoroscopy group a lesion was created in the AV node and the last application (1stAP, L_AP), the number of applications (N_AP), total RF duration (RF_T) and success rate. We included 176 pts with LS-AP (age 13.3±4 years, 73F) with SVT (76), WPW (96) or palpitations. In 118 pts the NavX was used during TS. We analyzed the procedural (duration of GA and procedure), X-ray (fluoroscopy exposure). Results: Fluoroscopic catheter ablation of cardiac arrhythmias in pediatric patients is a safe and effective procedure. Ablation was successfully performed in every patient. In 50 patients ablation was done with RF and in 13 with cryoenergy (all Kent bundles: 5 para-Hisian, 4 right postero-septal, 2 right antero-septal, 1 right anterior and 1 left postero-septal). All ablation procedures were performed without the use of fluoroscopy and without complication. At a mean follow-up of 15.0±11 months we observed 9 recurrences, 5 of them successfully reablated without fluoroscopy. In 1 case cryobalation of a para-Hisian AP was ineffective. In the NavX/Ensite group a lesion was created in the AV node and the last application (1stAP, L_AP), the number of applications (N_AP), total RF duration (RF_T) and success rate. We included 63 patients (mean age 13.1±3.3 years). An electrophysiological study was done with RF and in 13 with cryoenergy (all Kent bundles: 5 para-Hisian, 4 right postero-septal, 2 right antero-septal, 1 right anterior and 1 left postero-septal). All ablation procedures were performed without the use of fluoroscopy and without complication. At a mean follow-up of 15.0±11 months we observed 9 recurrences, 5 of them successfully reablated without fluoroscopy. In 1 case cryobalation of a para-Hisian AP was ineffective. In the fluoroscopy group a lesion was created in the AV node and the last application (1stAP, L_AP), the number of applications (N_AP), total RF duration (RF_T) and success rate. We included 176 pts with LS-AP (age 13.3±4 years, 73F) with SVT (76), WPW (96) or palpitations. In 118 pts the NavX was used during TS. We analyzed the procedural (duration of GA and procedure), X-ray (fluoroscopy exposure). Results: Fluoroscopic catheter ablation of cardiac arrhythmias in pediatric patients is a safe and effective procedure. Ablation was successfully performed in every patient. In 50 patients ablation was done with RF and in 13 with cryoenergy. Results: Fluoroscopic catheter ablation of cardiac arrhythmias in pediatric patients is a safe and effective procedure. Ablation was successfully performed in every patient. In 50 patients ablation was done with RF and in 13 with cryoenergy. Results: Fluoroscopic catheter ablation of cardiac arrhythmias in pediatric patients is a safe and effective procedure. Ablation was successfully performed in every patient. In 50 patients ablation was done with RF and in 13 with cryoenergy.
cardial APs with a R/S ratio < 1 (sensitivity 96%, specificity 72%, p < 0.001) and negative delta wave in lead V1 (sensitivity 74%, specificity 84%, p = 0.001). Epicardial posteroseptal APs were differentiated from endocardial APs by a negative delta wave in lead II (sensitivity 71%, specificity 99%, p < 0.001), R/S ratio < 1 in lead II (sensitivity 57%, specificity 79%, p = 0.03), and R/S ratio > 1 in V1 (sensitivity 57%, specificity 79%, p = 0.04).

Conclusions: Delta wave polarity and R/S ratio in lead V1 differentiate right endocardial posteroseptal APs from left endocardial APs. Delta waves in leads II, AVR, and V1, and R/S ratios in leads II and V1 estimate epicardial posteroseptal APs.

P3380 | BEDSIDE
Long-term outcome of intra-atrial reentrant tachycardia catheter 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 the spontaneous IART. We analyzed the influence of clinical factors (age, sex, type of CHD, age at surgical repair, systolic function of systemic and pulmonary ventricle, 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 52 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. 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. 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.

Conclusion: 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.

P3381

ABLATION OF ATRIAL FIBRILLATION I

P3382 | BEDSIDE
The Historic - AF Trial: European, prospective multicenter study of hybrid thoracoscopic and transcatheter ablation of persistent atrial fibrillation C. Mureretto1, G. Bisleri1, G.L. Polvani2, A. Curnis3, F. Rosati1, E. Maseri2, G. Fassini4, M. Moltrasio 4, C. Tondo5, R. Krakor5. 1University of Brescia, Department of Cardiac Surgery, Brescia, Italy; 2Cardiology Center Monzino IRCCS, Department of Cardiac Surgery, Milan, Italy; 3University of Brescia, Department of Cardiology, Brescia, Italy; 4Cardiology Center Monzino IRCCS, Department of Cardiology, Milan, Italy; 5THG Staudtliches Klinikum, Department of Cardiac Surgery, Dortmund, Germany

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 an hybrid fashion.

Purpose: The Hybrid Staged Operating Room and Intervventional 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 (LpAF). 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 LpAF 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 exit and/or entrance block were mandatory intraoperative end-points. Rhythm assessment was carried out by means of 72-hrs ECG-Holter or implantable loop recorders. In presence of AF recurrence, a staged EP evaluation and ablation was performed.

Results: All endoscopic 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 ablation. No ablation of the mitral isthmus was performed in the current study population. At 6 and 12 months follow-up a stable restoration of sinus rhythm was achieved in 90.7% (59/65), 88.8% (49/56) and in 93.3% (14/15) of patients respectively; according to HRS guidelines, the percentage of patients in sinus rhythm and with-out antiarrhythmic drugs were 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.

P3383 | BEDSIDE
Feasibility and safety of uninterrupted peri-procedural apixaban administration in patients undergoing radiofrequency catheter ablation for atrial fibrillation: results from a multicenter study L. Di Biasi1, D. Lakkireddy2, C. Trivedi3, T. Deneke3, M. Martinek4, S. Mohanty1, P. Mohanty1, J. Sanchez1, J.D. Burkhardt1, A. Natale1. 1Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Univ. of Texas and University of Foggia, Austin, United States of America; 2University of Kansas Medical Center, Kansas City; 3Heart Center Bad Neustadt, Bad Neustadt a.d. Saale, Germany; 4Elisabethiner University Teaching Hospital, Linz, Austria

Introduction: Periprocedural anticoagulation management with uninterrupted
warfarin with a “therapeutic INR” represents the best approach reducing both thromboembolic and bleeding complications in the setting of catheter ablation for atrial fibrillation (AF). The purpose of this study was to evaluate the safety and feasibility of uninterrupted apixaban administration in this setting.

**Methods:** We performed a prospective multicenter registry of AF patients undergoing radiofrequency catheter ablation at 4 institutions in USA and Europe with an uninterrupted apixaban strategy. These patients were compared with an equal number of patients, matched for age, gender and type of AF, undergoing AF ablation on uninterrupted warfarin. The apixaban group comprised consecutive patients who were on twice daily 5 mg Apixaban for at least 30 days prior to ablation. The last dose of apixaban was taken the morning of the procedure. A subset of 29 patients underwent dMRI to detect silent cerebral ischemia (SCI) in the apixaban group.

**Results:** A total of 1030 patients (200 patients in each group) were included in the study. The average age was 65.9±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. 3.8%, p=0.43) between the apixaban and the warfarin group respectively. There were no symptoms of 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.

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**P3385 | BEDSIDE**

**Rivaroxaban a new alternative to warfarin for atrial fibrillation ablation: a meta-analysis of embolic and bleeding complications**

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**Introduction:** Rivaroxaban (R) is being used more commonly pre and post-atrial fibrillation (AF) ablation due to its convenience. There are concerns that novel anticoagulants may be associated with more complications than warfarin (W). However, individual studies may be too small to accurately compare anticoagulation strategies given low procedural complication rates.

**Methods:** We conducted a meta-analysis of all published papers (n=3) and abstracts (n=5) to date and compared complication rates for peri-AF ablation use of R vs W (with or without heparin bridging). Bleeding complications included pericardial effusion, groin hematoma, and other bleeding; embolic complications included any clinical systemic embolism.

**Results:** The 955 pts on R were similar to the 1229 pts on W. R was not interrupted or stopped up to 48 hrs pre-procedure and restarted 3–24 hrs post-procedure; in 1030 (84%) pts, W was uninterrupted. Composite bleeding rates interrupted or stopped up to 48 hrs pre-procedure and restarted 3–24 hrs post-procedure; in 1030 (84%) pts, W was uninterrupted. Composite bleeding rates interrupted or stopped up to 48 hrs pre-procedure and restarted 3–24 hrs post-procedure; in 1030 (84%) pts, W was uninterrupted. Composite bleeding rates interrupted or stopped up to 48 hrs pre-procedure and restarted 3–24 hrs post-procedure; in 1030 (84%) pts, W was uninterrupted.

**Conclusions:** This meta-analysis demonstrates that R is a safe alternative anticoagulant for AF ablation. It is associated with no significant difference in bleeding or embolic events compared to W. However, more data is needed to determine the optimal time to discontinue and resume therapy. This data would inform the need and the design of the ultimate randomized trial of W vs R therapy.

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**P3386 | BEDSIDE**

**Ablation of atrial fibrillation I 565**

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**Background:** The new development of radiology-based ablation techniques renders percutaneous catheter ablation an important issue in cardiac electrophysiology. Aim of the study was to analyse the radiation usage in patients undergoing pulmonary vein isolation (PVI) and to evaluate the possibility to reduce radiation dose by optimized use of conventional fluoroscopy and 3D mapping system.

**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 cryoballon ablation.

**Conclusions:** Currently the median radiation exposure during PVI in Germany is 35 Gy*cm². Optimized fluoroscopy can reduce only the radiation dose to lower than 5 Gy*cm². Better introducing novel expensive technologies for fluoroscopy and 3D mapping result 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 cryoballon ablation.

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**P3387 | BEDSIDE**

**Ipsilateral pulmonary vein isolation using a new force-power-time formula reduces PV reconnection and improves outcomes in atrial fibrillation patients**

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**Introduction:** Contact force (CF) sensing technology reduces acute pulmonary vein (PV) reconnection and recurrence during the first year after PV isolation (PVI). The added value of formulas using CF, in combination with application time (Force-Time Integral, FTI) or CF with power and application time (Force-Power-Time Index, FPIT) in guiding PV ablation is unknown.

**Methods:** Eligible patients (n=100) with symptomatic paroxysmal atrial fibrillation (AF) were enrolled in this prospective trial, comparing ipsilateral PV CF sensing catheter with tip-integrated location sensor) guided by either FTI or FPIT. In the FTI group (n=50), radiofrequency (RF) was delivered until FTI reached at least 400 g/s; in the FPIT group (n=50), RF was delivered until FPIT reached targeted lesion depth (4mm posterior wall, 6mm anterior wall). In FTI group, FPIT values were lower than 5 Gy*cm². Better introducing novel expensive technologies for fluoroscopy and 3D mapping result 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 cryoballon ablation.
were unblinded 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. Isolateral 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 55%, p<0.001). A higher rate of PVI resistant to adenine (97% vs 85%, 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±24 min, p<0.0001). At 6 months follow-up, 8/30 (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 RF 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 PVI isolation by a single encirclement in 98% of veins. At 6 months follow-up, FPTI-guidance was associated with improved clinical outcome.

**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 substrate of atrial fibrillation and ablate perpetuating atrial re-entrant arrhythmias (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 (inter-electrode distance 1–2mm) was performed in 291 patients (218 male, age 66±11yrs) undergoing elective surgery during sinus rhythm (SR) and (induced) AF. Electrophysiological parameters within mapping quadrants covering the entire atrial epicardial surface were quantified and denoted in map units (SU) or cm².

**Results:** AF was non-inducible in 36 patients. Hemodynamic parameters (mean arterial pressure (MAP), right atrial pressure (RA), BIS score, ST-T segment alterations) before and during SR mapping were comparable (P>0.22). During AF, mean MAP (71±11 vs 67±10mmHg (p<0.001)) decreased. Total mapping time during SR or AF was respectively 3±1 min and 4±2 min. Beat-to-beat variation of SR cycle length and 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 catheter image integrated 3-dimensional electroanatomical mapping system**


**Background:** We explored whether a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping (F-EAM) system could result in a reduction 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 underwent 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 326–1401] cGy cm², p<0.001) in the EAM group were statistically significantly greater than those in the F-EAM group. The majority of reduction of fluoroscopy exposure was achieved after transpulmonary puncture, which was nearly zero-fluoroscopy exposure. In total, approximately 8% 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=0.382).

**Conclusions:** AF catheter ablation using a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping system was safe and resulted in a significant 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 acute 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 symptomatic, 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 ablation 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, post-procedural recovery patterns).

**Methods:** One hundred and ten patients (paroxysmal AF: 78 patients, persistent 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 segmental approach or a circumferential ablation strategy (CARTO; Biosense Webster) 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: 33 patients, 4 PVs: 16 patients). There was a slightly higher incidence of chronic PV reconnections related to the left-sided PV ostita 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 24 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 recovery of the PV-LA conduction of all four pulmonary veins. 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 PV isolation with 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 patients.

**P3391 | BEDSIDE**

**Cryoablation 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 success rates compared to the first Cryoballoon generation (CB) in the treatment of atrial fibrillation (AF). In this observational study, we aim to examine the impact of the LA surface area regarding the mid term freedom from AF after CBA vs. RF catheter ablation of persistent AF.

**Methods:** In total, 150 patients with symptomatic drug refractory persistent AF were controlled by matched pair 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 transeptal approach using second generation CryoSheath. Cryoballoon catheters were used in conjunction with intraumral multipolar mapping catheter. PVI with RF- catheter technique was performed as double transeptal Approach with 3 D mapping systems in RF- group wide antral circumferential ablation was performed. PVI as ablation endpoint was defined as complete elimination of all fragmented signals at PV antrum with verification of entrance- and exit- block. In 40 pts in RF-group 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 required at least 3 follow-up every 3 month in outpatient clinics with daily holter monitoring.

**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, fluoroscopy time was n.r.). 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 10 patients with RF and 2 patients with CBA reached primary endpoint (p<0.019). 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.

**Conclusions:** Novel CBA demonstrates favourable rates of clinical success with significantly higher patient 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.
Ablation of atrial fibrillation I / Ablation of atrial fibrillation II

P3392 | BEDSIDE
Catheter ablation of atrial fibrillation - Lessons from redo procedures
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Introduction: Pulmonary vein (PV) isolation is the cornerstone of catheter ablation of atrial fibrillation (AF) and may be extended by substrate modification in selected patients. More than one procedure is necessary in many patients.

Purpose: To explore electrophysiological and procedural findings as well as clinical outcome of AF ablation redo procedures.

Methods: The Leipzig AF Ablation Registry was screened for patients with redo procedures who had their first AF ablation between January 2008 and December 2011. Clinical, procedural, and follow-up data were analyzed. The ablation protocol in our institution consists of circumferential PV isolation in all patients. 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 76-Holters at 3, 6, 12 months, and yearly thereafter.

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. In 90%, 64%, 42%, and 0%, reconnection of at least one PV was found in the second, third, fourth, and fifth procedure (n=397, 87, 18, and 4, respectively). In 70%, 96%, 95%, and 100% respectively, additional modification was required. Freedom from AF/AT of patients with 2, 3, 4, 5 procedures was 66%, 58%, 71%, and 50% after a mean of 2.1, 1.6, 0.9, and 1.6 years, respectively. At least one severe complication occurred in 4.8% of patients.

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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Background: Pulmonary vein and coronary sinus isolation are both safe and feasible, though procedural outcome in humans is unknown.

Methods: 22 consecutive patients with longstanding persistent AF (mean age 62±7 years, 85% male, LA diameter 46±3 mm, AF duration 25±15 months, CHA2DS2-VASc score ≤ 2. Thrombi were encountered in 6 patients (0.9%); CHA2DS2-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 thrombi at p=0.041.

Conclusion: A simple clinical assessment may help to 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.

P3395 | BEDSIDE
A novel, safe and effective modality of treating persistent atrial fibrillation: concomitant left 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 percutaneous LAA (PVI) and LAA electrical isolation (LAAEI) on sinus rhythm and occlusion is both safe and feasible, though procedural outcome in humans is unknown.

Methods: 22 consecutive patients with longstanding persistent AF (mean age 62±7 years, 85% male, LA diameter 46±3 mm, AF duration 25±15 months, CHA2DS2-VASc score ≤ 2. Thrombi were encountered in 6 patients (0.9%); CHA2DS2-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 thrombi at p=0.041.

Conclusion: A simple clinical assessment may help to 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 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 catheter 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 duodacapolar catheter via the internal jugular vein to map the right atrium and the coronary sinus and place the absence of PV was present at the LV lead. In all cases 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 age- and sex-matched patients for sex, age and AF type that had CRT-D and underwent PV only ablation.

Results: The study population had a mean age of 63.9±13.5 years, 53% (82.8%) patients were male and all patients had non-paroxysmal AF. Mean LA size was 4.8±5.8 cm and moderate to severe left atrial scar was present in 67% of patients. Non-PV triggers were detected in 48 (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 15±6%±7 months follow-up, 42 (65.6%) 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 terminal mode (directly in SR, evolving into regular atrial tachycardia (AT) and subsequently into SR, or direct current (DC) cardioversion if PS after catheter ablation).

Methods and results: A systematic review was conducted in MEDLINE/PubMed and CochraneLibrary. In this meta-analysis were included randomized controlled trials, prospective cohort and observational studies including patients with PsAF in which AF terminal 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 1,798 patients. Mean follow-up was 26% (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, 73.7% (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.
tion), 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 cryoblation have 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 cryoblation after assessing the PV size and geometry by computer tomography. All cryoblation 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 intrathoracalegureal pressure or right phrenic nerve palsy occurred. If the PV potentials still remained, an extra application was delivered to that PV.

Results: In 76 (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 cryoblation is feasible and safe. The complete occlusion pattern of the pressure monitoring during cryoblation predicts an acute success for the PVI.
freedom from AF at 12 months FU for patients with paroxysmal indication, con-
sidering a blanking period (BP) of 3 months, was 67.8% (CI: 53.1–78.6%) in CB1
group and 77.8% (CI: 68.6–84.7%) in CB2.

Conclusions: The novel cryoballon Arctic Front Advance (CB2) has proven to
achieve, in a large clinical standard setting, significantly faster PVs times in com-
parison with the first-generation balloon, results also in lower acute procedural
complication rates and a 78% 1-year freedom from AF.

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 un-
derwent 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 pm-
larcision with a conventional approach. Activation time (ACT) was calculated using
invasive basket catheter导管. A 3-dimensional mapping system and circumferential mapp-
ing catheter were used. Voltage mapping using NAVX ensite (ST. Jude) software
with coronary sinus pacing around left and right pulmonary veins recorded. CPVA
ablation was then performed in regions of highest voltage in the antral regions in
a segmental fashion. The procedural endpoint was bidirectional block in each PV.

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 5±12 voltage points
were recorded for each PV antrum. The mean of maximum voltages areas per
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±2.4
vs. 33.6±17.7) and procedure times (233.8±31.6 vs 248.8±53.6) for the voltage
ablation were not different from control group (p>0.05). Voltage guided ablation
showed no superiority on widely used WACA in both isolation time and delay in
PV potentials during the procedure (p>0.05).

Full 24-hour holters were performed at 12 weeks in all pts. Recurrent AF > 30sec
duration was identified in 1/13 in Voltage guided ablation group and 5/20 in the
control group (p<0.05).

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
coupled with catheter contact sensing technology.

P3405 | BEDSIDE
The anticoagulant effect of heparin during radiofrequency ablation
(RFA) in patients taking apixaban and rivaroxaban
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Background: Measuring the anticoagulant effect of heparin during radiofre-
cuency ablation (RFA) in patients taking apixaban and rivaroxaban is challeng-
ing, since the activated coagulation time (ACT) does not seem to reflect the true
anticoagulant activity of these drugs. We therefore evaluated various coagula-
tion assays and compared the values with anti-factor Xa activity in order to better
guide intraprocedural heparin administration.

Methods: The study included 96 patients (mean age 61±12 years) who under-
went left atrial RFA procedures. All patients received 20 mg rivaroxaban once or 5
mg apixaban twice daily four weeks prior to the procedure. Dosage was modified
on the day of the procedure to 10 mg rivaroxaban or 2.5 mg apixaban twice daily.
During RFA, heparin i.v. was given to maintain an activated clotting time (ACT) of
270–300 seconds. Blood samples were before heparin administration, after 10,
60 and 360 minutes. Thromboplastin time (TPT), activated partial thromboplastin
time (aPTT), ACT and anti-factor Xa were measured.

Results: The anticoagulant effect of rivaroxaban was associated with an increase
in aPTT and ACT already before application of heparin. In contrast the effect of
apixaban was associated with an increase in TPT as compared to rivaroxaban.
As heparin dosage was led by the values of the ACT, patients with apixaban
received more heparin (IU/kg). This resulted in elevated anti-F xa levels in the
patients receiving apixaban as compared to rivaroxaban. However this was not
associated with an increase in bleeding complications.

Conclusion: We found variable responses of different FXa inhibitors rivaroxaban
and apixaban on global coagulation assays. This has to be taken into account
when performing ACT guided RFA.

P3406 | BEDSIDE
Relationship of lungs to left atrium in patients undergoing atrial
fibrillation ablation
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Background: The anatomic relationship between left atrium (LA) and lung tissue
(LT) has not been characterized. 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 under-
going 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 bronchi to LA regions commonly targeted during RFA of AF using
Osiris DICOM viewer.

Results: 100 patients (71 male, age 50±8 yrs, 46% paroxysmal, mean LA axial
255±5.5 cm²); 23% with LA enlargement, 33% with hypertension, 24% with
structural heart disease, 15% with obstructive coronary disease and 0% with ob-
structive 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 84%, minimum distance from LA endocardium to LT was 1.2±0.7 mm.
The right inferior PV ostum was -5 mm from LT in 94% (mean distance 2.4±0.8
mm). The right superior PV ostum 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 dis-
tance ±1.1 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 tho-
racic 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.

Conclusion: The lungs are intimately related to the LA in patients undergoing
RFA for AF. Whether LA RFA causes pulmonary complications merits further
study.

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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cular center, Osaka, Japan

Background: Reconstructions of isolated pulmonary vein (PV) is the major
cause of recurrence after ablation for atrial fibrillation (AF). In this study, we inves-
tigated the possibility that additional ablation on the ablation lines for PV isolation
(PVI) to obtain unreachability can reduce the reconstructions 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 to obtain unreachability by bipolar pacing at an out-
put 10 mA and 2ms pulse 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 ab-
lated to eliminate them. And then, we also checked that of ATP-dependent PVR
by injecting 0.4mcg/kg of adenosine triphosphates, 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<0.003).

Conclusion: The pace-and-ablate procedure after PVI could reduce the inci-
dence of PVR during procedure, and could improve the 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 theNavigStar RMT ThermoCool catheter guided by CARTO mapping and 30 with the Trigrum Fluor 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 60±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 new treated substratum to AF. Re-PVI was 80% vs 66.6% (P>0.30). Index procedure time (135.7±46.17 vs 182.89±68.46 min, P=0.006) and radiofrequency application time (424±4.5 vs 54.32±14.9 min, P=0.08) were longer in the Trigrum FluCA group; however, the respective total fluoroscopy time were similar (18.74±10.26 vs 28.57±14 min, P=0.48).

Conclusions: RMN guided ablation of PAF with the Trigrum Fluor 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 after multiple failed AF ablations (AA).

Methods: 21 pts (11 men, age 63±9 years), who had a recurrence of AA and undergo multiple RFCA (median 2, range 2–6) due to AF, were recruited in a prospective study. Bilateral voltage maps (endo/epi) were carried out. Low voltage zone (LVZ) was defined as bipolar amplitude <0.05mV and considered as unsuitable for RF ablation. If LVZ was present in either the left atrium (LA) or right atrium (RA) a dissection protocol was performed from RAA/LAA/CS. In case of spontaneous or induced AF, a successful atrial isolation/entrainment mapping was performed to locate the origin of the focus or reentrant circuit in order to eliminate AT.

Results: Re-PVI was performed in 11 pts (52%), SM 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 FO; 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 from IAG and 1 from epi roof of LA. Epi local capture in the vicinity of IAG was observed in a total of 17 patients, who received endo SL in LA and after endo confirmation of bidirectional block of SL. In 3 out of these 17 patients after receiving an epi SL, durations of pacing (beneath SL) to LAA were prolonged over 100 ms. Noninducibility was reached in all 21 patients. By the median 6 months of follow-up, 71% of patients remained in sinus rhythm without a significant increased major complication rate.

Conclusions: The combination of endo/epi RFCA aiming to recurrence of AA after multiple failed AF ablations may change the current concept of atrial ablation, especially for those who needs a 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.
for AF recurrence, while the annual rate of cardiovascular hospitalization was significantly lower in PAF vs PER (Rate*100pt/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 PTV (Pentamytr, Biosense) for ATs in the context of atrial fibrillation (AF) ablation.

**Methods:** All procedures using the PTV for AF, either during or persistent AF ablation were analyzed. A control group of number 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±50 points within 26±14 min were acquired per AT in the PTV 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 ishsthusms (n=25) were easily identified and ablated in the PTV (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±18 min versus 15±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 transcatheater 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) of patients 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±64.5 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 anesthesi related risk.

**Purpose:** We sought to determine the sedation levels with BIS monitoring in propofol sedation during AF ablation.

**Methods:** 50 consecutive patients (pts) (mean age 63±11 years, 24 male (69%), BMI 27.6±4.4 kg/m², mean CHA2DS2-VASc-Score 2.4±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 VISTATM, Covidien, Mansfield, 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 midazolam (mean 1.5±1.2 mg) bolus were administered. Mean procedural duration was 138.9±40.1 minutes. Mean BIS level was 48.4±7.7. Cumulative percentage of low BIS ≤45 (mean 36.6±7.0) was found in 44.0±28.8% of procedural time. No case of respiratory depression occurring required assisted ventilation occurred. Persistent 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-fluoroscopic sensor-based catheter navigation**

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**Introduction:** Nonfluoroscopic sensor tracking (NFST) within precorded x-ray loops offers the potential to perform catheter ablation of atrial fibrillation (AF) almost free from fluoroscopy use.

**Purpose:** Randomized comparison of standard AF ablation with or without NFST application.

**Methods:** Patients with AF were randomized into two groups before scheduled radiofrequency ablation: (1) catheter navigation using NFST 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 substrate 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 into 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.

**Conclusions:** Whether BIS guided monitoring during AF ablation procedures improves procedural outcome needs to be investigated.

<table>
<thead>
<tr>
<th>Procedure and follow-up</th>
<th>NFST group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroscopy time (min)</td>
<td>36.3</td>
<td>44.6</td>
<td>≤0.001</td>
</tr>
<tr>
<td>Fluoroscopy dose (Gy/cm²)</td>
<td>687±665</td>
<td>1899±1396</td>
<td>≤0.001</td>
</tr>
<tr>
<td>Procedure duration (min)</td>
<td>136±43</td>
<td>138±38</td>
<td>0.84</td>
</tr>
<tr>
<td>Radiofrequency time (min)</td>
<td>38±16</td>
<td>39±16</td>
<td>0.86</td>
</tr>
<tr>
<td>Add. substrate modification</td>
<td>6 (15%)</td>
<td>9 (23%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Periprocedural complications</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Success rate over 6-months</td>
<td>22/30 (73%)</td>
<td>18/22 (82%)</td>
<td>0.53</td>
</tr>
</tbody>
</table>
Conclusion: Radiation exposure can almost completely be abandoned from large parts of the procedure by using the novel NFST technology in addition to standard AF ablation technologies. “Lead-free” intervention following transeptal puncture is possible. This advantage can be achieved without the cost of negative consequences on procedure duration, risk, or clinical outcome.

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 explore 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 roof 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, a 3-D TEE was performed before the procedure to evaluate the PV morphology.

After discharge, patients were scheduled for repeated visits at the arrhythmia clinic at 1, 3, 6, 12, 24, 36, 48, 60 and 66 months after the ablation procedure.

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. Sixty-five out of 260 patients (25.0%) experienced an arrhythmia recurrence within the first 3 months after ablation requiring an electrical cardioversion. At 66-month follow-up, analysis of a 168-hour ECG recording revealed no evidence for an arrhythmia recurrence in 158/260 patients (60.8%). In 78/260 patients (30.0%), an AF recurrence within the first 3 months was classified as a recurrence of persistent AF (≥2 events per month). Sixty-five out of 260 patients (25.0%) experienced an AF recurrence within the first 3 months after ablation requiring an electrical cardioversion. At 66-month follow-up, analysis of a 168-hour ECG recording revealed no evidence for an arrhythmia recurrence in 158/260 patients (60.8%). In 78/260 patients (30.0%), an AF recurrence within the first 3 months was classified as a recurrence of persistent AF (≥2 events per month).

Conclusions: Catheter ablation of persistent AF can be performed safely and effectively using this ablation strategy (especially in patients with short-lasting persistent AF (<3 months)).

P3417 | BEDSIDE
Safety and feasibility of atrial fibrillation ablation in biological valve patients while on uninterrupted novel oral anticoagulant

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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: Patients were randomized to perform a first catheter ablation either through PVI alone or through PVI plus substrate modification based upon stepwise approach (CFAs and linear ablation). Data were recorded at 3, 6, and 12 months after both ablations. The subjects who experienced AF/AT recurrence were managed using the repeat ablation 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 occurred more frequently in patients treated with the stepwise procedure; 10/20 AT occurred in the stepwise group vs 4/33 in the PVI group. Adjusting for several potential confounders, the hazard ratio of 12-month AF/AT recurrence after the first ablation was 0.53 (95% Confidence Interval: 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 higher 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 ablation strategy. However, this approach had led to additive overall procedure and/or fluoroscopy times and more episodes of AT as compared PVI approach.

P3419 | BEDSIDE
Mitrail 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 perimittal flutter (PMF), 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 time in the LAA during pacing from the coronary sinus (CS).

Methods: 50 patients undergoing MI ablation (76 male, 61±8.1 years, Persistent AF: n=40). After a circular mapping catheter was positioned at the neck of the LAA, the MI ablation was performed at the earliest activation site of the LAA during pacing from the CS. The ablation catheter was equipped with a 3.5mm irrigated tip and utilized through a steerable sheath with a radiofrequency (RF) power of 35 W. When ablation by RF energy 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 the 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 in 22/26 patients (85%). Overall, complete conduction block at the MI was observed in 72/82 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 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, sensitherm, 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 mJ/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<0.05, 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 9.3±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**

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**Alims:** 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.

<table>
<thead>
<tr>
<th>Unipolar voltage (mV)</th>
<th>Bipolar voltage (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference voltage</td>
<td>Voltage close to ERP</td>
</tr>
<tr>
<td>Inferoposterior LA</td>
<td>2.64±1.04</td>
</tr>
<tr>
<td>Anterosuperior 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
Loss of contact force affects outcomes in atrial fibrillation ablation
Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic
Introduction: The pulmonary vein ablation catheter (PVAC) has been introduced to facilitate pulmonary vein isolation (PVI). Reconnection of pulmonary veins is considered to be the main source for recurrence of atrial fibrillation (AF) after ablation.
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 [111%, 72% male, mean age 58±6 years], undergoing redo procedure, were retrospectively evaluated. The mean time to redo procedure was 30±29 months. Redo procedure was analyzed for paroxysmal AF in 107 patients (65%), persistent AF in 55 (34%), permanent AF in 2 (1%). According to the ablation energy source 2 groups were identified: - Group 1: RF (143 patients, 87%); - Group 2: cryo (21 patients, 13%). Forty-five patients (27%), in whom the first procedure was realized more than 6 months after the first ablation, were analysed. The energy source of the first ablation was RF in 30 patients (87%) and cryo (first generation balloons) in 15 patients (33%).
Results: The use of cryo energy in the first procedure leaded to more frequent early AF redo procedure than the use of RF [respectively 26 patients (87%) vs 9 patients (60%), P=0.043]. On the contrary, using RF, reconnection was more frequent than using cryo in right inferior pulmonary vein (RIPV) [respectively 8 patients (53%) vs 7 patients (23%), P=0.044], and showed a trend of greater reconnection in left inferior pulmonary vein (LIPV) [respectively 26 patients (87%) vs 9 patients (60%), P=0.043].
Conclusions: Early redo procedures for AF after PVAC ablation had reconnection of at least one vein. Right PVs and a left common os are more likely to show conduction recovery. Reconnection occurs at a high incidence at the ridge between left atrial appendage and left PV ostia and at the posterior aspect of the right PVs. Prevalent sites of reconnection should attract special interest during PVI using the PVAC catheter. Standard use of a steerable sheath may help to improve durability of PVI.
Objective: We investigated hs Tropin utility and predictive value in patients with atrial fibrillation (AF) in the acute setting.

Methods: We studied 2038 consecutive patients undergoing coronary angiography between July 2013 and October 2014. In patients with ACS cardiac biomarkers (hs Troponin, Troponin T and cardiac creatinine) were obtained on presentation and if need again after 3–6 hours. In patients with Non ST-segment elevation myocardial infarction (NSTEMI) 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.

Conclusion: The diagnosis of ACS in patients with NSTEMI and AF on presentation revealed a rate of 28% (25/90) without significant stenosis. Hs Troponin was elevated in 60 of the 90 patients (74%) with a mean hs Troponin of 295±300. CK was elevated in 82 of 90 patients (91%) with a mean CK of 629±350.

P3429 | 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 on prognosis. With acute coronary plaque rupture and thrombosis the prognosis, despite adequate care, is worse than in other acute cardiac situations, e.g. takotsubo cardiomyopathy, where no epicardial coronary lesion is present. However, these situations are often indistinguishable in the emergency department by noninvasive methods.

Purpose: We hypothesised that inflammatory mediators matrix metalloproteinase-8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) would be of prognostic value in acute cardiac disease.

Methods: Serum samples were obtained in conjunction with coronary angiogram (CA) in 2072 successive patients scheduled for acute CA on clinical basis. Reperfusion was attempted in patients with NSTEMI and AF on presentation revealed a rate of 28% (25/90) without significant stenosis. Hs Troponin was elevated in 60 of the 90 patients (74%) with a mean hs Troponin of 295±300. CK was elevated in 82 of 90 patients (91%) with a mean CK of 629±350.

Conclusion: These data are the first to show that AF in the acute setting is frequently associated with hs troponin. One third of the patients showed no need of an intervention. These findings are of clinical decision making importance. Concentrations of patients with acute AF and myocardial ischaemia symptoms. Appropriate clinical guidelines must be established that also consider AF-related elevations in hs Troponin.

P3431 | BEDSIDE
Inflammatory mediator TIMP-1 is a prognostic marker for mortality in acute coronary syndrome without chest pain: in-hospital and 1-year prognosis

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Background: Chest pain is the most frequent symptom reported with Acute Coronary Syndromes (ACS). Its absence can sometimes mean a delay in the ACS diagnosis and have a negative influence on the clinical outcome. Patients who develop AHF during hospitalisation of patients with ACS presenting without chest pain, regarding in-hospital and 1-year follow up morbidity and mortality.

Methods: Prospective study of 1051 consecutive patients, diagnosed with ACS, presenting with chest pain during hospitalisation 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%; women).

Results: In group B, patients were older (B=71.65 years, DP=12.38 vs A=64.58 years, ±13.22, p<0.01) and had higher creatinine (B=1.52 mg/dL, DP=0.82 vs 1.24 mg/dL, ±0.85 p<0.01) and BNP levels (B=1162.86 pg/mL, DP=1118.03 vs 435.00, ±642.42 pg/mL, p<0.01) at admission. Killip class I was also more prevalent in group B (66.1% vs A=18.4%, p<0.01). They were more often diagnosed with non-ST elevation myocardial infarction (B=57.9% vs A=44.2%, p<0.01). Regarding in-hospital stay, group B patients had higher degree of negative outcomes (cardiogenic shock (B=14.6% vs A=5.5%, p<0.05), ischemic arhythmias (B=21% vs A=13%, p<0.01), cardio-respiratory arrest (B=14.6% vs A=5.2%, p<0.05)). Overall in-hospital death was also higher in group B (B=14.6% vs A=5.0%, p<0.01) as well as the primary composite endpoint (B=28% vs A=14.1%, p<0.01) in group B.

Conclusion: Patients who presented without chest pain had an overall higher rate of negative clinical outcomes.

P3432 | BEDSIDE
Myocardial injury 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 situation of 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) dyspnoea at rest or during minimal physical effort; 2) pulmonary congestion documented 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 (AHF+ vs AHF−) 71% vs 35%, OR=3.55; 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.

Conclusion: 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. Find CKD. Despite of having coexisting AHF and AMI, have poor in-hospital and postdischarge outcome.

Acknowledgement/Funding: Statutory grant ST-723 (Department of Heart Diseases, Wroclaw Medical University, Wroclaw).
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 unnecessary hospital admissions.

**Purpose:** To define the prevalence of myocardial injury in consecutive patients attending 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 third-generation cardiac troponin I assay in all patients, but only reported where requested by the attending clinician. Clinical characteristics, diagnosis, and outcomes 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 syndrome (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 3.35 [95% confidence interval 1.20–1.53] per doubling of troponin concentration). 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 compromise 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**

V. Kanic1, M. Volırath2, R. Ekart1, S. Becv1, B. Dvorsak1, Z. Kanic1, R. Hojs1.

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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 patients 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 were observed. Median follow-up time was 363 days (25th, 75th percentile: 2, 958). Kaplan-Meier estimation was used for unadjusted survival. Cox proportional analysis was used to establish possible independent predictors for in-hospital and long-term mortality. We controlled for age, gender, TIMI-flow before and after PCI, PCI of left main coronary artery, PCI of LAD, PCI of RCA, multi vessel PCI, drug eluting stents, GPI use and RD at admission. Distributions of continuous variables in the 2 groups were compared with the 2-sample t test. Distributions of categorical 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 ventilation 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**

**Angiographic findings and survival in patients undergoing coronary angiography after out-of-hospital cardiac arrest in Western Sweden**


**Background:** Sudden cardiac arrest (SCA) accounts for more than half of all deaths from coronary heart disease. Time to return of spontaneous circulation is the most important determinant of outcome but successful resuscitation also requires percutaneous coronary intervention in selected patients. However, proper selection of patients is difficult.

**Purpose:** We describe data on angiographic finding and survival from a prospectively followed SCA patient cohort.

**Methods:** We merged the RIKS-HIA registry (Register of Information and Knowledge About Swedish Heart Intensive Care Admissions) and SCAAR (Swedish Coronary Angiography and Angioplasty Registry) for patients hospitalized in cardiac care units in Western Sweden between January 2005 and March 2013. We performed propensity score-adjusted logistic and Cox proportional-hazards regression analyses on complete-case data as well as on imputed data sets.

**Results:** 638 consecutive patients underwent coronary angiography due to SCA. Severty of coronary artery disease was similar among SCA patients and patients undergoing coronary angiography due to suspected coronary artery disease (n = 37142). An acute occlusion was reported in the majority of SCA patients and was present in 37% of patients who did not have ST-elevation on the post resuscitation ECG. 31% of SCA patients died within 30 days. Long term risk of death among patients who survived the first 30 days was higher in patients with SCA compared to patients with acute coronary syndromes (p < 0.001).

**Conclusions:** Coronary artery disease and acute coronary occlusions are common among patients who undergo coronary angiography after sudden cardiac arrest. These patients have a substantial mortality risk both short- and long-term.
P3436 | BEDSIDE

Optimal blood pressure for favourable neurological outcome in adult patients following in-hospital cardiac arrest

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Background: The blood pressure over the first 24 hours following resuscitation is important in neurological recovery for patients sustaining transient brain ischemia.

Purpose: To investigate the relationship between blood pressure and neurological outcomes of patients resuscitated following cardiac arrest.

Methods: This was a retrospective observational study, from a single medical center, of adult patients between 2006 and 2012 who had in-hospital cardiac arrest and achieved sustained return of spontaneous circulation (ROSC). Multivariable logistic regression analysis was used to identify factors associated with a favourable neurological outcome at hospital discharge. Maximal mean blood pressure (MBP) during the initial 24 hours after sustained ROSC was used for analysis.

Results: Of the 319 study patients, 93 (29.2%) survived to hospital discharge and 56 (17.6%) achieved a favourable neurologic outcome. The mean MBP was 95 mm Hg. MBP above 85 mm Hg was found to be correlated with neurological outcome. There may be a threshold blood pressure value of 88 mm Hg (OR 4.04, 95% CI 1.41–13.03) above which there is increased risk of cerebral injury. MBP between 85 and 115 mm Hg (OR 8.80, 95% CI 3.13–28.55); 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 value that is important in neurological recovery for patients sustaining transient brain ischemia.

Acknowledgement/Funding: This study was funded by the academic research branch.

Background:

To investigate the relationship between blood pressure and neurological outcome. The optimal blood pressure is important in neurological recovery for patients sustaining transient brain ischemia.

Methods:

To investigate the relationship between blood pressure and neurological outcome in adult patients following in-hospital cardiac arrest. Maximal mean blood pressure (MBP) during the initial 24 hours after sustained ROSC was used for analysis.

Results:

Of the 319 study patients, 93 (29.2%) survived to hospital discharge and 56 (17.6%) achieved a favourable neurologic outcome. The mean MBP was 95 mm Hg. MBP above 85 mm Hg was found to be correlated with neurological outcome. There may be a threshold blood pressure value of 88 mm Hg (OR 4.04, 95% CI 1.41–13.03) above which there is increased risk of cerebral injury. MBP between 85 and 115 mm Hg (OR 8.80, 95% CI 3.13–28.55); 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 value that is important in neurological recovery for patients sustaining transient brain ischemia.

Acknowledgement/Funding:

This study was funded by the academic research branch.

P3437 | BEDSIDE

Clinical profile, treatment, and outcomes of patients with type B acute aortic syndromes: findings from a large multicenter Italian registry

G. Norscini1, T. Piva2, G. Melandri 1, C. Rapezzi1, G.P. Perna2.

Background:

The outcome of AAS Italian patients enrolled in AESA 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 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 in line with that reported by the current international literature.

Methods:

To assess the epidemiological characteristics, clinical presentation, diagnostic strategies, treatment, and outcome of patients with type B Acute Aortic Syndrome (AAS).

Results:

AESA registry enrolled 190 patients with Type B AAS: 122 (65%) with DA, 49 (25%) 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 (52%), abdominal pain (39%), malignant pain (14%), 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% 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%, 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 AESA 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.

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 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 month.

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 per-procedure myocardial injury (23.6% vs 35.7%, P<0.05). At follow up of 6 month, intensive statin treatment also reduced MACE (6.8% vs. 12.2%, P<0.05). Both group had similar incidence of hepa-totoxicity (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=0.06). 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 peri-procedural myocardial injury and MACE at no cost of safety.

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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.

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Conclusions:

Intensive statin treatment pre PCI in elderly Chinese patients can reduce peri-procedural myocardial injury and MACE at no cost of safety.
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).

Conclusions: Two-year clinical outcome of BES is similar to that of EES in patients with bifurcation lesions.

**P3440 | BENCH**
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 (CUTLR), 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 independently of the RISK and SAFE pathways. STAT5 seems to be a unique signaling marker of PerC in rabbits, and to further elucidate its mechanisms.

Methods: Anesthetized rabbits were subjected to 30-min ischemia (isic) 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 AT1 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 assessment.

Blood samples were drawn at baseline and at rep for malondialdehyde (MDA) and nitrotyrosine (NT) assessment. Results: The inhibition of JAK-2, Src and ATC did not abrogate the infarct size limiting effects of PerC (29.3±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). STAT5 was activated in PerC groups independently of the presence of AG, whereas no STAT5 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 an inverse 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 myofibroblast-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 myofibroblast-count.

Results: LV dimensions were smaller and ejection fraction (EF) was higher after alginate-GH compared to alginate alone. Increased neo-vascular density and myofibroblast-count were found in the infarct and peri-infarct areas after alginate-GH (Table).

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<th>Control</th>
<th>Alginat e-GH</th>
<th>Alginat e-restrai nt</th>
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</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>
</tr>
<tr>
<td>ESD (mm)</td>
<td>2.55±0.47</td>
<td>4.28±0.95</td>
<td>4.58±0.38</td>
<td>3.12±0.21**</td>
</tr>
<tr>
<td>ESD (mm)</td>
<td>6.27±0.24</td>
<td>4.03±0.47</td>
<td>5.50±1.71**</td>
<td>3.89±3.23</td>
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<td>EF (%)</td>
<td>46.4±0.34</td>
<td>6.27±0.24</td>
<td>3.61±0.44</td>
<td>3.76±0.44</td>
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<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>
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<tr>
<td>Angiogenesis (%)</td>
<td>0.05±0.05</td>
<td>0.05±0.05</td>
<td>3.88±1.11</td>
<td>3.88±1.11</td>
</tr>
</tbody>
</table>

Data are mean ± SD. EDD, end diastolic dimension; ESD, end systolic dimension; EF, ejection fraction. **p<0.01 vs control; †p<0.01 vs control, *p<0.05 vs control, ‡p<0.05 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 neovascularization and myofibroblast-density in the peri-infarct area.

Acknowledgement/Funding: ADV, EB, MK were supported by a scholarship from the Experimental Research Center ELPEN (Greece)

**P3443 | BENCH**
Vasoparotin peptide inhibits endoplasmic reticulum stress and attenuates 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 unclear. Our study is focused on the effects of vasoparotin peptide – natriuretic 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 VNP 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 VNP (10–8 mol/L).

Results: The diabetic state aggravated MI/R injury and showed more severe myocardial functional impairment than normal state. VNP treatment significantly improved ±LV dp/dtmax and LVSAP, reduced LVEDP, and decreased infarct size, apoptosis index, caspase-3 activity, serum CK and LDH levels (n=8, P<0.05). Moreover, VNP 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 analog, while 8-BrcGMP (1 mg/kg, i.p., 20 min before R), the selective inhibitor of PKG. Moreover, pretreated DM rats with TUDCA (50 mg/kg, i.p.), a specific inhibitor of ER stress, couldn’t further promote the VNP’s cardioprotective effect. In additional experiments, H9c2 cardiomyocytes were subjected to hypoxia/reoxygenation (H/R, 3 h/6 h) and incubated with or without VNP in vitro. Gene knockdown of PKG1α with siRNA blunted VNP’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: VNP protects diabetic heart against MI/R injury by inhibiting ER stress and apoptosis. Gene knockdown of PKG1α with siRNA blunted VNP’s inhibition of ER stress and apoptosis (n=6, P<0.05), while overexpression of PKG1α resulted in significant decreased ER stress and apoptosis.

Acknowledgement/Funding: Supported by the NSF (81270330 and 813000190) and the Shaanxi Province S & T Program (2013KXX-89).

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 diabetes 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 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 Pentobarbitone 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 larger IS (53±1.8% and 65±4.2% respectively, p<0.05) as compared to 11mmol Glucose. The non-selective SGLT inhibitor Phlorizin to inhibit glucose uptake in non-diabetic SDR hearts reduced IS with 22mmol Glucose to 37±5.8% and had no effect on IS with 11mmol Glucose. Moreover, we demonstrated for the first time that this excess injury can be abolished in diabetic heart, reflecting established epidemiological outcome data in AMI. We have now analyzed the temporal kinetics of cardioprotection by tetrazolium chloride-based planimetry.

Conclusion: 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 the NSF (81270330 and 81300190) and the Shaanxi Province S & T Program (2013KXX-89).

P3446 | BEDSIDE
 Oxidative DNA damage in acute myocardial infarction

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Background: Oxidative damage of DNA in acute myocardial infarction is caused by free oxygen radicals excessively released at reperfusion. We evaluated possibility of using comet assay method for measurement of oxidative DNA damage in patients with acute myocardial infarction.

Methods: Comet assay measure DNA damage and repair in peripheral leukocytes, oxidized pyrimidines with endonuclease III (ENDO III) and oxidized purines with formamidopyrimidine-DNA glycosylase (FPG).

Results: Blood samples were obtained from 23 patients with STEMI, before and after primary PCI from aorta and coronary sinus, with follow up 6, 12 and 24 hours. After 30±6 min. upper-limb blood pressure cuff inflation and 5 min deflation. Venous blood samples were obtained at baseline before RIPC and after 30 min, 1, 6 and 24 hours and daily up to 7 days. Isolated mouse hearts were mounted on a Langendorff apparatus and perfused at a pressure of 100 mmHg with modified Krebs-Henseleit buffer (37°C) before undergoing 20 min global ischemia and 120 min reperfusion. Before ischemia, the hearts were perfused for 15 min with dialysed plasma (cut off 12–14 kDa, 1:20 dilution). Infarct size was assessed by TTC-staining. Infarct size over time was analyzed using one-way repeated measures ANOVA.

Results: Dialysates from healthy volunteers undergoing RIPC reduced infarct size in the bioassay hearts no later than after 30 min after the completion of the manoeuvre. The cardioprotective effect lasted for at least 6 days and vanished thereafter.

Conclusion: 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
M.C. Barsotti1, L. Botta1, T. Santoni1, F. Felice1, S. Burchielli2, A. Puccio2, A.M. Piras4, F. Chiellini3, R. Solari5, R. Di Stefano1, 1University of Pisa, Department of Surgical, Medical, Molecular and Critical Area Pathology, Pisa, Italy; 2Fondazione Santa Cristina G. Monasterio, Pisa, Italy; 3University Hospital, Histopathology Department, Pisa, Italy; 4BIOLab - UdR INSTM - Department of Chemistry and Industrial Chemistry - University of Pisa, Pisa, Italy; 5University of Pisa, Department of Chemistry and Industrial Chemistry, Pisa, Italy
Background: Endothelial progenitor cells (EPCs) contribute to ischemic repair by paracrine factor secretion, with hypoxic stress up-regulating factors related to vessel repair. No in vivo test of conditioned medium (CM) has been demonstrated effective for ischemic tissue revascularization. Nanoparticles (NPs) for controlled release in ischemia might represent a further improvement. Purpose: To characterize the in vivo effect of hypoxic EPC-CM-loaded NPs, comparing it to hypoxic EPC-CM.
Methods: EPCs were obtained from peripheral blood of healthy donors and cultured for 24 h at 1%O2 in growth factor- and serum-free medium to obtain CM. 36 rats were divided into 3 groups: control (vehicle), EPC-CM, EPC-CM NPs. For each animal, 500 μL injections were performed at 3 sites into the ischemic hindlimb, immediately after ischemia and after 1 week. The effect of ischemia was evaluated both using Laser Doppler Blood Flow imaging (ratio between ischemic and contralateral limb), histology (hematoxylin/eosin, H&E, staining) to evaluate the neovascularization and immunohistochemistry to evaluate capillary (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. control (p<0.05) and CM-NP vs. CM (p<0.05). In control, tissue showed signs of ischemia but main vessels were preserved, while in 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<0.005 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 arteriogenesis. Use of controlled release in 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
P. Jakob1, D. Heg2, R. Klingenberg1, N. Rodondi3, P. Vogt4, F. Mach5, S. Windecker5, C.M. Matter1, T.F. Luescher1, U. Landmesser1, 1University Hospital Zurich, Cardiovascular Center, Department of Cardiology, Zurich, Switzerland; 2University of Bern, Institute of Social and Preventive Medicine (ISPM), and Clinical Trials Unit, Department of Clinical, Bern, Switzerland; 3Bern University Hospital, Emergency Clinic, Department of Medicine, Bern, Switzerland; 4University Hospital Centre Vaudou (CHUV), Department of Cardiology, Lausanne, Switzerland; 5Geneva University Hospitals, Cardiovascular Center, Department of Cardiology, Geneva, Switzerland; 6Bern University Hospital, Cardiovascular Center, Department of Cardiology, Bern, Switzerland
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 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 into the circulation in pathophysiological cardiovascular processes, such as in patients with acute myocardial infarction, has been observed and selected circulating miRNAs (c-miRNAs) have been tested for their potential as biomarkers. However, an array based screening of c-miRNA-levels in a multi-center prospective cohort with patients presenting with an acute coronary syndrome (ACS) 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. Levels of 752 c-miRNAs were then analyzed in plasma samples. On average, 290 c-miRNAs were detected per sample, with 92 c-miRNAs detectable in all samples. Importantly, 13 c-miRNAs were significantly altered (p<0.05) in patients presenting with STEMI and experiencing a MACE as compared with patients without MACE at 1 year FUP. c-miRNAs significantly associated included c-miR-18, c-miR-15 and c-miR-19a, 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 ability to predict MACE.
Acknowledgement/Funding: Swiss National Foundation - SNF

P3449 | BEDSIDE
The difference in rates of postprocedural ischemia in side branch and main branch after coronary bifurcation stenting detected with intracoronary electrocardiography
D.V. Vassilev1, K. Karamfilov1, R.G. Gil2, G.R. Rigitalle3, 1University Hospital Alexandrovska, Cardiology, Sofia, Bulgaria; 2Clinical Hospital of the Ministry Of National Defence Affairs, Cardiology, Warsaw, Poland; 3General Hospital of Rovigo, Rovigo, Italy
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 (ieECG) and the exploration of causation mechanisms.
Methods: After placement of intracoronary guidewires in the main branch (MB) and side branch (SB) of the coronary bifurcation, the residual ischemia in MB was expressed and compared with hypoxic EPC-CM. EPC-CM-NPs were loaded for the treatment of ischemia. Under the assumption that the main branch is the culprit vessel, SB ostial stenosis was detected with the un insulated proximal wire ends were connected to unipolar V leads. Intracoronary unipolar ECGs were recorded before, during and after stent placement and at the end of the procedure. The maximal ST elevation during intervention and 5 min after the procedure was recorded in SB and MB. After PCI, the coronary wire was placed in every distal vessel with reference caliber >1.0mm, 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 ieECG was 12±9 mm in MB and 8±7 mm in SB (p=0.044). At the end of the procedure, the distribution of ieECG 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 ieECG were the ratio of R/S waves at the beginning of PCI in main branch OR (3.584, 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 TSSTC 14.2% vs. STC 16% (p=0.031). However, the significant association between the MB residual ischemia and STC could be due to small SB residual ischemia.
Conclusion: The end-procedural PCI 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: N. Keles1, M. Caliskan2, B. Dogan2, N.N. Keles1, F. Aksu1, O. Kostek2, B. Isilden4, A. Ozgu2, 1SB Goztepe Hospital, Cardiology, Istanbul, Turkey; 2SB Goztepe Hospital, internal medicine, Istanbul, Turkey, Turkey; 3ottu government hospital, erzurum, Turkey; 4SB Goztepe Hospital, biochemistry, Istanbul, Turkey
Background: The aging suppressor gene klotho encodes a single-pass transmembrane protein that is released into plasma as its N terminal fragment (NO) and to protect against endothelial dysfunction. In some recent trials, showed that higher klotho levels is associated with lower cardiovascular disease prevalence. Epidermal fat thickness (EFT) and cutaneous intima-media thickness (c-IMT) that are clinically related to subclinical atherosclerosis. Flow-mediated dilatation (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. 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 (0.30–0.60), p=0.03) and c-IMT (0.80 (0.60–
Background: Acute chest pains without troponin raise are particularly challenging in patients with past medical history of coronary artery disease (CAD).

Methods: We analysed retrospectively 1149 STEMl 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 frequent women (19 vs 30.4%;p=0.014) and had higher prevalence of hypertension (57 vs 71.7%;p<0.008). On admission, group 2 presented more often Killip >1 (18 vs 42.4%;p<0.001), cardiogenic shock (2.9 vs 23.1%;p<0.001), anaemia (20.7 vs 39.8%;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% vs 29.3%;p<0.001). They required more often amnion support (4.3 vs 6.6%;p<0.001), intra-aortic balloon pump (4.3 vs 6.6%;p<0.001) and mechanical ventilation (2.6 vs 14.5%;p<0.001). They also had higher prevalence of malignant 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 admission 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 pacemaker more frequently (71.4 vs 60.3%), presented more often KCS (71.4 vs 37.2%;p<0.001), left ventricular dysfunction (10 vs 34.8%;p<0.001), but less right ventricular dysfunction (7.1 vs 28.4%;p<0.001). Compared with IMI pts, AMI pts had higher risk of in-hospital [OR 9.04, 95% CI (2.87–28.50);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].

Conclusions: 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.

**Discussion**

HABV is associated with poor outcome in patients presenting with chest pain and negative ECG for myocardial infarction. The prognosis is adversely affected by increased prevalence of high-risk features. The incidence is 9.6/100000/year in Europe and 3.2/100000/year in the USA, with a mortality of 6–10%.

HABV could be a potential marker for ongoing myocardial ischaemia, cardiac function and haemodynamic impairment.
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 or pathological evidence of NOMI.

Results: 2456 patients between 1991 and 2014 were included into the analysis. Thirteen patients (0.5%) suffered from NOMI and 7 of those died (54%).

Patient characteristics

<table>
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<th>Post-op</th>
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<td>15 (41.7)%</td>
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<td>12 (34.3)%</td>
<td>10 (28.6)%</td>
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<td>22 (62.9)%</td>
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<td>13 (37.1)%</td>
<td>11 (31.4)%</td>
<td>8 (22.9)%</td>
<td>6 (17.1)%</td>
<td>3 (8.6)%</td>
<td>1 (2.9)%</td>
</tr>
<tr>
<td>2013</td>
<td>34</td>
<td>20 (58.8)%</td>
<td>14 (41.2)%</td>
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<td>14 (41.2)%</td>
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P3455 | BEDSIDE
Effective heart rate control by ivabradine in patients with acute heart failure
J. Treptau1, O. Jeske1, L.C. Nappi1, A. Menon1, B. Schiefer2, A. Schaefer1, J. Bauersachs1, J. Tongers1, Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany; 2Philips University of Marburg, Department of Cardiology, Marburg, Germany

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 β-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 yrs, 49 males vs. 20 females) acutely with ivabradine (2.5 to 5.0 mg twice a day on standard care dose). Following admission patients were allowed a run-in period of 20 min, p<0.05 vs. hospital discharge, 79±16 bpm, p<0.01) without hemodynamic alteration (systolic/diastolic blood pressure at discharge: 111±16/63±10 mmHg).

Discuss: NOMI is 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. CCRP, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; PEA, pulseless electrical activity.

P3457 | BEDSIDE
Acute coronary syndromes without chest pain: a high risk group?
P. Magalhaes, S. Leao, F. Cordeiro, P. Mateus, S. Carvalho, J.I. Moreira on behalf of National Registry of Acute Coronary Syndromes. Hospital of Vila Real, Dept. of Cardiology, Vila Real, Portugal

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 ACS pts without chest pain (WOCPC) 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 clinician’s diagnosis and in-hospital mortality (IHM). 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 WOCPC were mostly males (57.2%) and significantly older, more frequently diabetic and hypertensive and with a higher prevalence of previous heart failure (24.2%) and syncope (21.9%). Time to first medical contact was similar between groups but time from symptoms onset to admission (TSHA) and time from first medical contact to admission were significantly higher in pts WCP (median 289 vs 191 min, p<0.001) and 194 vs 110 min, p<0.001 respectively. 2–3 vessel disease was more frequent in this group (60.7% vs 45.9%, p<0.001) and they were less likely to undergo reperfusion therapy (41.0% vs 67.4%, p<0.001). During hospitalization pts WCP had more frequently HF (42.3% vs 14.1%, p<0.001), atrial fibrillation (10.7% vs 4.8%, p<0.001), stroke (2.4% vs 0.7%, p<0.001), major bleeding (3.1% vs 1.4%, p<0.001) and higher IHM (11.2%).

Discussion: In this study, the main indication for WOCP use remains patients with poor LV function undergoing elective or urgent CABG surgery. A decrease in WCP 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.
complications 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 myocardial 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 outpatients 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-cytometry in order to evaluate peripheral EPC levels (EPC/ml). Tissues (CD34+VEGFR2+) levels were assessed on a right anterior oblique 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 23% 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 patients. Conclusion: Patients with ischemic heart disease have higher EPC density value (EPC/mm²) and are more likely to have lower EPC blood levels when compared with no CAD patients. Furthermore, the differences in EPC level suggest that stable ischemic heart disease has an impact on EPC level both in tissue and blood.

P3459 | 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.

Conclusions: We investigated the effects of global RANKL inhibition and selective inhibition of RANKL derived from different cellular sources on post-ischemic cardiac function and remodelling.

Methods: MI was induced by permanent ligation of the left descending coronary artery. We established a model of selective inhibition of RANKL from hematopoietic and mesenchymal cellular sources, we exploited the specificity of the monoclonal anti-human RANK 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 unfractionated bone marrow leads to engraftment of hematopoietic, but not mesenchymal precursors. 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 increased 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 untransplanted 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-1β 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

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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 dosing of IC adenosine as well as to determine minimal side-effects and above which no further increase in flow can be expected.

Methods: In 30 patients, Doppler-derived flow velocity measurements were obtained in 10 right coronary arteries (RCA) and 20 left coronary arteries (LCA) free and after IC bolus injection of 2 μg adenosine infused as a serial dose in 4 steps (0, 2, 6 and 8 μg) with measurements performed before and after each dose. The primary endpoint was a 50% increase in the hyperemic index (HI). The secondary endpoints were the maximum increase in HI and the maximal hyperemic flow velocity reached in a given artery (Qmax, %).

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Results: QOmax 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 atrioventricular blocks was 40% after injection of 100 μg in the RCA, and was 15% after injection of 200 μg in the LCA. The epicardially attached miniaturized 3D accelerometer enabled 3D accelerometer vs tissue lactate

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.

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P3463 | BEDSIDE
Low molecular weight dextran usage in intracoronary imaging guided percutaneous coronary intervention was associated with high incidence of filter no re-flow phenomenon
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Background: Intravascular frequency-domain optical coherence tomography (OCT) image acquisition with low molecular weight dextran L (LMD-L) could reduce the total amount of contrast media without loss of image quality. LMD-L is a highly viscous solution, however, there were no data about the influence of LMD-L on the PCI with filter distal protection device.

Purpose: The purpose of this study was to evaluate whether LMD-L has negative effect on PCI with a filter distal protection device or not.

Methods: We retrospectively reviewed consecutive 110 patients who underwent PCI with a filter distal protection device. They included 43 cases of acute myocardial infarction with ST elevation (39.1%), 34 cases of non-ST elevation acute coronary syndrome (30.9%), and 33 cases of stable angina (30%). We included proximal to the anastomosis. Flow in LIMA was stepwise reduced by 25% from 100% (BL) to 75%, 50%, and 25% for 18 min each. From the 3D accelerometer signals peak systolic velocity was obtained by time integration of the acceleration signals. The reference method to detect myocardial ischemia was assumed proximal to the anastomosis. Flow in LIMA was stepwise reduced by 25% from 100% (BL) to 75%, 50%, and 25% for 18 min each. From the 3D accelerometer signals peak systolic velocity was obtained by time integration of the acceleration signals. The reference method to detect myocardial ischemia was assumed proximal to the anastomosis. Flow in LIMA was stepwise reduced by 25% from 100% (BL) to 75%, 50%, and 25% for 18 min each. From the 3D accelerometer signals peak systolic velocity was obtained by time integration of the acceleration signals. The reference method to detect myocardial ischemia was assumed proximal to the anastomosis.

Conclusions: LMD-L usage might facilitate a filter no re-flow phenomenon in OCT-guided PCI. When we use LMD-L in conjunction with a distal protection device, we should pay attention for the possibility of filter no re-flow phenomenon.

P3464 | BENCH
Human mesenchymal stem cell (hMSC)-derived exosomes upregulate Bcl-2, a cross talk between apoptosis and autophagy, reducing ischemia / reperfusion injury
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Purpose: Evidence suggests the beneficial effects of MSC-based therapy is mediated via paracrine effects, e.g. exosome (Exo) release, rather than direct MSC differentiation and integration in injured tissues. exosome-derived Exo have potent cardioprotective effects in multiple ex vivo and in vivo animal models. However, little is known of role in regulating apoptosis and no reports exist on any potential role regulating autophagy.

Methods: Myoblast H9c2 cells underwent 16 hr 0.2% O2 hypoxia/2 hr re-oxygenate culture (H-R). Cells were treated with 1μg/ml Exo, 3-MA or rapamycin (Rapa); a known anti- or pro-autophagic agent. Cell viability WST assay, cell injury-induced LDH release, a flow-based apoptosis assay and GFP-LC3 labeled autophagosomes were measured. Isolated hearts underwent 20 min ischemia/60 min reperfusion (I/R); with or without Exo. Cardiac function was monitored throughout and LDH release was measured during reperfusion. Both H9c2 cells and isolated hearts were collected for WB analysis.

Results: Exo reduced I/R injury as indicated by higher cell viability, WST activity and reduced LDH and apoptosis (Exo vs. H-R, p < 0.05). 3-MA showed similar protective effects. Rapa-induced injury was partially blocked by Exo. Increased cardiac functional recovery by ~2-fold (vs. I/R) and reduced LDH release. WB from both H9c2 and tissue demonstrated that Exo increased the LC3-II ratio and p62, indicators of reduced autophagy. Exo also inhibited autophagosome formation (Fig). Bcl-2 was significantly upregulated by Exo but not by 3-MA. Exo down regulated Tril and upregulated mTORC1/p-S6P1.

Conclusions: Exo reduces apoptosis and autophagy in I/R via. u-regulation of
BoI-2. Inhibition of Traf6 and activation of mTORC1 are additional mechanisms in inhibiting apoptosis and autophagy.

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P3465 | BENCH
Activation of orphan nuclear receptor ROR-α, but not ROR-beta and ROR-gamma, protects against myocardial ischemia/reperfusion injury
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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, RORα, -γ, and -η, have been discovered separately. However, the roles of RORs in the heart have never been investigated.

Methods and results: The endogenous RORα and RORγ expression was detected in the human and mouse heart tissues, as well as isolated cardiac myocytes and fibroblasts. RORα, but not RORγ or RORγ, was significantly up-regulated in mouse heart tissue and human atrium sample after in vivo ischemia/reperfusion (I/R) injury. Synthetic RORα agonist (SR1078) and SR3335 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 Beclin 1 over-expression, 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). The aforementioned cardioprotective effects of ROR agonists were impaired in the setting of cardiac-specific gene silencing of RORα, but not RORγ or RORγ, subtype. Furthermore, RORα sg/sg mice, but not RORγ-null or RORγ-null mice, exacerbated MI/R-induced oxidative stress, and aggravated apoptosis and autophagy dysfunction. In contrast, cardiac RORγ overexpression, but not RORγ or RORγ overexpression, decreased MI/R injuries. We further found that RORγ inhibited gp91phox luciferase activity. Furthermore, deletion of the C-terminals of RORα, or RORα-siRNA resulted in the loss of the RORα ability for the inhibition of gp91phox luciferase activity, and CHIP assay showed that RORγ antibody could pull-down the DNA-protein complex. Thus, RORα directly binds to the regulatory sequence of gp91phox gene through ROR-responsive element.

Conclusion: Our study provides the first evidence that RORα acts as a novel endogenous cardioprotective receptor. RORα, but not RORγ or RORγ, is a novel receptor against MI/R injury, supporting for the drug development strategies specifically targeting RORα for the treatment of ischemic heart diseases.

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P3466 | BEDSIDE
The investigation of the dynamic thiol-disulphide 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 angina. The plasma thiols (SH) is water-soluble and cytoplasmic antioxidant protein-disulphide reductase molecules. It is exclusively associated with the sulfur-containing tripeptide glutathione (γ-glutamyl-cysteinyl-glycine). A review of the literature demonstrates that the dynamic thiol-disulphide homeostasis has not discussed in acute coronary syndrome.

Purpose: The study aims to investigate the dynamic thiol-disulphide homeostasis in acute coronary syndromes.

Methods: The study population consisted of 133 patients with ACS, 38 patients with stable angina (SA) and 47 voluntary healthy subjects. Plasma SH and disulphide (SHSs) levels were measured by a novel and automated spectrophotometric method. The thiol-disulphide homeostasis was calculated as SH/SHHS 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/SHHS ratio was similar 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±7.40 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.

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P3467 | BEDSIDE
The effect of high loading dose of atorvastatin in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention on microvascular perfusion
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Background: Statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor), 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 microcirculatory 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 IMR. IMR are 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 66 patients were divided into 2 groups, atorvastatin group (32 patients) and placebo group (34 patients). Baseline clinical, 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 value. 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. 1.2, p=0.34) showed no microvascular function as assessed by IMR were not difference between both groups (median 41.54 vs. 41.60, p=0.61).

Conclusion: Administration of high loading dose of atorvastatin (80 mg) before primary PCI in STEMI patients didn’t improve microvascular perfusion as measured by index of microvascular resistance compare to placebo.

Acknowledgement/Funding: self-funded

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?
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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. Among 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.

Methods: This study is a post-hoc study of the TTM trial, which randomized 939 patients to 24 hours of TTM of 33 oC or 36 oC. 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 interventions (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.

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

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Background and Introduction: Men and women who suffer an out-of-hospital cardiac arrest (OHCA) differ in characteristics such as location of arrest, bystanders performing cardiopulmonary resuscitation or probability of defibrillation. Women are also reported to receive fewer interventions in hospital and it is unknown whether the effect of target temperature management (TTM) is the same 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: Among a total of 290 patients 45 received IABP as a rescue therapy. Among 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).

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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.
**P3472 | BEDSIDE**

Mehran contrast nephropathy risk score: is still useful ten years later?

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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).

**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 (34%) and hypertension and worse renal function and anemia (p < 0.001). The OR for different score components in Mehran’s population versus our study was similar except for DM, hypotension and IABP (1.6%, 2.68% 2.55% Vs 0.9%, 1.89% and 2.66% 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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**Introduction:** Evidence supporting the benefit of thrombus aspiration (TA) on clinical outcomes is limited. We wanted to assess its clinical benefit during primary PCI (PPCI) in a real-world STEMI population.

**Methods:** Retrospective cohort study of 1534 STEMI patients who underwent primary PCI between 2004 and 2011. We performed a propensity-matched analysis to draw up two groups of 334 patients paired according to whether or not they had been treated with TA. Prognostic value of TA to predict mortality during follow-up was analyzed using Cox regression.

**Results:** There were not differences between patients with and without TA regarding mortality (7.4% 67%, p=0.673); infarction (2.7% 2.9%, p=0.856) or heart failure (8.3% 8.5%, p=0.923). After propensity score matching, results were similar between the two groups for these events (7.5% 6.9%, p=0.764; 2.7% 3.0%, p=0.816, 8.4% 7.8%; p=0.777 respectively). During the follow-up (3.9±2.8 years) there was not association of TA with mortality (HR 0.76, 95% CI 0.50-1.16, p=0.207) and HF (HR 1.24, 95% CI 0.77-2.01, p=0.375). The rate of reinfarction was higher in patients with TA (HR 2.24, 95% CI 1.28-3.91, p=0.004).

**Conclusion:** We have not find benefit on clinical outcomes of TA in a real-world unselected STEMI population. This study highlights the importance of an optimal selection of patients during PPCI in order to do or not to do TA.

**P3473 | BEDSIDE**

Acute coronary syndrome and atrial fibrillation a world of many questions


**Introduction:** Atrial fibrillation (AF) is a very common arrhythmia in patients (P) with cardiovascular disease. Acute coronary syndromes (ACS) remains an important risk factor for the onset of AF.

**Purpose:** To evaluate the differences between patients with ACS and AF on admission or during in-hospital stay regarding the cardiovascular risk profile, therapeutic approach, in-hospital mortality (IHM) and major cardiac events (MACE) follow-up of 17±9 months.

**Methods:** We reviewed 1039 P admitted with ACS, 38.9% STEMI; 41.2% NSTEMI; 15.6% unstable angina; 4.3% unspecified myocardial infarction. P were divided in 2 groups according to the presence of AF: group A (with AF 12.5%, 131 P) and group B (without AF 87.5%, 980 P). We compared demographic, clinical, laboratory and echocardiographic characteristics, performed therapy, coronary disease severity, IHM and MACE.

**Results:** The P with AF were older (75 vs. 67, p < 0.001) and more hypertensive (87% vs 75%, p = 0.022). Had lower incidence of diabetes (30.5% vs 38.9%, p = 0.049) and smoking (14.5% vs 36.6%, p = 0.001); with more coronary disease history (36.6% vs 25.7%, p = 0.008), stroke (19.8% vs 7.6%, p = 0.001) and HF (37.4% vs. 13.6%, p < 0.001). The presentation as NSTEMI was frequenter (51% vs 38.9%, p = 0.006). Had worse HF (Killip Kimmoto class ≥ 3, 10.7% vs 8.7%, p = 0.008) on admission. There was no significant difference in NT-proBNP on admission (8000 vs 5830 pg/ml, p = 0.072) and maximum troponin (51.1 vs 51.5 umol/L, p = 0.987). They presented larger left atria (45 vs. 39 mm in M mode, p = 0.001) and higher pulmonary artery systolic pressure (PASP) (39 vs 35 mmHg, p = 0.0024). No significant differences in relation to left ventricular ejection fraction (43% vs 47%, p = 0.052).

 Coronarography was less performed in these P (85% vs 93%, p = 0.002), with lower revascularization rate (73% vs 83%, p = 0.027). Bare metal stents were most used, but with no t difference (50% vs 46%, p = 0.364). Medical therapy was similar in both groups, with the exception of dual antiplatelet therapy at the time of release (p = 0.019).

 IHH was overlapping in both groups (6.1% vs 5.9%, p = 0.942). At follow-up, there was no significant difference in the incidence of MACE (30.4% vs 27.7%, p = 0.06) but a higher mortality was found (27% vs 17%, p = 0.007).

**Conclusions:** In ACS P there is a high prevalence of AF. These P have a more severe clinical profile, the presence of AF being associated with adverse events including increased mortality at follow-up. Revascularization therapy should be individualized taking into account the overall risk of the patient.

**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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**Background:** The ratio of early mitral inflow velocity to tissue Doppler mitral annulus (E/e') and isovolumic relaxation time (IVRT) are simple, non-invasive tools that can predict mortality in acute coronary syndrome (ACS).

**Objective:** To validate Mehran contrast nephropathy risk score: is still useful ten years later?

Evidence supporting the benefit of thrombus aspiration (TA) on clinical outcomes is limited. We wanted to assess its clinical benefit during primary PCI (PPCI) in a real-world STEMI population.

**Methods:** Retrospective cohort study of 1534 STEMI patients who underwent primary PCI between 2004 and 2011. We performed a propensity-matched analysis to draw up two groups of 334 patients paired according to whether or not they had been treated with TA. Prognostic value of TA to predict mortality during follow-up was analyzed using Cox regression.

**Results:** There were not differences between patients with and without TA regarding mortality (7.4% vs 6.7%, p = 0.673); infarction (2.7% vs 2.9%, p = 0.856) or heart failure (8.3% vs 8.5%, p = 0.923). After propensity score matching, results were similar between the two groups for these events (7.5% vs 6.9%, p = 0.764; 2.7% vs 3.0%, p = 0.816, 8.4% vs 7.8%; p = 0.777 respectively). During the follow-up (3.9±2.8 years) there was not association of TA with mortality (HR 0.76, 95% CI 0.50–1.16, p = 0.207) and HF (HR 1.24, 95% CI 0.77–2.01, p = 0.375). The rate of reinfarction was higher in patients with TA (HR 2.24, 95% CI 1.28–3.91, p = 0.004).

**Conclusion:** We have not find benefit on clinical outcomes of TA in a real-world unselected STEMI population. This study highlights the importance of an optimal selection of patients during PPCI in order to do or not to do TA.
systolic heart failure. A total of 61 patients were included. Clinical data are outlined in Tab.1. Both groups underwent simultaneous echocardiographic and hemodynamic evaluation. For the purpose of the study, according to the published data PCWP >18mmHg was a cut-point for E/e’ value estimation.

**Results:** There was statistically significant difference in mitral E/e’ ratio between ADCFH patients and in CS (27±11 vs. 13±5, p=0.0011). 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 ADCFH patients. We observed statistically significant difference of E/e’ ratio in patients subgroups listed on PCWP value <18 and ≥18mmHg in ADCFH group; 19.2±5 vs. 30.5±11 p=0.00831 respectively and in CS group 11.4±2 vs. 17±7 p=0.0492 respectively.

**Conclusion:** In patients with cardiogenic shock complicating ACS and in the patient with ADCFH tissue Doppler-derived mitral E/e’ ratio may be a reliable and simple tool in predicting elevated PCWP.

**P3478 | BEDSIDE**

**Mini-invasive circulatory support systems and extracorporeal membrane oxygenation in the management of cardiogenic shock and refractory cardiac arrest: results from a prospective registry**

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**Purpose:** Mini-invasive circulatory support systems and particularly vено-arterial extracorporeal membrane oxygenation (ECMO) has been recently introduced for circulatory support in the management of critical conditions caused by severe cardiac failure.

**Methods:** We analyzed a prospective registry of 110 primarily non-surgical patients (mean age 61 (30–82) years, 83% were males), treated in our institution by Impella 2.5 (N=2), PulseSath (N=16), TandemHeart (N=17), and ECMO (N=75). The major indication for circulatory support therapy was cardiogenic shock, followed by refractory cardiac arrest, arrhythmic storm, and support of high-risk interventions.

**Results:** Median duration of circulatory support was 2 days, maximum 62 days. The all-cause 30-day mortality was 30.0%; in the subgroup of 51 patients with severe cardiogenic shock as the reason for circulatory support the 30-day mortality was 44.4%. In patients with refractory cardiac arrest, where ECMO was introduced during continuous chest compressions (extracorporeal cardiopulmonary resuscitation, ECPR), 4 individuals from 18 treated survived with good neurological outcome. We found significant survival differences between subgroup with urgent circulatory support placement and patients with semi-urgent or planned support (30-day mortality 46% vs. 11.6%, P < 0.001). We did not find differences between survivors and non-survivors in the major characteristics including age or left-ventricle ejection fraction. Multiple logistic regression analysis revealed that urgent device placement and cardiac arrest before implantation were independent predictors of death.

**Conclusions:** Mini-invasive circulatory support systems and particularly vено-arterial ECMO are promising tools in the management of severely compromised patients with rapidly progressing cardiogenic shock or refractory cardiac arrest. Frequently the mechanical circulatory support in these high-risk patients represents the last chance to survive.

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**P3477 | BEDSIDE**

**Impact of acute heart failure in patients with non-ST elevation acute coronary syndrome by their functional classification and the application of early invasive strategy**

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**Background:** Little is known about the outcomes of non-ST-elevation acute coronary syndrome (NSTE-ACS) complicated with acute heart failure (AHF). Further, early invasive strategy (EIS) is recommended in the clinical guidelines but difficulty on its real-world application is noted.

**Purpose:** We aimed to quantify the short-term impact of 1) AHF condition on the in-hospital outcome by their functional classification and also 2) the “real-world” application.

**Methods:** Between 2009 and 2014, 3287 patients with NSTE-ACS were enrolled in our interhospital Cardiovascular Studies, an ongoing prospective multicenter registry. AHF was defined as PCI performed within 48 hours after presentation. The individual and composite outcome of in-hospital death, cardiogenic shock after the procedure, stroke, major bleeding, and new requirement for hemodialysis were analyzed.

**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).

**Conclusions:** As novel markers of cardiac injury MMP-8 and TIMP-1 identify acute cardiac pathology of various aetiologies, irrespective of coronary status. In ACS, to prevent worsening of the patients’ condition, coronary angiogram (CA) should not be delayed. In other settings postponing, or even omitting, CA could be beneficial.

**Purpose:** We hypothesised that systemic inflammatory mediators matrix metalloproteinase 8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) could identify acute cardiac injury and distinguish ACS from other acute cardiac conditions.

**Methods:** Serum samples were obtained in conjunction with CA in 3794 successive coronary artery bypass grafting (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) were measured using enzyme-linked immunosorbent assay (ELISA). Of the elective (N=1627) patients 653 had no coronary artery disease (no-CAD), and 974 had stable CAD. Of the acute patients 2072 had ACS, and 95 did not (ACS-like).

**Results:** Both MMP-8 and TIMP-1 concentrations were significantly higher in the acute patients (ACS and ACS-like, p < 0.001) relative to the stable patients (stable CAD and no-CAD). The concentrations of MMP-8 and TIMP-1 did not differ within stable patients (no-CAD vs CAD, p=0.411 and p=0.599, respectively). In acute patients MMP-8 concentrations did not differ significantly, but TIMP-1 concentrations were significantly higher in ACS patients than in ACS-like patients (p=0.174 and p<0.001, respectively).

**Conclusions:** Serum levels of inflammatory mediators

**Acute intensive cardiovascular care II / Acute cardiac care in the emergency department II**

589
Different clinical findings at the chest pain unit: do women spend more time seeking emergency room?


Purpose: The aim of this study was to evaluate the impact of neurologic status on the outcome of patients with cardiogenic shock.

Methods: Patients were recruited from the Japanese Circulation Society Shock registry, a prospective, observational, multi-center, cohort study. A total of 986 consecutive patients with cardiogenic shock were enrolled. Patients’ consciousness levels were evaluated using Japan Coma Scale (JCS), which is a one-axis coma scale and widely used in Japan. JCS was composed by four levels; JCS0 (unarousable), JCS1 (not fully alert but awake without any stimuli), JCS2 (arousable with stimulation), JCS3 (unarousable). The primary endpoint was all cause death at 30-days.

Results: A total of 978 patients (mean age 70.2±14.2 years, 66.3% male) were eligible for analysis. The incidence of all cause death was 34.2%. At 30-days follow-up, the incidence of all cause death was significantly higher in JCS3 group compared with lower 3 groups (JCS0: 15.3% vs. JCS1: 24.3% vs. JCS2: 35.9%; JCS3: 55.8%, p<0.001). Similar results were observed in a subgroup of 721 patients excluded out-of-hospital cardiac arrest. On multivariate analysis, JCS was an independent predictor of all cause death at 30-days (HR 1.40, 95% CI 1.14–1.73, p<0.002).

Conclusion: Neurologic status as a predictor of short-term outcome in patients with cardiogenic shock.
Acute cardiac care in the emergency department II

P3483 | BEDSIDE
An updated heart fatty acid binding protein assay facilitates improved risk stratification for 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 whether it is possible to combine high-sensitive Troponin T (hs-cTnT), 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: hs-cTnT and hFABP were measured on presentation and two hours later in patients presenting to an emergency department with possible ACS without STE 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 males. A positive index test was an ECG positive for new or worsening ST-elevation MI (STEMI) has been excluded by the initial ECG. 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 (85.5%) as negative of whom 12 were false negatives (Sensitivity 94.7% [95% CI 91.0% to 97.0%]. A sensitivity of >99% ([98.6% 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 95.7%]). 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 hs-cTnT and hFABP with a cutpoint of 4.3 ng/mL to the index test comprising hs-cTnI and ECG reduced the rate of false negatives whilst maintaining a clinically useful proportion of low risk patients at around 40%.

Acknowledgement/Funding: hs-cTnT assays were provided free of charge by Randox Cardiology. Funding by the Health Research Council of NZ & 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 recognized, yet unmet clinical need for rapid risk stratification for 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) at presentation versus the 1h-algorithm based on hs-cTn).

Methods: In a prospective international multicentre diagnosis 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 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 strategy. Efficacy was quantified as the percentage of the overall patients assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: LOD = 5 ng/L, 1h-algorithm 0–<12 ng/L and 0–<1-<3 ng/L, and hs-cTnI Abbott: LOD = 2 ng/L, 1h-algorithm 0–<5 ng/L and 0–<1-<2 ng/L) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied if the index test (hs-cTn) results were negative (≤5ng/L).

Results: Acute myocardial infarction was the final diagnosis in 17% of patients. Using hs-cTnT, the safety was very high and comparable with both algorithms (LOD: NPV 99.8%, 95% CI 99–100% versus 1h-algorithm: NPV 99.9%, 95% CI 99.6–100%, p ns). Regarding efficacy, LOD allowed rule-out in 24% of patients versus 58% with the 1h-algorithm (p <0.001). Using hs-cTnI, the safety was very high and comparable with both algorithms (LOD: NPV 100%, 95% CI 99–100% versus 1h-algorithm: NPV 99.9%, 95% CI 99.6–100%, p ns). Regarding efficacy, LOD allowed the rule-out in 16% of patients versus 52% with the 1h-algorithm (p <0.001).

Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI, irrespective of the underlying hs-cTn assay. While LOD has the obvious advantage of allowing rule-out already with the measurement at presentation, the 1h-algorithm is much more effective and more than doubles the number of patients eligible for rule-out.

P3485 | BEDSIDE
Heart score with and without a single troponin testing to rule-out acute coronary syndrome

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Introduction: Ruling out acute coronary syndrome (ACS) in emergency department (ED) is challenging. In patients with possible ACS and non-diagnostic electrocardiogram (ECG), current guidelines recommend multiple troponin tests increasing length of stay before discharge and ED overcrowding. Heart score assigns 0 to 2 points to 5 items: History, ECG, Age, Risk factors, Troponin. Score >1 can exclude ACS with a high sensitivity at ED admission. Further more, using the first 4 items (i.e. not considering troponin), a modified ‘HEART’ score <1, should exclude ACS without requiring any biomarker testing.

Purpose: To evaluate the performances of the HEART score and of a modified ‘HEART’ score not considering troponin in ED chest pain patients.

Methods: Prospective observational bi-centric study. Patients admitted to ED for non-traumatic chest pain were included and followed up at 6 weeks. The primary endpoint was the upper limit of the 95% confidence interval (CI) of major adverse cardiac events (MACE) including acute myocardial infarction, coronary revascularization by percutaneous coronary intervention or coronary artery bypass graft surgery or death (unless clearly non-cardiac).

Results: 643 patients were enrolled, 2 among them were lost and MACE occurred in 61 patients (9.5%) to the formal 6-week follow-up. At ED admission, HEART score was <3 for 404 patients (63.0%), None of them had MACE during follow-up: false negative rate 0% [CI 0.0–0.9], sensitivity 100% [CI 94.1–100], negative predictive value 100% [CI 99.1–100], specificity 70.0% [CI 65.8–72.3], positive predictive value 25.8% [CI 13.9–41.2] and the ‘HEART’ score (without troponin) was <1 in 200 patients (31.2%) and none of them had MACE: false negative rate 0% [CI 0.0–0.9], sensitivity 100% [CI 94.1–100], negative predictive value 100% [CI 98.2–100]. Among them, a sensitive troponin I assay was performed for 119 patients: all tests were under reference range.

Discussion: In patients with a HEART score <3 or a ‘HEART’ score <1, the 6-week MACE rate was very low. HEART score appears safe to rule out ACS and to allow discharge after a single troponin test. In addition, ‘HEART’ score might be useful on anamnestic and clinical-diagnostic data without any biological test in a significant proportion of patients.

Conclusion: In patients admitted to ED for non-traumatic chest pain, HEART and ‘HEART’ scores seem accurate to rule out ACS and may lead to significant decrease in troponin test requirement and ED length of stay. A larger multicentric study is needed to confirm these results.

P3486 | BEDSIDE
High sensitivity troponin T in the rule-out of acute coronary syndrome at the emergency department: the age matters


The best use of high sensitivity troponin T (hs-tnt) in the rule-out of myocardial infarction (MI) is still unknown. Values >14 ng/L should be regarded as the cut-off for a MI. However, multiples cardiac and no cardiac causes can elevate hs-tnt levels in absence of MI.

Methods: We retrospectively analyzed all measurements of hs-tnt at the emergency department (ED) during one year.

Results: We reviewed 17251 hs-tnt measurements in the ED, in 6459 patients (62% male), age 69.2±15 years. 9099 (52.7%) determinations were >14 ng/L. Selecting only concentrations >14ng/L, the diagnosis at discharge was “MI” in 28%. 41% was attributed to other cardiac disease other than MI and 31% were diagnosed with non-cardiac origin. MI classified patients into two groups: ≤65 yo (n=1112) and >65 yo (n=2108). In younger patients group, diagnosis was MI in 48% (vs 18%, p=0.02). Non cardiac condition was the diagnosis in 28% of ≤65 yo vs 38% in elderly population (p=0.03). No differences were found between groups in cardiac but non MI elevation.

Conclusion: hs-tnt elevation in patients under 65 yo is more often due to MI.
P3487 | BEDSIDE

Underlying cause for pre hospital cardiac arrest - incidence of culprit lesions after successful resuscitation and their predictability by ECG recordings

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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%.

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 angiography as the underlying mechanism for OHCA.

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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Purpose: 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.

Methods: We conducted electronic search of RCT. The primary endpoint was all-cause mortality. Favorable neurological outcome was defined as modified Rankin Scale ≤ 3.

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 differences from TH for all-cause mortality (OR 0.95 [95% CI 0.71–1.28], p=0.73). Subgroup analysis for survival is limited.

Conclusion: Our meta-analysis showed that TH in patients resuscitated from out-of-hospital CA does not improve mortality, favorable neurological outcomes, or new onset arrhythmias or re-arrest. Overall survival rate and odds of neurological re-infarction should be evaluated 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 during inotropic stimulation with 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 subset of the LEVosimendan in Acute heart Failure (LEAF) trial.

Methods: A total of 61 patients developing clinical signs of heart failure within 48 hours after a primary percutaneous coronary intervention-treated ST-elevation myocardial infarction (excluding 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 were significant 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 vs. 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

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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 (TO), at the end of
operation (T1), at 6 hours, 1 day, and 3 days postoperatively (T2, T3, and T4, respectively) in order to assess levels of cardiac Troponin I (cTnI) and Copeptin. Standardized clinical events were recorded and used to compute rates of major adverse cardiovascular events (MACE), and evaluate the occurrence of low output syndrome (LOS). Predictive power was investigated by means of ROC curve and Hosmer-Lemeshow analyses; Delong method was used to compare ROC curves.

**Results:** Hospital mortality was 5/166 (3%), LOS occurred in 8/166 (4.8%) patients, and incidence of MACE was 9/166 (6%). Postoperative peak value of Copeptin (25.3±13.1 pmol/L) was reached at T1, whilst peak cTnI concentration (2.1±0.66 ng/ml) at T2. At T1, Copeptin showed a significant predictive power with respect to LOS (AUC 0.86, 95% CI 0.81–0.92, H-L p=0.69), significantly better than cTnI (AUC 0.77, 95% CI 0.63–0.80, H-L p=0.31); with difference p=0.006. With regard to MACE occurrence, best predictive power at T1 was again shown by Copeptin (AUC 0.82, 95% CI 0.78–0.85, H-L p=0.45), with respect to cTnI (AUC 0.74, 95% CI 0.66–0.76, H-L p=0.25), with difference p=0.04. At T2, predictive power of both markers for LOS (difference p=0.27), and MACE (difference p=0.38) were similar. Copeptin highest accuracy points were found at >19 pmol/L for predicting LOS, and at ≥16 pmol/L for predicting MACE.

**Conclusion:** Copeptin dosage following CABG early and reliably identifies the postoperative development of complications such as LOS, and MACE. 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 cardiogenic shock**

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**Background:** Conduction abnormalities are common and affect survival in acute heart failure and myocardial infarction, but their role in cardiogenic 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%, LAHB 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 adjusted for hemiblock (LAHb 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 0.91–5.2, 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 infusion (Dob). Pressure-volume analysis was used to determine LV systolic function under pressure-volume manipulation. 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 infusion (Dob). Pressure-volume analysis was used to determine LV systolic function under pressure-volume manipulation.

**Methods:** 9 anesthetized, 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 LV pressure-volume pressure of 100 mmHg (LVV-Pes100) was taken as 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.

### P3493 | BEDSIDE

**Culprit-only or complete revascularization in patients with non-ST segment elevation acute coronary syndromes: predictors of mortality in patients with non-st segment elevation acute coronary artery disease: a propensity score matching-based analysis**

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**Background:** In patients with non-ST elevation acute coronary syndrome (NSTEMACS) and multivessel coronary artery disease (CAD), the strategy of same 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 NSTEMEACS 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 NSTEMEACS study sample had a total of 460 multivessel CAD patients, after exclusion of clinical indications for CR, as shock. 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 predefined higher risk groups for mortality/morbidity.

**Results:** A strategy of CR was performed in 128 (28%) of NSTEMEACS 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 0.7% 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. 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.

**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.
Long-term outcome after extracorporeal membrane oxygenation due to refractory cardiac shock

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Background: In patients with cardiacogenic shock refractory to standard treatment, implantation of left ventricular assist device 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 in patients undergoing ECMO implantation due to refractory cardiac shock in a high volume tertiary care centre.

Methods: Eighty patients with refractory cardiac 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 cardiacogenic shock complicated by acute coronary syndrome (n=51, 63.8%), acute non-ischaemic heart failure (n=17, 21.2%), deterioration of valvular heart disease (n=9, 11.3%) and interventional complications during percutaneous coronary intervention or transfemoral aortic valve replacement (n=3, 3.7%). Mean ECMO support lasted 7.0±6.7 days (range 1–54). Although initial ECMO support was successful in 45 patients (56.3%), in hospital-mortality 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 was 70.0% as only 24 patients were alive at discharge. Despite ECMO support, long-term prognosis of patients with cardiacogenic shock complicated by periprocedural myocardial infarction may improve clinical outcomes

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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 perianestheic coronary interventional procedures (PI) CABG complicated by periprocedural MI may lead to 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, use of inotropes or intra-aortic balloon pump and the urgency of CABG. The mortality rate was determined 18 to 130 (median 48) months after CABG.

Results: A history of MI (35 vs 15%, p<0.003) or chronic kidney disease (10 vs 3.8%, p=0.01) were more frequent in patients who underwent immediate PCI as compared with no-CATH patients (11.8 vs 25%, p<0.04). There was also a trend to higher long-term survival in patients who underwent PCI (Figure). Multiple regression analysis showed that immediate PCI after CABG complicated by periprocedural MI independently reduced long-term mortality rate (odds ratio 0.48 (0.20–0.96), P=0.046).

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

P3494 | BEDSIDE

Long-term outcome after extracorporeal membrane oxygenation due to refractory cardiac shock

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 trial comparing TAVR with 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 months after TAVR and SAVR. LV mass was determined as the difference between end-diastolic volume (EDV) and end-systolic volume (ESV).

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 TAVR 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 TAVR group (p=0.0002). The difference in LV mass regression between groups was correlated with differences in end-diastolic volume (EDV). In the TAVR group at 12 months, EDV increased from 87±6 to 98±6 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=0.01), and in those with mild PVL by −9±9 ml (p=0.02).

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. Further development in transcatheter valve technology to minimize paravalvular leak may be important to optimize long-term results after TAVR.

P3495 | BEDSIDE

The immediate percutaneous intervention after bypass surgery complicated by periprocedural myocardial infarction may improve clinical outcomes

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Background: New parameters to improve risk stratification and predict outcome in patients with aortic stenosis (AS) are needed. Left ventricular (LV) mechanical dispersion by strain echocardiography reflects heterogeneous myocardial contraction and is a novel marker of sudden cardiac death.

Purpose: We aimed to explore the prognostic value of mechanical dispersion in AS patients, and hypothesized that mechanical dispersion can be an additional clinical tool in risk assessment of these patients.

Methods: We included 55 patients (56 women, 75±9 years) with moderate to severe AS. Global longitudinal strain (GLS) was assessed by speckle tracking echocardiography from a 16 LV segments model. Mechanical dispersion was calculated as standard deviation of time from Q/R on ECG to peak strain in 16 LV segments. To compare LV myocardial dispersion between patients with moderate to severe AS, we performed a univariate analysis and a multivariate logistic regression analysis.

Results: Average aortic stenosis area was 0.7±0.2 cm². Most patients had LV septal hypertrophy (12±2 mm) and preserved LV ejection fraction (EF) (57±10%). Aortic valve replacement (AVR) was performed in 37 (67%). During 36±14 months follow-up, 15 (27%) patients died (no 30-day mortality after AVR). LVFE and GLS did not differ between survivors and non-survivors (58±9 vs 54±13, p=0.16, and −17.0±3.4 vs. −16.7±4.0, p=0.78, respectively). Mechanical dispersion was the only echocardiographic parameter that differed between survivors and non-survivors (56±18 vs 63±20 g, p=0.02). C-statistics for mechanical dispersion showed an AUC of 0.70 (0.55–0.86) and a value of >67 ms indicated worse survival (log rank <0.01) (Fig.1).

Conclusion: LV mechanical dispersion was significantly higher in the AS non-
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P3498 | BEDSIDE
Dynamic 3-dimensional echocardiographic assessment of mitral valve in patients with functional mitral regurgitation caused by lone atrial fibrillation

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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, NPA and PML angle were 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.

P3499 | BEDSIDE
Predictive factors of left ventricular outflow tract obstruction after aortic surgery in patients with severe aortic stenosis


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Background: Asymmetric septal hypertrophy frequently coexists with severe aortic stenosis (AS) and is associated with 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 studied retrospectively before and after surgery by transhoracic 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, aortic-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.

P3500 | BEDSIDE
A cross-sectional study of endocardial lead-related tricuspid regurgitation: towards proposing a new practical 2D/3D echocardiographic approach for better risk stratification

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Background: Recently published studies revealed poor long-term prognosis for patients with significant endocardial lead-related tricuspid regurgitation (ELTR). Using three dimensional transesophageal echocardiography (3D-TTE), we tried to propose a simplified morphological classification of ELTR.

Methods: A cross-sectional study, all patients with all types of implanted endocardial leads were evaluated. 3D-TTE images of the tricuspid valve (TV) were obtained and TR severity was graded accordingly.

Results: Between May 2014 and January 2015, a total number of 145 patients (81 male, mean age 73±11 years, 64 pace makers and 81 implantable cardiac defibrillators) were included.

Based on mobility of the leads and their relative 3D position to the TV, patients were classified into low risk or high risk groups (Fig.1).

Conclusion: 1) Hemodynamically significant ELTR occurs commonly after device implantation. 2) Lead mobility and 3D characterization of lead-valve interaction can potentially be used for risk stratification of ELTR. 3) Complementary 3D-TTE evaluation of TV should routinely be considered in echocardiographic evaluation of patients with endocardial implanted devices.
ters of patients undergoing TAVI with or without BAV with a self-expanding bioprosthesis. 

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 transathoracic echocardiogram prior to the procedure and before discharge. 

Results: The direct group had less moderate/severe paravalvular leakage and similar mortality rates compared to patients with non-direct TAVI.

Conclusions: Patients undergoing direct TAVI have 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) with significant mitral regurgitation (MR ≥2+) undergoing percutaneous mitral valve (MV) repair using mitral mitraclec 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, mitraclec procedure resulted in significant reduction of MV regurgitation (2.5±0.4 vs FU, 1.4±0.7, p<0.001) and amenolerted NYHA functional class (3.0±0.5 vs. 2.3±0.6, p<0.001). Echocardiographic revealed reduced left atrial (LA) minimal (75±31 vs 70±32 ml, p<0.01) and maximal volumes (106±39 vs 96±35 ml, p<0.01), reduced LA volume index (57±19 vs. 51±19 ml/m², p<0.01) accompanied by decreased pulmonary systolic artery pressure (PASP, 42±12 vs. 44±14 mmHg, p<0.001) and increased LA systolic strain (10.2±4.1 vs 12.3±6.1%, p<0.01). Active emptying fraction showed no significant 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±4.6 vs 13.9±5.7%, 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 mitraclec 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<0.001) 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 predictor of clinical recovery after mitraclec procedure.

Conclusions: In heart failure patients percutaneous MV repair results in a significant 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 no permanent atrial fibrillation 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.

P3503 | 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 periprocedure transesophageal echocardiography (TEE) with post procedure transthoracic echocardiography (TTE) for the diagnosis of AR.

Methods and results: Among 163 patients undergoing TAVI under TEE guidance, TEE and TTE images were reviewed separately and blinded to each other. The median time between TEE/TAVI and TTE was 4 days (IQR2–10). 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=6±2 mmHg, p<0.001) 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±2 mmHg, p<0.01 for both). No differ-

ences 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: When compared to TEE performed days after TAVI, periprocedure TEE under-diagnosed the presence of AR. This might be explained by a lower BP immediately after TAVI, compared to follow-up, as well as mild short-term progression of AR.

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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

<table>
<thead>
<tr>
<th>Mitral valve parameters</th>
<th>Before AV repair (n=14)</th>
<th>After AV repair (n=14)</th>
<th>p-value (before vs. after AV repair)**</th>
<th>Controls (n=16)</th>
<th>p-value (controls vs. before AV repair)**</th>
<th>p-value (controls vs. after AV repair)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterolateral-posteromedial diameter (mm)</td>
<td>41.6±6.0</td>
<td>39.0±8.4</td>
<td>0.10</td>
<td>39.6±5.5</td>
<td>0.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anteroposterior diameter (mm)</td>
<td>36.6±5.8</td>
<td>35.1±5.6</td>
<td>0.19</td>
<td>36.5±4.5</td>
<td>0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anular height (mm)</td>
<td>10.3±2.2</td>
<td>6.0±2.2</td>
<td>&lt;0.01</td>
<td>10.3±1.7</td>
<td>0.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anular height to commissural width ratio</td>
<td>0.24±0.05</td>
<td>0.16±0.05</td>
<td>&lt;0.001</td>
<td>0.26±0.04</td>
<td>0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coaptation height (mm)</td>
<td>56.1±15.4</td>
<td>45.4±15.4</td>
<td>0.002</td>
<td>55.5±11.3</td>
<td>0.60</td>
<td>0.013</td>
</tr>
<tr>
<td>Tenting area (mm²)</td>
<td>109.1±43.4</td>
<td>73.5±30.3</td>
<td>0.005</td>
<td>102.4±25.6</td>
<td>0.91</td>
<td>0.009</td>
</tr>
<tr>
<td>Aorto-mitral angle (°)</td>
<td>112.6±9.6</td>
<td>121.1±8.3</td>
<td>0.018</td>
<td>108.7±8.6</td>
<td>0.23</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Paired t-test, **independant samples t-test.
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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 60.4±13.3). MV annular morphology was retrospectively assessed by dedicated quantification software.

Results: The distribution of valve-sparing root replacement with AV reimplantation 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 annulus to commissural width ratio were significantly decreased after AV repair, as were the coaptation height and tenting area. The aortic-mitral 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.

P3505 | BEDSIDE

Mitral/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 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 yrs; 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 parasternal long-axis view. 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), 2 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=0.79). 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 a significant reduction of LAVI (77.2±14.8 ml vs. 68.5±13.0 ml; P=0.03), LVED (254±92 ml vs. 242±89 ml; P=0.04), and a 10% (ESC) or 0.10% (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 scenarios.

Methods: Inclusion criteria were patients with LTE (CAD) to define outcome in these scenarios.

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 patients died (annualized death rate 0.42%), 27 patients (2.7%) suffered an MI (annualized revascularization rate 4.7%), 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 (HR) by blood pressure at rest at 1.1 years (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 in wall motion score index with exercise (HR=0.98, 95% CI: 0.83–0.99, P=0.009) and an incremental prognostic value of ExE, P=0.03). Clinical or ECG testing positivity was not predictive. The number of ExE required to detect an ischemic case was 12.9.

In conclusion, ExE still offer prognostic information in patients with LPP of CAD although the number of studies needed to detect a patient at risk is very high.

The great diagnostic power of stress echocardiography

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Purpose: We aimed at assessing the impact of AV repair on the MV annular geometry. The echocardiographic 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.

Methods: Retrospective analysis of prospectively collected data on patients with normal ExE study. Overall mortality, myocardial infarction (MI) before any revascularization, and revascularizations during follow-up (FU) was assessed. In conclusion, patients with positive exercise ECG testing in absence of positive ExE may still have CAD, mainly in non-LAD vessels. Although overall mortality seems not to be associated to the non-imaging positive patients, these patients might benefit from revascularization.

P3508 | BEDSIDE

Usefulness of negative supine bicycle exercise stress echocardiography in patients with end stage renal disease evaluated for renal transplantation

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Background: Exercise capacity is a well known and robust prognostic factor
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 under 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 fatal 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 stratify patients with little risk of cardiac death 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.

# P3590 | BEDSIDE

**Blunted stress upregulation of stroke volume index is related to impaired end-diastolic volume reserve**

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Background: In the normal heart, when exercise is performed, left-ventricular stroke volume (SV) increases in response to the decrease in end-diastolic volume (LVEDV) while end-systolic volume (LVESV) decreases significantly. Little is known of end-diastolic volume (EDV) re-recruitment during physical or pharmacological stress in patients with negative stress echocardiography (SE) and all coronary artery disease; 324 dilated cardiomyopathy, studied with SE during exercise and peak stress from raw measurement of LV EDV and ESV by biplane Simpson rule.

Methods: We studied 460 patients that underwent DSE within 1 year prior to orthotopic liver transplantation (OLT) between 2004–2011. Clinical and DSE data was recorded. Primary outcome predictor of combined death and heart failure hospitalization.

Results: Clinical and DSE data are shown in Table 1. 30-day events occurred in 14 (3%) patients of the Group I with a higher CI increase (+ 1.89 L/min/m² vs. rest); 573 patients decreased the LVESV and the LVEDV (group II, increased systolic function and decreased relaxation; CI + 1.71 L/min/m² vs. rest); 136 patients increased the LVSV 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: 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.
In patients with symptoms of stable, exercise-induced angina, the 73 (95%), 62 (80%) and 64 (83%), respectively. Forty patients (52%) developed WMA, ECG changes or angina.

Background: Transmural myocardial ischemia is known to determine a typical sequence of events characterized by left ventricular wall motion abnormalities (WMAs), ST-segment depression = 1 mm (STD) in any lead and onset of chest pain if it occurred. The times of appearance of myocardial left ventricular WMAs, ST-segment depression during coronary angiography under continuous echocardiographic and 12-lead ECG monitoring, and patients were invited to immediately report chest pain if it occurred. The times of appearance of myocardial left ventricular WMAs, ST-segment depression = 1 mm (STD) in any lead and onset of chest pain if it occurred.

Results: At coronary angiography, 1-vessel, 2-vessel and 3-vessel disease was found in 29 (33%) patients. At least one among angina, ST and WMAs induced during DST in 77 patients (85.9%), whereas no abnormal findings were induced by DST in 10 patients (11.5%). Among patients with at least one abnormal finding during DST, WMAs, ST and angina were induced in 73 (85%), 62 (80%) and 64 (83%), respectively. Forty patients (52%) developed at least one among angina, ST and WMAs induced during DST; in the latter patients, WMAs, ST and angina were the first abnormal manifestation of myocardial ischemia in 9 (22%), 19 (47%) and 12 (30%), respectively. The severity of coronary artery disease did not significantly influence this kind of results (data not shown).

Conclusions: In patients with exercise-induced angina, the classical ischemic cascade does not seem to be consistently reproduced during DST-induced myocardial ischemia, which can variably be manifested initially by WMA, ECG changes or angina.

P3513 | BEDSIDE

Dobutamine-induced changes of longitudinal strain predict longterm mortality in severe heart failure

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Background: We investigated the dobutamine-induced changes of left ventricular (LV) multidimensional deformation and their relation with prognosis in patients with severe chronic systolic heart failure.

Methods: In 100 patients with advanced heart failure, we performed a low dose dobutamine echocardiography study, including speckle tracking imaging. The patients' mortality was during 5 year of follow-up. Brain Natriuretic Peptide was also measured.

Results: Dobutamine infusion increased LV ejection fraction (EF), LV outflow tract Doppler velocity time integral (LVVTI), global longitudinal, circumferential, radial strain and strain rate (p < 0.05). Patients with cardiac death at t=16 (No: 32) had lower longitudinal strain and strain rate at rest (−7.9±1.4 vs. −9.8±2.5% and −0.47±0.15 vs. −0.63±0.22 L/sec, P = 0.001) and low dose dobutamine (−7.05±2.7 vs. −14.9±4.3 and −0.37±0.18 vs. −0.95±0.37 L/sec, P < 0.001). Smaller differences were observed for circumferential and radial strain and strain rate (p < 0.05).

All among indices, the dobutamine-induced changes (Δ) in longitudinal strain and strain rate were the best predictors of cardiac death (HR: 2.4 (95% CI: 1.5–3.7) p < 0.001, and HR: 2.3 (95% CI: 1.4–3.6) p < 0.001, area under the ROC curve of 91% (95% CI: 85–97) and 88% (95% CI: 81–95) respectively) with an independent and additive predictive value in a model including age, sex, resting LVEF, LVVTI, longitudinal strain (or rate), ΔEF, ΔLVVTI (as measures of contractile function) and type of cardiomyopathy (model x2=84.06 increased to x2=86.15 and x2=84.06 to x2=87.3 after inclusion of Δ 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 of longitudinal myocardial deformation indices of LV function are the best predictors to stratify the risk for cardiac death.

P3514 | BEDSIDE

Value of additional diastolic strain rate analysis at rest, during dobutamine stress and recovery in detecting significant coronary stenosis

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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: 44 patients (mean age 65±8 years) with moderate and high probability of CAD were evaluated by DSE. CAD was defined as having ≥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 late radial DSR significantly increased in the CAD (-) group (-1.86 is to −2.88 is, p=0.012) though not in the CAD (+) group (+1.95 is to −2.28 is, p=0.754). Similar 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 ΔBASE to MIN, early longitudinal ΔBASE to MIN, late circumferential ΔBASE to MIN, early circumferential ΔMIN to MAX, late radial ΔMIN 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.

P3515 | BEDSIDE

Prognostic utility of stress testing and novel cardiac biomarkers in 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) & sECG biomarkers for CAD in postmenopausal women at low to intermediate risk for CAD.

Methods: 366 postmenopausal women [age 54±5 yrs, Framingham risk 7±4%] were prospectively studied during simultaneous CSE & sECG. Abnormal CSE was defined as new or worsening WM abnormality at stress; abnormal sECG was defined as ≥1 mm horizontal/downsloping ST segment depression during stress testing. 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% Cls] 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 sECG was in 21 (7%) women. In 33 women with abnormal CSE, sECG 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 82/38% (18 vs 293/6%) (p=0.014), respectively. Overall, abnormal vs. normal sECG, P=0.001, Figure. Resting BNP was higher in women with MACE vs. without [BNP pg/ml: 70±106 vs 33±39.9, P=0.001]. Abnormal sECG 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 BNP was associated with MACE [HR 2.9 (1.1–7.3), P=0.028].
Conclusions: Severe ultrasound contrast replenishment increased the risk of AV without baseline LBBB who presented AV block had severe contrast replenishment associated to AV block. Patients with severe replenishment (n=20) had greater after ASA. Alcohol dose, CK level and contrast-enhancement volume were not.

Background: Inhaled prostanoids improve right ventricular (RV) function in pul-

Santiago, Chile

Acute changes in right atrial function after iloprost inhalation in

S. Tuohinen1, T. Skytta 2, V. Virtanen 1, M. Virtanen 1, T. Luukkaala 3,

myocardial walls, an ultrasound tissue characterization study

The early impact of breast cancer radiotherapy on myocardial tissue

evaluated before and immediately after RT. Twenty patients had right-sided, and

Methods: Patients with symptomatic left ventricular obstruction referred for ASA

sessed by echocardiography ultrasound contrast.

P3519 | BEDSIDE

Myocardial scar evaluation by 2D contrast echocardiography


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. Purpose: 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 car-
diomyopathy) who underwent cMR and 2D-CE-Echo for clinical indications. Two-
dimensional echocardiography images were acquired with a low mechanical in-

index (MI=0,1) so that normal myocardium appears hypo-echoic, whereas region with scar brighter. We used transpulmonary contrast agent to improve border def-

minition and evaluate the trans-mural extent of scar. Results: After a total of 638 patients (25% with cMR) 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%) and sub-endocardial (sensitivity=74%, specificity=84%) infarct. Disagreement between 2D-CE-echo and cMR was principally due to false nega-
tive (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

Perioperative management of an echocardiographic model to predict significant

paravalvular regurgitation after TAVI

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Aim: Paravalvulvar 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 par-

avalvular 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 trans-
catheter echocardiography (TCE) and contrast echocardiography (CE).

Background: Inhaled prostanooids improve right ventricular (RV) function in pul-

monary arterial hypertension (PAH) patients. Effects on right atrial (RA) func-
tion have not been studied. We evaluated acute changes in RA function post inhaled iloprost in patients with PAH.

P3516 | BENCH

Contribution of ultrasound contrast in predicting conduction disturbances due to percutaneous alcohol septal ablation

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Background: Alcohol has been incriminated in the risk of permanent atrio-ventricular (AV) block during alcohol septal ablation (ASA). We sought to evaluate the association between the risk of AV block and alcohol diffusion assessed by echocardiography ultrasound contrast.

Methods: Patients with symptomatic left ventricular obstruction referred for ASA were included in the study (n=42). Patients with previous pacemaker implantation were excluded. Measures to prevent permanent AV block were a slow alcohol injection and the use of ultrasound contrast agent to avoid multiple septal injec-
tions. Myocardial contrast-enhancement volume was quantified from full volume 3D apical views with contrast replenishment graded as severe when right and left ventricle were filled by contrast during the 3 cardiac cycles after contrast delivery.

Results: Despite the use of a limited alcohol dose (2.3±0.7 mL) and only one pa-
tient with >1 septal injection, 10 (23.8%) patients experienced permanent AV block after ASA. Alcohol dose, CK level and contrast-enhancement volume were not associated to AV block. Patients with severe replenishment (n=20) had greater contrast replenishment associated to AV block. Finally, no AV block was observed in patients without baseline LBBB and severe contrast replenishment.

Conclusions: Severe ultrasound contrast replenishment increased the risk of AV block during ASA and may be a marker of alcohol diffusion.

P3517 | BEDSIDE

The early impact of breast cancer radiotherapy on myocardial tissue properties in 2D echocardiography with increased echodensity of the myocardial walls, an ultrasound tissue characterization study

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Background: Radiotherapy (RT) in the thoracic region is associated with in-
crease in risk for cardiac morbidity and mortality. The aim of this prospective single-center study was to assess whether ultrasound tissue char-
acterization (UTC) can indentify early RT related myocardial lesions.

Methods: Seventy-eight eligible patients with early stage breast cancer were evaluated prospectively, and 10 (13%) patients had right-sided, and

fifty-eight left-sided breast cancer. None received chemotherapy. A comprehen-
sive echocardiographic examination included 3D measurements and UTC anal-
ysis, segment analysis, 2D-CE-Echo allowed the identification of cMR scars with a sensitivity of 60% and specificity of 99%. Hence, 2D-CE-Echo could be used to identify myocardial scar and its transmural extent.

Conclusions: The early impact of breast cancer radiotherapy on myocardial tissue properties in 2D echocardiography is increased echodensity of the myocardial walls, an ultrasound tissue characterization study.
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.

Results: Mean age was 82.7±5.6 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 variables found to be statistically significant, and considered clinically relevant were used to develop a multivariable prediction model. The primary endpoint was significant paravalvular regurgitation, defined as grade ≥2 according to VARC-2 criteria.

Conclusions: Mean eGls (sd in patients with/s without significant CAD was found at rest (−22.6 (4.1)%/−23.3 (3.3)%, p=0.27), but a highly significant difference was detected during Adenosine infusion (−23.7% (5.5)%/−28.3% (4.1)%, p<0.0001). ROC curves were produced and the area under the curve (AUC) for changes in eGls (eGls at rest – eGls during stress) was 0.79. The best accuracy (78%) was achieved if the cut off value was <2.3% indicating that patients with less than 2.3% increase in (i.e. more negative) eGls during Adenosine infusion has significant CAD. This cut off value yielded a sensitivity of 64% and a specificity of 85%.

Conclusion: Endocardial Gls during Adenosine Se may be used as a noninvasiv tool to stratify patients suspected of CAD. However, there seems to be a wide overlap in the increase in strain induced by Adenosine in patients with and without significant stenoses.

Acknowledgement/Funding: Region Health Research Fund of Central Denmark Region. • J og O Madsens Fund.

P3523 | BEDSIDE Stress speckle tracking: an underestimated tool in detecting myocardial viwatios in Adenosine SE.

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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 patients were 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 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 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. Mean 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.

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P3521 | BEDSIDE Accuracy of adenosine 2D strain stress echocardiography in the detection of coronary artery disease in patients with chest pain

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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. Semiautomatic 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 CA’s 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<0.12). Significant CAD - defined as one or more stenoses above 70% - was present in 44 (33%) of the patients: 48% had 1-vessel disease (1VD); 36% 2VD and 16% 3VD.

Results: No difference in mean eGls (sd) in patients with/without significant CAD was found at rest (−22.6 (4.1)%/−23.3 (3.3)%, p=0.27), but a highly significant difference was detected during Adenosine infusion (−23.7% (5.5)%/−28.3% (4.1)%, p<0.0001). ROC curves were produced and the area under the curve (AUC) for changes in eGls (eGls at rest – eGls during stress) was 0.79. The best accuracy (78%) was achieved if the cut off value was <2.3% indicating that patients with less than 2.3% increase in (i.e. more negative) eGls during Adenosine infusion has significant CAD. This cut off value yielded a sensitivity of 64% and a specificity of 85%.

Conclusion: Endocardial 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 strain induced by Adenosine in patients with and without significant stenoses.

Acknowledgement/Funding: Region Health Research Fund of Central Denmark Region. • J og O Madsens Fund.
**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 DSE was performed and 50 patients with significant lesions in coronary arteries confirmed in coronaryography (18 female; mean age 62±9 years). Rotation was measured at basal and apical levels of LV. We compared rotation measured at aortic valve closure (RvAC) and twist (T) calculated as a difference of basal and apical RvAC. 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 group, see Table

**Conclusion:** Endystolic rotation as well as twist of the LV are intrinsic features of LV mechanics, constant despite changing inotropic and chronotropic challenge. Contrary, the significant differences between groups with CAD and without CAD, indicate that ischemia impacts on rotational parameters.

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**Conclusions:** Stress strain rate values obtained from speckle tracking are highly sensitive and specific in detecting myocardial viability in comparison with cardiac MRI. A complete echocardiographic study, including CPOM was provided by LV mass (M) to convert the units to watts/100 g: CPO = K M–1 (g). Patients were followed-up for the end point 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 the 3rd tertile exhibited the worst LV EF% (26±6 vs 32±5 vs 34±5; p<0.0001), VO2 max (13±4 ml/kg/min vs 14±4 ml/kg/min vs 20±5 ml/kg/min; p<0.0001) and E/e′ (16±5 vs 12±8 vs 10±3; 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.

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**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.

**Results:** 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 prospective study (PROS) using GE Vivid7 or 9 echocardiography. Tissue Doppler Imaging (TDI) is a powerful tool to assess myocardial function, especially in patients with severe LV dysfunction. TDI is well validated in patients with severe LV dysfunction to assess the potential energy stored in LV mass, it provides indirect information about the efficiency of such transformation.

**Aim:** This study was designed to assess the value of CPOM in the prognostication of patients with chronic stable heart failure (HFrEF) submitted to 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 afterload of LV filling pressure, was carried out at baseline. CPOM was calculated as the product of a constant (K=2.22 × 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 end point 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, CPO (HR 0.17, 95% CI 0.002–0.016, p=0.0004) was selected as the most powerful independent predictor of mortality or ventricular assist device (VAD) implantation.

**Conclusion:** The multivariate analysis identified CPOM as a powerful independent predictor of mortality or ventricular assist device (VAD) implantation. These findings suggest that CPOM may be useful in the risk stratification of patients with HFrEF.
negative predictive values (NPV 56%). In the PROS study, feasibility was high (PWVe 75%, E/e’ 90%, LAVI 59%, E/A 95%, Edeq 90%, SF 91%, PSve 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 PWP was impaired by low PPV (EF < 50% 18%, EF ≤ 50% 65%) 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%).

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.

P3529 | 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 transtricuspid echocardiography (STTe) can quantitative measure strain 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). We measured 2D LV global longitudinal strain (GLS) and circumferential strain (GCS) (absolute values) using STTe, and compared with controls.

Methods: A total of 105 subjects, 41 with HCM (31 male, 62±15 yrs), 40 with severe AS (19 male, 77±7 yrs, transaortic maximum velocity 4.8±0.6 m/s, aortic valve area index 0.46±0.12 cm²/m²), and 24 controls (12 male, 54±18 yrs) underwent STTe (Vivid E9). Apical 4-, 2-, and 3-chamber views for GLS and parasternal short-axis views of the mitral valve, papillary muscle, and apex for GCS were acquired.

GLS was defined as all 17 averaged LV segments.

Results: Whole, endocardial, and epicardial layer GLS were significantly smaller in HCM than in controls (all p <0.001), and were significantly smaller in severe AS than in controls (all p <0.001). There were no significant differences in endocardial GCS at any site among the 3 groups. Endocardial GCS at the mitral valve and papillary muscle was significantly positively correlated with LVEF (R=0.447 and 0.34, respectively) in HCM. Similarly, in severe AS, endocardial GCS at the mitral valve and papillary muscle was significantly positively correlated with LVEF (R =0.472 and 0.556, respectively).

Conclusions: In HCM and severe AS with preserved LV EF, 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 LVEF.

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 53 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 LVEDV 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). There was a significant correlation between 3D LVEDV mass and all 3D strain components (from r=0.71 for 3DGDS to r=0.63 for 3DGCS, all p <0.05). 3D GCS had the strongest association with 3D LVEDV mass (r=0.82, p <0.001). For segmental deformation, as compared to controls, HCM patients had lower 3D longitudinal strain whatever the LWWT (controls: −20.5±7 vs. 1st quartile: −16.9±6, p <0.05) whereas circumferential strain was increased in none- and poorly hypertrophied segments (controls: −19.2±6.0 vs. 1st: −21.2±6.0 and 2nd quartile: −20.8±6, both p <0.05).

Conclusions: 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.

P3531 | BEDSIDE

Global myocardial mechanics with 3-Dimensional speckle tracking echocardiography in hypertrophic cardiomyopathy

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Background: Interstitial fibrosis as well as myocardial fibre disarray and non-contractile excision (TAPSE), and pulsed Doppler peak velocity at the tricuspid annulus (s') as an assessment of RV systolic function, and investigated the relationships between echocardiography-derived parameters of RV systolic function with CMR-derived measurement of RVEF and the impact of TR grade on these relationship.

Results: In patients with ≤ mild TR (n=129), FAC, TAPSE and s’ showed significant correlation with CMR-derived RVEF (p<0.0001, r=0.596, p=0.0121, r=0.220 and p=0.011, r=0.283, respectively). On the other hands, in patients with ≥ moderate TR (n=13), both TAPSE and s’ had no significant correlation with CMR-derived RVEF. FAC had a good correlation with CMR-derived RVEF (p<0.0001, r=0.758) in patients with significant TR.

Conclusion: FAC correlates best with CMR-derived RVEF, and its correlation is not affected by TR grading. TAPSE and s’ didn’t show significant correlations with CMR-derived RVEF in patients with significant TR.
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 Artida 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: −8.6±5.4% vs. −17.8±2.4%; GCS: −24.13±6.8% vs. −34.9±4. %, p < 0.001 for both). 3D area tracking (AT) was also significantly impaired compared to controls (HCM vs. controls, −33.6±7.5% vs. −47.9±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 function. Further contribution 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 magnetic resonance (CMR) imaging for further contribution to LV mechanics with aging. The influence gender in age-related LV remodeling and torsion in asymptomatic Asian population remains largely unknown. Multivariate logistic regression analysis showed that LAe’sr was an independent predictor of LA dysfunction (odds ratio 3.30, p < 0.05).

Conclusion: Impaired LA e’sr function evaluated by LA strain rate was a promising parameter for LA dysfunction in patients with acute ischemic stroke.

P3533 | BEDSIDE

Novel vendor independent software for right ventricular quantification by 3D echocardiography shows good reproducibility and improved accuracy in comparison with cardiac magnetic resonance

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Background: According to the recent ASE/EACVI guidelines, three-dimensional echocardiography (3DE) is strongly recommended for assessing right ventricular (RV) volumes and ejection fraction.

Purpose: This study aimed to test a novel semi-automated software algorithm for 3DE RV analysis in terms of: (1) accuracy and reproducibility versus cardiac magnetic resonance (CMR); (2) accuracy and analysis time with respect to the previous software.

Methods: 48 patients (age range 14–82 years, 28 men) with various cardio-vascular diseases (ischemic 44%, congenital 19%, cardiomyopathy 21%, other 16%), scheduled for a clinically indicated echo and CMR study >48 hours apart, were prospectively enrolled. RV 4- and 6-beat full volume datasets (31±9 vps) were acquired using Vivid E9 scanner (GE) and analyzed with novel vendor-independent 4D RV-Function 2.0 software (TomTec). Subsets with suboptimal image quality were not excluded. Reproducibility and accuracy in comparison with previous RV-Function 1.2 release (TomTec) was tested in 15 random datasets.

Results: There was a wide range of RV end-diastolic volumes (EDV 93–349 ml), ejection fractions (EF 35–76%), and image quality (optimal = 2/3 datasets), RV volumes were smaller by 3DE than by CMR (163±58 vs 179±66 ml, p < 0.001), while EF was comparable (55±8% vs 53±1% p = 0.053). RV 3D semi-automated analysis by novel software showed an excellent correlation and agreement (bias/SD) with CMR analysis (r=0.94 and 17 ml±24 ml for EDV; r=0.86 and 1.4±4.8% for EF, p < 0.001 for both), being also 5-fold faster (5 vs 25 minutes, p < 0.001).

Using intra-class correlation (ICC) analysis, intraobserver reproducibility of 3DE on same datasets was excellent and similar to CMR’s (ICC 0.97 vs 0.99 for EDV; 0.89 vs 0.91 for EF), while interobserver variability was larger than CMR’s (ICC 0.94 vs 0.99 for EDV, 0.74 vs 0.87 for EF). In comparison with 1.2 release, analysis by 4D RV-Function 2.0 reduced the bias and narrowed the limits of agreement versus CMR (2±14 ml vs 13±27 ml for EDV, 1.4±4.8% vs 6.2±10.9% for EF), with no significant time benefit (5 vs 6 minutes editing, p<NS).

Conclusion: Novel vendor-independent software enables a reproducible and more accurate 3DE quantitative analysis of RV volumes and ejection fraction than previous version. These findings are relevant for both research and clinical practice, particularly for echo labs aiming to implement 3DE for RV analysis in a multi-vendor setting.
The aim of the present study is to identify a novel disease locus/gene by fatty or fibrofatty replacement. It is recognized worldwide as the second most myocardial disorder characterized by progressive cardiomyocyte death, followed by septal hypertrophy and dilatation. Sequencing (NGS) technology was then applied in order to identify a novel locus 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 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 didn't reveal the presence of any additional variants except for a novel intronic variant (c.766+8C>A) in TIMM43 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 segregation of the novel disease locus was mapped on chromosome 19p13.3 and a critical region of 2 Mb was defined.

Acknowledgement/Funding: This study was funded by University of Padua Research Grant TRANSCAP, Padua; the University of Padua Grant CPD133979/13, Padua; Veneto Region Target R.

P3535 | BENCH
Constitutively active phosphatase inhibitor-1 improves cardiac contractility in unchallenged mice but is deleterious in a model of pressure-overload

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 (lncRNAs) are expressed in humans but their functions are largely unknown. We searched for IncRNAs influencing intracellular capacity in patients with viral (CVBS) cardiomyopathy and assign immunoregulatory functions to a small tRNA-like processing product of the IncRNA MALAT1.

Methods and results: To identify functions of the MALAT1-mascRNA 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 tRNA-like product mascRNA was highly enriched in immune cells. Antisense oligonucleotide (ASO)-mediated mascRNA ablation in macrophages led to massive induction of FASLG, FAS, TNF-a, and IL6, whereas the primary transcript MALAT1 was expressed in all immune cells and cardiomyocytes. The proband and additional 44 family members were genotyped by a SNP array (370,000 markers) and a multipoint linkage analysis using an invader assay. 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 didn't reveal the presence of any additional variants except for a novel intronic variant (c.766+8C>A) in TIMM43 gene. The segregation of this variant among all the available family members excludes an association with the disease phenotype.

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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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Methods and results: To identify functions of the MALAT1-mascRNA 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 tRNA-like product mascRNA was highly enriched in immune cells. Antisense oligonucleotide (ASO)-mediated mascRNA ablation in macrophages led to massive induction of FASLG, FAS, TNF-a, and IL6, whereas the primary transcript MALAT1 was expressed in all immune cells and cardiomyocytes. The proband and additional 44 family members were genotyped by a SNP array (370,000 markers) and a multipoint linkage analysis using an invader assay. 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 didn't reveal the presence of any additional variants except for a novel intronic variant (c.766+8C>A) in TIMM43 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 segregation of the novel disease locus was mapped on chromosome 19p13.3 and a critical region of 2 Mb was defined.

Acknowledgement/Funding: This study was funded by University of Padua Research Grant TRANSCAP, Padua; the University of Padua Grant CPD133979/13, Padua; Veneto Region Target R.

P3535 | BENCH
A novel locus on chromosome 19p13.3 linked to arrhythmogenic cardiomyopathy
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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 (lncRNAs) are expressed in humans but their functions are largely unknown. We searched for IncRNAs influencing intracellular capacity in patients with viral (CVBS) cardiomyopathy and assign immunoregulatory functions to a small tRNA-like processing product of the IncRNA MALAT1.

Methods and results: To identify functions of the MALAT1-mascRNA 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 tRNA-like product mascRNA was highly enriched in immune cells. Antisense oligonucleotide (ASO)-mediated mascRNA ablation in macrophages led to massive induction of FASLG, FAS, TNF-a, and IL6, whereas the primary transcript MALAT1 was expressed in all immune cells and cardiomyocytes. The proband and additional 44 family members were genotyped by a SNP array (370,000 markers) and a multipoint linkage analysis using an invader assay. 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 didn't reveal the presence of any additional variants except for a novel intronic variant (c.766+8C>A) in TIMM43 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 segregation of the novel disease locus was mapped on chromosome 19p13.3 and a critical region of 2 Mb was defined.

Acknowledgement/Funding: This study was funded by University of Padua Research Grant TRANSCAP, Padua; the University of Padua Grant CPD133979/13, Padua; Veneto Region Target R.

P3538 | BENCH
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 address this, we adapted ribosome profiling to reliably monitor genome-wide protein synthesis in heart and multiple tissues. The primary transcript MALAT1-derived mascRNA has important immunoregulatory potential, which is modulated by mimetic or antisense drugs has cardiovascular therapeutic potential.

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 86% 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 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 didn't reveal the presence of any additional variants except for a novel intronic variant (c.766+8C>A) in TIMM43 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 segregation of the novel disease locus was mapped on chromosome 19p13.3 and a critical region of 2 Mb was defined.

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and there is limited evidence of translational buffering. Remarkably, we observe hundreds of strain-specific differences in gene expression that are apparent only at the translational level, almost doubling the number of differentially expressed genes detected between strains. Genome-wide protein synthesis rates measured by ribosome profiling are a better proxy for protein levels compared to RNA sequencing. Integration of genetic, transcriptional and translational datasets identifies distinct signatures in 3’UTR variation, RNA binding protein motifs, and mRNA expression that are associated with translational regulation of gene expression. Intriguingly, many genes regulated at the translation level have been implicated in human disease in genome-wide association studies (GWAS). Taken together these data document novel and extensive translational control of important cardiac and metabolic genes and pathways and show that a large number of genes associated with heart and liver traits by GWAS are regulated translationally. Capturing these individual differences in the translated genome will lead to new insights into the genes and regulatory pathways underlying disease phenotypes.

P3539 | BENCH
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 was 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 characterised a transgenic mouse model with a cardiac-specific overexpression of hDSC2. Echocardiography and (immuno)histology were used to characterise the functional and structural defects in our DSC2 mouse model. These experiments were complemented by Western-blot analysis and qRT-PCR experiments to characterise 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 transgenic mice in comparison with non-transgenic 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.

P3540 | BENCH
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 a part of sydromic 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. Assayed 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 of MH2 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 aim of our study was to define genetic background of TAAD. In familial TAAD, all relatives with TAAD carried identified variants. Based on combined clinical and genetic data, syndromic TAAD was diagnosed/confirmed in 9 pts (7-Marfan syndrome, 1-Loeys-Dietz syndrome, 1-Sprinten-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 causative mutations adds to heterogeneity of the genetic background of TAAD.

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P3541 | BENCH
Gene expression in myocardial tissue and peripheral blood cells: potential RNA-biomarkers for myocarditis identification

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Introduction: Myocardial inflammation following 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 of 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, ADCCY7) out of 30 tested 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.

P3542 | BENCH
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 (MYBP3/C) are one of the most common causes of hypertrophic cardiomyopathy (HCM). HCM 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 morpholin 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 morpholin target gene 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.

P3544 | BENCH
Detection of novel TTN truncating variants in patients with unexplained left ventricular systolic dysfunction and genotype-phenotype correlations
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Purpose:
In order to explore the role of TTN truncating mutations in the pathogenesis of dilated cardiomyopathy and unexplained left ventricular systolic dysfunction (LVSD), we performed genome-wide and targeted next-generation sequencing (NGS) strategy in selected patients with unexplained LVSD.

Methods:
We screened 200 unrelated Polish patients with unexplained LVSD for TTN truncating variants. The analysis was performed using the exome sequencing service at the Centre for Biostructure, Warsaw, Poland. In addition, we performed targeted NGS using the TruSight One sequencing panel (Agilent, Santa Clara, CA) in 66 selected patients from families with unexplained LVSD. The sequencing was performed using the Illumina NextSeq 500 platform. The variants were classified based on the American College of Medical Genetics and Genomics guidelines.

Results:
We identified 16 novel TTN truncating variants in 18/66 (27.3%) patients. The variants were found in 16 different families and were distributed across the TTN gene. The most common variant was an in-frame deletion in exon 20 (7/16; 43.7%). The variants were classified as pathogenic, likely pathogenic, or of uncertain significance.

Conclusion:
Our results suggest that TTN truncating variants are a significant cause of unexplained LVSD in a subset of Polish patients. Further studies are needed to confirm these findings in a larger cohort and to elucidate the pathogenic mechanisms of these variants.

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enrichment and innervation to ensure integration with the surrounding myocardium.

**Methods:** Polycaprolactone (PCL) fibres conjugated with the osteopontin-derived adhesive motif (Gly-Pro-Arg-Val/lumina) and the growth factor capturing heparin binding peptide (Hep, adventitial) were electrospun. SVP were seeded on the adventitial layer. Peptides and SVP effect on endothelial cell (EC) adhesion and migration was evaluated.

**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 Hep peptide distribution. SVP attachment on the adventitial side of the H/S was assessed by immunostaining (H/S+SVF). Seeded scaffolds were cryopreserved for up to 2 weeks, preserving 70% viability. Seeding of SVP on H/S scaffolds increased EC coverage on the luminal side by 4 fold, compared to H/S scaffolds alone. When SVP were seeded on CTF scaffold the increase was more modest, indicating a synergic effect between SVF and the progenitor cells. We investigated the ability H/S+SVF scaffolds to influence EC migration in a wound healing assay. Indeed, the presence of SVP in the adventitial layer increased EC wound closure capacity, supporting a role in re-endothelialisation of the graft. The ability of SVP to promote healing was confirmed in a cell-free cardiac migration assay.

**Conclusions:** We engineered a vascular scaffold combining progenitor cells and a gradient of functional molecules showing their synergistic effect in promoting EC coverage.

**Methods and results:** We engineered MSCs with integrin-linked kinase (ILK), a pleiotropic protein enhancing progenitor cells 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 and the 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 induce any significant improvement in cardiac remodeling, 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 after MI.

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**P3547 | BENCH**

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 SIRT6 in cardiac repair, and its role in macrophages remain unknown. Therefore, we aimed to determine the role of MQ SIRT6 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) male mice 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 male mice and their WT litter mates and analyzed cardiac MQ phenotype by flow cytometry using the markers: CD68 vascular cell adhesion molecule (VCAM), CD40 ligand (CD40L), and CD11b (F4/80). CD14+CD11b+ macrophages were used to study scaffold vascularization. Transmission electron microscopy was performed to confirm the presence of vascular and nervous ultrastructures. Results: H/E and Masson’s and Gallego’s modified trichrome staining provided a histological description of the pericardial-derived scaffold. Newly formed nerve fibers, composed of several amyelinated axons as the afferent nerve endings of the pericardium were discerned, within the scaffold, nerve structures composed of several amyelinated axons, and vascular structures with erythrocytes within the lumen, confirming functional conduits with blood flow.

**Conclusions:** In summary, this study demonstrates for the first time the neoinformation of vessels and nerves in cell-free cardiac scaffolds applied over infarcted tissue. Thus, the search for an optimal scaffold that preserves the natural tunnels necessary to vascularize and nerves and with the porosity to nest cells may be crucial to ensure a functional and successful engineered bioprosthesis.

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**P3548 | BENCH**

The longevity gene SIRT6 switches macrophages into an anti-inflammatory phenotype and improves cardiac function after myocardial infarction in mice

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P3550 | BENCH
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 damage the heart 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 activity.
Purpose: 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 (0.1μM) and pro-apoptotic (1μM) 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 Annexin V/PI staining, respectively. The percentage of selected intracellular signal 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% in 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.

P3551 | BENCH
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 extensively discussed. However, optimal method of CPC transplantation is still elusive because of low graftability and unclear treatment effects 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 RADAR1 as a scaffold. Addition of IGF-1 and specially modified self-assembling peptide with the active motif of RGD sequence, improved three-dimensional spreading 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 confirmed it inside of the pericardial space by using parietal pericardium (pericardial grafting method). Histological and immunohistochemical staining showed that the number of VWF-positive capillaries in treatment group was higher than that of control group. CPC-scaffold transplantation restored the volume of the left ventricle by increasing the proportion of capillaries and microvessels. Furthermore, CPC transplantation improved the deficit of cardiac function (fractional shortening: 22.6±5.0% and 39.7±8.7%, p < 0.05, n=5). The scaffold was detected by the combination of horse anti-rabbit antibody and al-labeled avidin, scaffolds were globally detected in the scaffold area 1 week after, but sparsely 4weeks after transplantation. To examine whether graft CPCs survive in the scaffold, FISH analysis of sex-mismatched transplantation to female mice showed that CPCs derived from male mice were globally detected in the scaffold area 4weeks after transplantation. By using CPCs expressing red fluorescence protein (RFP), many RFP-positive CPCs were detected in the scaffold area 2 weeks after transplantation with pericardial grafting method. On the other hand, there were not detected with direct injection method. These results were well-vascularized, biodegradable and protected by parietal pericardial transplantation. Pericardial grafting of CPC-scaffold is a useful method to improve cardiac function and graftability of transplantation after MI in mice.

P3552 | BENCH
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-differentiated cardiomyocytes (iPSC-CMs) to establish a model in vitro and in vivo of ACT for understanding the underlying pathomechanisms.
Methods and results: iPSCs from healthy human individuals were directly differentiated into pure cardiomyocytes (95%) for two month and exposed to 0.1, 0.5, 1 μM DOX for 24h. We investigated the cell survival of DOX-treated iPSC-CMs using Annexin V/PI staining resulting in a mortality rate of 30% after 5μM DOX. 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 TN (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 Fluor4. 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 expression of ROS and viability 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 confirmed it inside of the pericardial space by using parietal pericardium (pericardial grafting method). Histological and immunohistochemical staining showed that the number of VWF-positive capillaries in treatment group was higher than that of control group. Immunofluorescence study showed that there were many CD31-positive capillaries with or without smooth muscle cell actin-expressing perivascular cells in the graft area. By using biotin-labeled self-assembling peptide and fluorescence-labeled avidin, scaffolds were globally detected in the graft area 1 week after, but sparsely 4weeks after transplantation. To examine whether graft CPCs survive in the scaffold, FISH analysis of sex-mismatched transplantation to female mice showed that CPCs derived from male mice were globally detected in the scaffold area 4weeks after transplantation. By using CPCs expressing red fluorescence protein (RFP), many RFP-positive CPCs were detected in the scaffold area 2 weeks after transplantation with pericardial grafting method. On the other hand, there were not detected with direct injection method. These results were well-vascularized, biodegradable and protected by parietal pericardial transplantation. Pericardial grafting of CPC-scaffold is a useful method to improve cardiac function and graftability of transplantation after MI in mice.
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 injured myocardium. Cardiac cells are subjected to mechanical and electrical forces, which regulate gene expression and cell function. Therefore, an effective intracoronary 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 (cardiacADTPCs); and 2) examine the effect of electromechanical stimulation cardiacADTPCs within a myocardial infarction (MI) model in mice.

Methods: CardiacADTPCs 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 Live & Dead assay. The cellular construct was implanted in the murine heart and animals were sacrificed at 3week post-implantation. 40 animals were randomly distributed: without cells (control Mi, fibrin Mi) and with stimulated or non-stimulated cells (stimulated Mi and sham). Echocardiography, gene and protein analysis were also carried out.

Results: In vitro electromechanical stimulation on cardiacADTPCs showed increased expression of cardiac transcription factors, structural genes and calcium handling related genes. After 3 weeks of in vitro culture in the fibrin construct, cells exhibited high viability and remained labeled. Cell treatment resulted in functional improvement of left ventricular ejection fraction (LVEF) relative to post-infarction values; indeed, stimulated cardiacADTPCs 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 cardiacADTPCs, but also scarce migration to make the MI tested.

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, maturation and migration to infarcted myocardium. All together, electromechanical stimulation of therapeutic cells previous implantation could be a valuable tool for cardiac regeneration approaches.

Allogeneic cardiac-reparative cell therapy for acute myocardial infarction. Preliminary results of the CAREMI clinical trial
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Background: The high prevalence of ischemic heart disease and the absence of effective treatments have encouraged searching for feasible alternatives to treat this pathology. Different types of stem cells have been tested in clinical trials with the aim of activating endogenous cardiac-regenerative responses after STEMI.

Purpose: We designed a “First-In-Man” clinical trial to evaluate the safety and the efficacy of allogeneic cardiac progenitor cells (CPC) in this setting.

Methods: The CAREMI trial comprises 2 consecutive phases: an open-label dose-escalation phase (n=49). STEMI patients (p) successfully treated with primary PCI, with dose-escalation phase (n=6) and a randomized double-blind placebo-controlled

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References:
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Background and purpose: Mesenchymal stem cell populations (MSCs) are a promise source of stem cells for cardiac regeneration approaches. However, not 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 therapeutic properties of resident and transplantable MSC populations.

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 release of cytokines and secreted proteins 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: IL1α, IL1β, IL-6 and TNF-α (p<0.05). On the other hand, SC MSC phenotype and cytokine profile were less affected by MI. Next, to assess the 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 MSC origin, MI 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 enhanced 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 changes in LV diastolic diameter and volume, compared with WT cMSCs (2.4 fold and 2.5 fold decrease, p<0.04) and saline treatment group (2.9 fold and 3 fold decrease, p<0.04).

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.

Stem cells and cell therapy I / Stem cells and cell therapy II

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 endothelium (at 24h, 1 week, 3 and 6 months) 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 were included in this study, 31 with advanced CLI (Rutherford category 5.6) not eligible for revascularization were treated with intramuscular (n=30) or intrarterial (n=31) application of 40ml of BM-MNCs concentration. Patients with limb salvage at 6-month follow-up were considered as responders to cell therapy. The concentrations of blood 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...
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 12.6±4.0 μmol/l, p=0.05). Importantly, the number of delivered BM-MNCs significantly correlated with decrease in ADMA concentration at 3-month follow-up (r=0.006, n=−0.45), and with decrease in TNF-α concentration at 6-month follow-up (r=0.009, n=−0.51). There was no correlation with number of applied CD34+ cells, or with dosage of administered atorvastatin.

Conclusions: Administration of BM-MNCs could positively influence angiogenesis and endothelial function by decrease of ADMA concentration and by attenuation of oxidative stress. Regulation of ADMA-NO axis and improvement of anatherosclerosis and endothelial function by decrease of ADMA concentration and by attenuation of oxidative stress.

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P3557 | BENCH
Granulocyte colony-stimulating factor promotes the proliferation of cardiac side population cells by AKT-GATA4 pathway
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Background: Granulocyte colony-stimulating factor (G-CSF) was initially reported to induce myogenic regeneration by promoting mobilization of bone marrow stem cells or side population cells to the injured heart after myocardial infarction. However, the number of cardiac side population cells (CSPs), one of candidate progenitor cells for cardiac stem cells, has been reported to be able to differentiate into cardiovascular cells in vitro and in vivo. Our previous study showed that G-CSF improved cardiac function against ischemic-reperfusion injury by Stat3/HSF1 pathway in animal study. However, whether the cardiac-protection of G-CSF is associated with the effect on CSPs is unclear.

Purpose: We aim to study the effect and the potential mechanisms of G-CSF on CSPs.

Methods: MI model was established by ligature of left anterior descending artery in mice. Mice were treated with recombinant human G-CSF (100μg/kg/day) or saline by subcutaneous injection for 7 days consecutively after MI. CSPs were isolated and counted from mice by fluorescence-activated cell sorting (FACS) analysis. In vitro, CSPs from neonatal rat were purified and cultured with or without G-CSF. The proliferation of cultured CSPs was analyzed by luminescent cell viability assay.

Results: After MI, the ratio of CSPs was increased 2-fold compared to sham mice, and G-CSF greatly promoted the effect. In vitro, G-CSF significantly enhanced the proliferation of CSPs in concentration-dependent manner. Further analysis showed that G-CSF increased phosphorylated-AKT and expression of GATA4 in cultured CSPs. AKT inhibitor dramatically suppressed G-CSF-induced-proliferation of CSPs in vitro and in vivo. It also inhibited the upregulation of GATA4 in G-CSF in cultured CSPs. Si-GATA4 not only effectively downregulated the expression of GATA4 by about 80%, but also partly abolished the phospho-AKT induced by G-CSF in cultured CSPs. In addition, G-CSF-induced-proliferation of CSPs was greatly reversed by si-GATA4 in vitro. G-CSF-treated-CSPs demonstrated a cell layer similar to the left pulmonary artery luminal cell layer. Cell proliferation/remodelling/repairing capacity, including electron microscopy images of the luminal side of the recellularized grafts, showed that transplanted CSPs could express α-MHC, one of markers of cardiomyocytes at 2 week after MI. Cardiac function was significantly improved by CSPs transplantation at 4 week after MI.

Conclusions: G-CSF greatly activated AKT signaling, the phospho-AKT upregulated the expression of GATA4, which in turn, promoted the activation of AKT, resulting in the proliferation of CSPs. Thus, G-CSF may exert cardiac-protective effect against MI by promoting the proliferation of CSPs and support myocardial regeneration in injured heart.

P3558 | BENCH
Analysis of secretory profiles of pro-angiogenic paracrine factors in clinical trials of stem cell therapy for myocardial infarction
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Introduction: Great expectations were put on stem cell therapies for myocardial infarction (MI) over the last decade. However, inconsequent results of large clinical trials have hampered a wider application in patients who have suffered a MI. Whereas the REPAIR-AMI trial evidenced quite convincing results, no detectable effects of stem cell transplantation were found in the ASTAMI-trial. As paracrine mechanisms in stem cell therapy have received more and more attention recently, we sought to compare cell separation protocols of these trials with special emphasis on paracrine signalling.

Materials and methods: Mononuclear cells were obtained from peripheral blood and from bone marrow aspirates and were processed according to the ASTAMI and REPAIR-AMI protocols. In brief, cells in the ASTAMI protocol were resuspended in sodium chloride solution supplemented with 20% of autologous plasma and were kept at 4°C, whereas in the REPAIR-AMI protocol cells were cultured in X-Vivo 10 medium supplemented with 5% of autologous plasma, and were kept at room temperature. Cell culture supernatants were analyzed for pro-angiogenic factors using ELISA (e.g. Interleukin-8, GRO-alpha, ENA-78, MCP-1, VEGF).

Results: Cells treated according to the REPAIR-AMI protocol secreted remarkably higher amounts of pro-angiogenic factors compared to the ASTAMI protocol (e.g. Interleukin-8 9.79±mg/ml ±2.9 SEM vs. 930.4 pg/ml ±483.5 SEM, p=0.0022). Keeping cells at higher temperatures significantly boosted secretion of pro-angiogenic factors. Moreover, the addition of autologous serum was superior to AB serum for further increasing secretion of pro-angiogenic factors.

Conclusions: Here we could show that the REPAIR-AMI protocol was far superior regarding the secretion of pro-angiogenic factors. During the culture period these factors were enriched in great amounts in the supernatant when cells were treated in accordance to the REPAIR-AMI protocol. Based on recent studies showing that paracrine signalling represents a major influencing factor in stem cell therapy, we believe that the efficacy of clinical trials in MI patients could be increased by improved protocols for cell processing. The fact that almost no pro-angiogenic factors were present in the supernatant of cells processed according to the ASTAMI-protocol might explain the failure of the ASTAMI-trial.

P3559 | BENCH
In vivo implantation of tissue engineered vascular graft using newborn piglet thyimus derived stem cells: a proof of concept study
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Background and introduction: Prosthetic replacement grafts are used in congenital heart defects surgical surgery. However, these grafts have limited durability and often require repeat operations because of the lack of growth potential. Tissue engineering has the promise to produce a graft with growing/remodelling/repairing capacity. To test such a device, a large animal model of congenital heart defect is needed for in vivo testing.

Purpose: We aimed at isolating and characterising mesenchymal stem cells (MSCs) from newborn piglet thyimus and using these cells to tissue engineer vascular grafts. Additionally we established a novel recovery piglet model for left atrial appendage artery grafting to test tissue-engineering grafts.

Methods: MSCs were isolated from newborn boar thyimus and expanded in vitro. Oil Red, Alizarin Red and Alcian Blue stainings were, respectively, used to test adipogenic, osteogenic and chondrogenic differentiation potential of isolated MSCs. Graft and cell imaging was carried out by histology, fluorescence and scanning electron microscopy. Cells were seeded onto the acellular porcine small intestine sub-mucosa and grown in a bioreactor. Cell-seeded scaffolds were shaped into conduits and implanted into left pulmonary artery of 12 kg piglets. At 1–6 months following surgery, echocardiography was carried-out and grafts were harvested and analysed.

Results: Thyimus-derived MSCs (pTMSCs) displayed fibroblast-like morphology and were capable of differentiating into osteo-, adip- and chondro-phenotypes. Protocols for seeding stem cells onto a naturally occurring scaffold, routinely used in cardiac surgery, were optimized. Live cells, previously proliferated with 20% serum at room temperature, were then cultured in X-Vivo 10 medium supplemented with 20% serum at room temperature. Cell culture supernatants were analyzed for pro-angiogenic factors using ELISA (e.g. Interleukin-8, GRO-alpha, ENA-78, MCP-1, VEGF).

Materials and methods: Mononuclear cells were obtained from peripheral blood and from bone marrow aspirates and were processed according to the ASTAMI and REPAIR-AMI protocols. In brief, cells in the ASTAMI protocol were resuspended in sodium chloride solution supplemented with 20% of autologous plasma and were kept at 4°C, whereas in the REPAIR-AMI protocol cells were cultured in X-Vivo 10 medium supplemented with 5% of autologous plasma, and were kept at room temperature. Cell culture supernatants were analyzed for pro-angiogenic factors using ELISA (e.g. Interleukin-8, GRO-alpha, ENA-78, MCP-1, VEGF).

Results: Cells treated according to the REPAIR-AMI protocol secreted remarkably higher amounts of pro-angiogenic factors compared to the ASTAMI protocol (e.g. Interleukin-8 9.79±mg/ml ±2.9 SEM vs. 930.4 pg/ml ±483.5 SEM, p=0.0022). Keeping cells at higher temperatures significantly boosted secretion of pro-angiogenic factors. Moreover, the addition of autologous serum was superior to AB serum for further increasing secretion of pro-angiogenic factors.

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P3560 | BENCH
The adult myocardium has a robust endogenous cardiomyocyte proliferation potential
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Introduction: The degree of cardiomyocyte (CM) turnover in the adult myocardium has been since decades a matter of hot debate with many controversial published results. In young adult CMs, 0.06% spans from 0.5% up to 40% per year. Furthermore, the key aspect of the phenomenon at stake is not the mere best approximation of normal CM turnover but rather the actual myocardial potential to replace lost CMs by injury or ageing.
Purpose: To assess the endogenous cardiac capacity for CM replenishment after incremental amounts of pure CM death.

Methods: Transgenic mice non-mutant 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 (R26R) locus to express an "erasable" STOP sequence in front of the Dopaxia toxin A gene (R26R-stop-DTA). Using double transgenic myh6-mER-Cre-mER/R26R-stop-YFP mice, we showed that TAM labeled 80% of total c-kit+ bone marrow cells were recombined to 80% of all c-kit+ cardiac cells as they were all either CD45+ or CD31+ cells. When gating the low expression in several pro-cell survival or cardiopoietic factors (IGF-1, HGF, peptide) from quiescent saline-controls. In vitro analysis revealed that in situ activated eCSCs showed an increased proliferation (determined by bromodeoxyuridine (BrdU) labeling), with a significant increase in the clonogenicity and cardiomyocyte formation when compared to quiescent eCSCs. To identify the alterations of activated eCSCs to iPS-CSCs in the previously activated in situ induced pluripotent stem cells (iPSCs) and protein biochemistry to study Vici syndrome. In this study, we aim to generate iPSCs from Vici syndrome patients carrying EPG5 mutations (Vici-iPSCs) and analyze the cellular and molecular features of Vici-iPSC-derived cardiomyocytes (Vici-iPSC-CMs) and non-cardiomyocytes (Vici-iPSC-nCMs).

Results and methods: Skin fibroblasts from a Vici syndrome patient with EPG5 mutation (c.4952+1 G > A) were reprogrammed into Vici-iPSCs by using lentivirus containing four Yamanaka factors Oct4, Sox2, Klf4 and Myc. The generated Vici-iPSCs were proved for their pluripotency and verified with the EPG5 mutation by sequencing. Vici-iPSCs and control-iPSCs were directly differentiated into functional cardiomyocytes using a standardized serum-free protocol by modifying the Wnt pathway with GSK3β inhibitor CHIR99021 and Wnt pathway inhibitor IWP2. To study the CM of Vici-iPSC-CMs display hypertrophic phenotype, we measured the cell surface areas and found that Vici-iPSC-CMs were significantly bigger than control-iPSC-CMs, however, the volume of the cells demonstrated by flow cytometry analysis showed no differences. Preliminary data showed that the embryonic cardiac genes, e.g., CD90, were downregulated in Vici-iPSC-CMs compared to Vici-iPSC-nCMs showed significant autophogosome accumulation than control cells by both Western blotting and immunofluorescence staining analyses. These findings suggest that the autophagy defects in Vici-iPSC-CMs are different with Vici-iPSC-nCMs.

Conclusions: Our data demonstrated that the differentiated cells from Vici-iPSCs can recapitulate the disease phenotype in vitro and can be used to study the underlying molecular mechanisms in Vici syndrome.

P3561 | BENCH

In situ activation of endogenous cardiac stem cells alters their secretome, miRNome, potentiating their regenerative capacity on the injured heart.

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Introduction: Recently, we have demonstrated that resident tissue-specific c-kit+ endogenous cardiac stem cells (eCSCs) are the central element for myocardial regeneration in adult rodents. However, the first mouse model for c-kit+ cells in adult life has been established. To investigate whether a tamoxifen (TAM)-inducible Cre knock-in the c-kit Exon1 efficiently recombine c-kit+ eCSCs in the adult myocardium for reliable cell fate mapping.

Methods: Heterozygous c-kitCreERT2 Tg/+ mice were crossed with the global double transgenic Cre reporter mouse (R26R-TmG) that express in the ROSA26 (R26) locus a membrane-targeted tandem Tomato dimer (mT) prior to Cre expression and membrane-targeted green fluorescent protein (mG or GFP) after Cre.

Results: CreERT2 knock-in in the c-kit Exon1 produces 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 replace c-kit+ cardiomyocytes in the CM content of the c-kit CreERT2 Tg/+ mouse, about 15%, were recombined by TAM. Thus, the c-kitCreER(T2)/+ mouse, therefore, an endogenous cardiac stem cell fate map strategy, it impossible to appropriately quantify the cardiac cell progeny, using this approach, we identified that activated eCSCs had a greater regenerative capacity than quiescent eCSCs. These miRs regulated a specific network of cell-cycle and survival target genes as revealed by RNASeq analysis. We also identified expression analysis of activated eCSCs identified up-regulation of miR-21*, miR-221 and miR-874, and down-regulation of miR-92b*, miR-598–3p and miR-299 relative to quiescent eCSCs. These miRs regulated a specific network of cell survival target genes as revealed by RNASeq analysis. We also identified that activated eCSCs had a greater regenerative capacity than quiescent eCSCs, with injured hearts (ISO+S-FU cardiomyopathy) recovering function more following treatment with activated than quiescent eCSCs.

In conclusion, activation of the c-kit+ eCSC population in vivo substantially alters the eCSC5 secretome and miRNome, associated with alterations of their biological characteristics and properties. These effects are associated with an enhancement of the regenerative capacity of eCSCs, suggesting that utilisation of eCSCs for myocardial regeneration.
Conclusions: Combined SW-BMDMSC therapy is superior to either alone for improving LVEF, reducing infarct size, and inhibiting LV remodeling. That of LVEF among all groups (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 4 than those in group 3 (p < 0.001). Protein (MMP-9, TNF-α and NF-κB) and cellular (CD14+, CD40+) levels of inflammatory biomarkers, protein expressions of oxidative stress (oxidized protein, NOX-1, NOX-2), apoptosis (Bax, caspase-3, PARP), infarct size, and LV dimensions showed a pattern opposite to that of LVEF among all groups (all p < 0.05).

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-BMDMSC), and group 5 (AMI-SW-BMDMSC) were sacrificed by day 60 and the hearts were collected for studies. Baseline LV injection fraction [LVEF (%)] 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 3 than that in groups 4 and 5, and significantly higher than those in group 3 (p < 0.001). Cellular and protein levels of VEGF, CXCR4, and SDF-1a 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 4 than those in group 3 (p < 0.001). Protein (MMP-9, TNF-α and NF-κB) and cellular (CD14+, CD40+) levels of inflammatory biomarkers, protein expressions of oxidative stress (oxidized protein, NOX-1, NOX-2), apoptosis (Bax, caspase-3, PARP), infarct size, and LV dimensions showed a pattern opposite to that of LVEF among all groups (all p < 0.05).

Conclusions: Combined SW-BMDMSC therapy is superior to either alone for improving LVEF, reducing infarct size, and inhibiting LV remodeling.

P3564 | BENCH
Therapeutic potential of induced pluripotent stem cells in monocrotaline-induced pulmonary arterial hypertension
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Background: Pulmonary arterial hypertension (PAH) is a group of diseases characterized by increases in vascular resistance and the remodeling of pulmonary arteries. Severe inflammation, demonstrated by the accumulation of inflammatory cells in the lung and elevated levels of specific cytokines in bloodstream, has been suggested involving in PAH. Regenerative cell therapy emerged as a potential treatment for PAH through regulating the host’s immune response. In this study, induced pluripotent stem cells (iPSCs) were investigated for their effects in the development of monocrotaline (MCT)-induced PAH in rat.

Methods: MCT-induced PAH rats received either iPSCs or the conditioned medium of cultured iPSCs (iPSC CM) via intravenously injection. Functions of right ventricle after iPSC-based therapy were evaluated by the measurement of systolic pressure of Rv and the ratio of Rv/Lv weight. Inflammation in MCT-induced PAH rats were assessed by immunohistochemistry, qPCR or ELISA as say of the lung specimens or serum. The underlying molecular mechanism of iPSC-based therapy on PAH was focus on the NF-κB signaling by analyzing the phosphorylation level of NF-κB molecule.

Results: iPSC-based therapy, either iPSCs or iPSC CM, significantly restored the function of right ventricle by reducing systolic pressure and action potential, and pteryphophy of the vascular walls of pulmonary arteries in MCT-induced PAH rats. Inflammation in lung tissue of MCT-induced PAH rats was attenuated shown by IHC staining for markers CD68 and MHC-II and quantitative RT-PCR for genes il-1b, il-6, il-12a, il-12b, il-23 and il-10. The anti-inflammatory effect of iPSC-based therapy in group 4 that treated with reduced secretion of TNFα and IL-1β into the culture medium of human pro-inflammatory macrophages. Suppression of NF-κB phosphorylation was proved to be the underlying mechanism of iPSC-based therapy in PAH by IHC and western blot.

Conclusions: The iPSC-based therapy improved the function of Rv and alleviated the inflammatory situation of MCT-induced PAH rat, which might be a potential therapeutic PAH in the future.

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P3565 | BENCH
Human cardiac stem cells and saphenous vein-derived pericytes show a molecular interaction involving DPP-4/SDF-1 turnover and additively 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, secreto-me, 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-deoxyuridine - Edu (i.p. 50μg) every 2 days over all 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, GFO, SCF), in agreement with previous studies. Differences in SVPs were shown by Ang-1/2 levels; CSCs secreted SVs. Interestingly, when cells are cultured in mutual contact for 48 hrs, the release of SDF-1 in cell supernatants is significantly increased (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 SDF-1-degrading enzyme. 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 recruiting 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 arteries and microvessel-like capillaries.

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.

P3566 | BENCH
Quantitative analysis of cardiomyocyte contractile kinetics and force generation using automated morphologic similarity measure
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Background: Stem cell-derived cardiomyocytes are increasingly used for studying cardiac physiology and pathophysiology in vitro. However, current techniques for functional assessment of CMs are optimized for mature myocardial cells and are not well suited for the study of stem cell derived CMs that lack distinct cellular edges and well-developed sarcomeres.

Purpose: To develop an unbiased automated methodology for the quantitative assessment of force generation and contractile kinetics of cardiomyocytes at different developmental states concurrently with other physiological measures such as calcium cycling and action potential.

Methods and results: We have performed pairwise statistical similarity measures between all frames in a video of human stem cell-derived cardiomyocytes contracting on a flexible substrate. We then generated a similarity matrix that represents a comprehensive assessment of change in cell morphology over time to compute the contraction kinetics. In adult cardiomyocytes this approach produced contraction curves highly similar to those generated by traditional edge detection technology with a Pearson’s correlation coefficient of 0.98. We further calculated as calcium cycling and action potential.

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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
been applied to 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 regard-
ing 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 pa-
tients 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 examinations. Long-term follow-up (up to 5 years) revealed
a mortality rate of 36.5% (50/137 patients). Twenty patients (14.6%) received a
redo-MVR. Furthermore, the majority of the remaining patients (73/137 patients, excluding dead
patients and those who underwent conventional MVR), clinical follow-up (>3
years after pMVR) was achieved in 91.8% (67/73 patients, median follow-up 48
months). Of these, 34 patients presented with NYHA functional class II (64.2%).
In survivors with available long-term echocardiographic follow-up (>3 years af-
ter pMVR, 53/73 patients, median echocardiographic follow-up of 47 month),
MR grade ≤2 was present in 86.8% of patients (46/53 patients). More detailed
echocardiographic parameters will be presented at the congress.

Conclusions: For the patient 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 sustain-
able in selected real world patients with severe symptomatic MR.

P3570 | BEDSIDE
Influence of ischemic and nonischemic cardiomyopathy on mortality
and regurgitation after MitraClip results from the Dresden
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 inter-
ventionally percutaneous method of repair of the mitral valve that mimics the
surgical edge-to-edge Alfieri technique through mechanical coaptation of the mitral
leaves. High surgical risk may limit the purpose of this procedure. 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 Dresden 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 measured using 3D-E (phillips).
Decision upon MitraClip procedure was made in the interdisciplenary heart team
accordingly. Patients follow up was 3 and 6 months after successful procedure with
transhorasthal and transesophaegeal echo (TTE, TEE) and clinical examination.

Baseline characteristics showed a mean age of 78 years (57–97 years), with an
ischemic cardiomyopathy in the ischemic cardiomyopathy group (69%). 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) showed a mean LVEF of 52% and 55%, respectively. Imple-
mentation 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 23.9% 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 fea-
sible in patients with ischemic or nonischemic cardiomyopathy with similar pro-
duced results. Two year mortality was twice times higher in patients with ICM, especially in those with severely reduced LVEF <30%. A preoperative ascis-
septoral transthorasthal measured ejection fraction and log. Euro2-Score helps to
identify patients with high mortality in this community of surgical high risk pa-
tients.

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 shape and size of both effective re-
gurgitant 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 mea-
suring the EROA and the regurgitant volume (RVol).

Purpose: To assess the agreement between the severities of the FMR deter-
mined using 2D 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 pe-
riod. The severity of FMR was firstly assessed according to current guidelines
cutoffs. For 2D PISA, EROA and RVol. 3D PISA volume was measured offline
to each frame of the MR flow, using dedicated software package (ePIE 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 clas-
sified as mild, moderate and severe, using the same current guideline cutoffs for

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
2D analysis, 44% of the patients had mild, 25% moderate, and 31% severe FMR. Using 3D peak PISA and 3D cutoffs, 6% of the patients had mild, 19%
moderate, and 75% severe FMR, with a low inter-rater agreement with the 2DE
analysis (k=0.24, CI 0.03–0.52). Using 3D mean PISA, 63% of the patients had
mild, 16% moderate and 22% severe FMR, with a moderate inter-rater agreement
with the 2D 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

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Mitraclip implantation. Kaplan–Meier curves and the log-rank test revealed that proBNP was still higher in FMR patients at 6 months and 12 months after the NYHA class similarly improved in patients with DMR and FMR. However, NT-proBNP was lower in patients with FMR. Logistic EuroSCORE was comparable between the two groups. N-terminal pro-B-type natriuretic peptide (NT-proBNP) was higher and LVEF was lower in patients with 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-proBNP) was higher and LVEF was lower in patients with FMR. Logistic EuroSCORE 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-proBNP was still higher in FMR patients at 6 months and 12 months after the mitraclip implantation. Kaplan–Meier curves and the log-rank test revealed that the all-cause mortality was comparable between patients with DMR and FMR.

Purpose: We aimed to clarify the difference in the characteristics and long-term outcomes of patients underwent mitraclip between DMR and FMR.

Method and result: In a total of 206 consecutive patients after the mitraclip 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 NYHA class was similar between the two groups. N-terminal pro-B-type natriuretic peptide (NT-proBNP) was higher and LVEF was lower in patients with FMR. Logistic EuroSCORE 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-proBNP was still higher in FMR patients at 6 months and 12 months after the mitraclip 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 mitraclip implantation were comparable between DMR and FMR.

Acknowledgement/Funding: Japan Society for the Promotion of Science

Survival rate after MitraClip

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 mitraclip 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 mitraclip 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 underwent mitraclip between DMR and FMR.

Method and result: In a total of 206 consecutive patients after the mitraclip 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-proBNP) was higher and LVEF was lower in patients with FMR. Logistic EuroSCORE 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-proBNP was still higher in FMR patients at 6 months and 12 months after the mitraclip 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 mitraclip 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 of retrograde femoral access to close Mitral Paravalvular 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 Percutaneous Closure of MPVL in patients with double aortic and metallic prostheses.

Methods: Consecutive patients with double prostesis (DP) who underwent percutaneous MPVL closure in our institution were included. Antegrade and retrograde approach consisting of crossing the wire across the aortic prosthesis in order to access and cross the perivalvular mitral leak were used. Arterious venous loop (AVL) were also performed in all cases but one. The devices used in all interventions were Amplatzer 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 follow-up was 46±32.1 days Retrograde approach with AVL was performed in 17 patients (88%). All procedures were hemodinamically well tolerated. Technical success rates were 88%, (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 interference. At follow-up 50% of the patients presented significant 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 consideration during the procedure.

P3574 | BENCH
Non invasive ultrasonic chordal cutting
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Objective: Chordal cutting targeting leaflet tethering has been described to improve the efficacy of annuloplasty during ischemic mitral regurgitation surgery. Histotripsy is a novel ultrasonic 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 cardipulmonary bypass and invasive surgery in infarcted heart.

Methods: Experiments were performed in vitro in explanted sheep heart (N=5) and in vivo in sheep beating heart (N=3, 40±4 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 8us duration, peak negative pressure of 17 MPa, repetition frequency of 100Hz) placed orthogonal to the direction of 64±0 μm distance. In vivo, the procedure was applied on the thorax cavity was filled with water. We analysed MV coaptation 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 baseal chordae and the integrity 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 of the leaflet were completely cut. The mean procedure time was 19 (±9) 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 objected.

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 frequently challenging in these patients and a special diagnostic workup is necessary 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 intracellular 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 promoting the pathogenesis of Tropheryma whipplei-induced IE (TWIE). Methods: Markers of microbial translocation and systemic immune activation, bacterial derived Lipo polysaccharide (LPS), endotoxin core antibodies (Endo-Cab), 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 tissue 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 p=0.0161, sCD14 p=0.0019). Values of sCD14, that not differed from patients with intestinal barrier dysfunction (p=0.3356), remained still high after therapy induction (p=0.0222), indicating sustained immune response. Low levels of LPS (p=0.04) in the context of high Endo-Cab 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 infective endocarditis undergoing surgery during their lifetime position of surgical mortality was 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: A retrospective analysis of patients with 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 performed a multivariable logistic regression analysis to determine their predicting factors of mortality.

Results: Among 1101 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, perianalum 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%). Staphylococcus 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 0.1–0.8, 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 1.1–8.4, p=0.028) were the independent risk factors for hospital 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.
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 (PPI).

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 PPI implantation after the procedure. Patients requiring a PPI implantation significantly longer (14.5±3.33 vs 10.74±2.33 ms (p=0.0003)). They also had at baseline a longer AH: 143.8±48 vs 107.4±23 ms (p<0.002), 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 PPI 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 PPI implantation after TAVI.
Aortic valve disease

litus (DM), especially insulin treated, on short- and midterm outcomes following TAVI remain to be defined.

**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, 586 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 reinventions 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) compared with patients without diabetes. In order to define the prognostic power of HbA1C 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 >6.5 was 2.571, p=0.033 (CI 95% 1.077-6.136) compared with HbA1C <5.7. Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

**Conclusions:** History of DM does not significantly effect rates of complications revealed that DM was not independentely correlated with death. In mild AS patients with heart failure, aortic valve intervention or transcatheter aortic valve implantation (TAVI) may benefit this group of patients in terms of determining timing of intervention.

**AORTIC VALVE DISEASE**

**P3585 | BEDSIDE**

**Rapid progression of mild to moderate aortic stenosis in patients with end stage renal disease**

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**Background:** We aim to explore progression of mild to moderate AS in ESRD patients by using full cardiac imaging. Unlike patients on dialysis, AS is a common entity in ESRD patients and severe AS requiring valve replacement is frequent in this group of patients.

**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 assessed by peak systolic pressure gradient (PGN, 10 μg/ml), 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±24.0 months. Change of AVA and MCS according to their initial HbA1c measured at 1, 3 and 10 years were significantly different. From mild AS, PGN acceleration was significantly faster in ESRD than control (p<0.01). In control group, acceleration rates of MSPG and PGN were higher according to peak systolic pressure gradient (PGS), mean systolic pressure gradient (MSPG), and aortic valve area (AVA) calculated by continuity equations as well as current guidelines.

**Conclusions:** In patients who underwent TAVI, however a less controlled disease as manifested by elevated HbA1c may be associated with increased mortality.

**P3586 | 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 prosthesis 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 [1027–618] pg/ml vs 1039 [212–1865] pg/ml, p=0.02). The incidence of leak in the overall population was 65%, being moderate to severe in 16 pts (11%). In pts with leak, the presence of pre-TAVI moderate to severe AR was associated with a higher baseline NYHA functional class (p=0.03) and with a more significant functional improvement (>2 NYHA stages) during the follow up (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 differences between these pts and the overall population, in what concerns to functional class, NT-proBNP and cardiovascular events during the follow up.

**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 valvarus interstitial cells (VICs) activation and their transformation into osteoblastic phenotype seem to be the crucial step in AS development. Statins, which are very effective in atherosclerosis treatment, have been found to be generally ineffective in delaying the AS progression.

**Aim:** 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, 10μg/mL) or TNF-α (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 TNF-α stimulation (9.6-fold, 8.8-fold and 12.7-fold, respectively, all p<0.01). Proinflammatory stimulators also increased calcification process (8.4-fold, 7.4-fold and 10.4-fold, respectively, all 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 (12% and 82%, respectively, p<0.01). Similar effects were observed for 1 and 1 μM rosuvastatin (TF mRNA reduction by 31% and 91%, respectively, and calcification by 42% and 92% respectively, all 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 suggests 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.
His bundle recording during and after TAVR to predict early and late atrioventricular block


Background: Early and late atrioventricular blocks (AVB) are frequent during trans-aortic valve replacement (TAVR) leading to permanent pacemaker (PPM) implantation. Whether His Bundle recording (HBR) during and after TAVR can predict AVB remains a matter of debate.

Objective: To correlate HV interval during and after TAVR with early and late AVB occurrence.

Methods: Between January 2013 and December 2014, HBR was assessed prospectively before balloon inflation (HV1), 15 minutes after (HV2), and at day 2 and 5 for Sapiens and CoreValve (HV3) in all pacemaker-free patients undergoing TAVR. PPM was implanted when permanent AVB persisted over day, or if parovascular AVB occurred within the first 5 days or if HV3 > 80ms. Logistic regression 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±9.3 and of whom 50 (57%) were female were recruited. Corevalve was predominantly used (59%) for Sapiens and HV2 and HV3 were 56±17ms, 70±18ms 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 and 3 for sick sinus 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 preservation 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=0.35 and p=0.01 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.

Increased levels of NT-proBNP are associated with reduced exercise capacity and peak oxygen consumption in asymptomatic patients with chronic aortic regurgitation

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Background: In patients with chronic, haemodynamically significant aortic 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 chronic 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 severe, chronic AR and no indication for aortic 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±82 ml and the aortic regurgitant fraction 34±13%. VO2peak was 35.8±8.9 ml/kg/min, 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 aortic regurgitant fraction was not predictive of VO2peak. Higher levels of NT-proBNP were independently associated with poorer exercise capacity and VO2peak (Figure).

Conclusion: Our results indicate that in asymptomatic patients with moderate or severe AR and moderately dilated left ventrices, exercise capacity is preserved and remodelling is primarily adaptive. An increased level of NT-proBNP is associated with a reduced VO2peak, possibly heralding the onset of adverse remodeling.

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P3589 | BEDSIDE

Bisphosphonates inhibit calcification of aortic valve in an experimental model of aortic valve stenosis

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Background: Local delivery of bisphosphonates has been recently proven to inhibit calcification of the arterial wall in an experimental model of atherosclerosis. The aim of the present study was to evaluate the anticalcific action of bisphosphonates on the aortic valve in an experimental model of aortic 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 aortic calcification of the aortic valve by measuring aortic valve area (AVA). Subsequently eight animals were treated with local delivery of a mixture containing 500 μg zoledronate that was delivered on the cusps of the aortic valve, by a dedicated balloon catheter. A placebo mixture was administered 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 aortic valves were fixed in 10% neutralized buffered formalin solution for 24 hours. The cusps were embedded in paraffin waxes. 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 histomorphometric analysis using Image Pro Plus, version 5.1. The calcified areas were expressed as the percentage 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 aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (21.3±1.17 vs 21.9±3.12, p=0.53). In all animals the local delivery of zoledronate 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±1.60% of the area, p<0.0001). Similarly 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 26.22±1.69% of the area, p<0.0001). No differences were observed between the cusps of the placebo and the controls. (26.92±1.60 vs 26.22±1.69, p=0.23).

Conclusion: Local delivery of bisphosphonates on the aortic valve can inhibit calcification in an experimental model of aortic stenosis.

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Screening of GATA family reveals genetic variants in GATA5 gene in individuals with bicuspid aortic valve

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Background: Bicuspid aortic valve (BAV) is one of the most common heart diseases, with prevalence between 1%-2% in the general population. It has a proposed 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 aortic 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 aortic valve (TAV) (mean age 72.1±9.4 years, 56.2% male), diagnosed by transthoracic echocardiography. DNA was obtained from peripheral blood and stored in the Biobank of our center. Exons and flanking introns of GATA4, GATA6 and GATA6 genes were analyzed by Sanger sequencing. Polyphen2 and SIFT programs were used to predict the pathogenic potential 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 rs41305803 (p.Asp230→Val) in GATA5 resulted significantly associated with the presence of BAV (OR=2.2; 95% CI [1.23–3.95]; p=0.024). 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 previously described, but synonymous, each in an individual with TAV (p.H274=G in GATA5 and p.Asn458=Val in GATA6) were identified.

Conclusion: A new GATA5 potentially pathogenic variant and a common polymorphism appear to contribute to the development of BAV. Our results support the involvement of this gene in the presence of BAV.
Conclusions: for heart failure were consistent across all the groups predictor of mortality. After adjustment, persistent severe Phy after 1 month was an independent pre-
ator of mortality. 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].

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 10mmHg respectively.

of the patients had improved to below moderate MR at 30 days and 1 year, re-
duced pulmonary artery systolic pressure. Among Group 1 62.5% and 77.7%
needs to be revisited.

Background: A certain degree of pulmonary hypertension (Phy) is very com-
mon in patients undergoing Transcatheter Aortic Valve Replacement (TAVR) and a severe Phy is known to negatively affect the outcome. However, a clear understand-
ing of the incidence, the clinical impact and the evolution of the different grades of Phy in the setting of TAVR is lacking.

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=520). The two groups were compared in regards to baseline clinical, echo and procedural characteristics. In hospital, 30 days and 1 year out-
comes were assessed. Univariate and multivariate Cox regression analyses were performed to test the independent effects. Kaplan-Meier assessment was com-
50 AS patients (50% males, age 85±6 years) treated by TAVR under-
got 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 pre-
dicator 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).

Conclusions: 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 inde-
pendently predicts mortality.

P3593 | BEDSIDE

Baseline Mitral Regurgitation in Transcatheter Aortic Valve Replacement Patients: Does it Impact 1 Year Mortality?


Background: The prevalence of concomitant moderate to severe Mitral Regurgi-
tation (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=520). The two groups were compared in regards to baseline clinical, echo and procedural characteristics. In hospital, 30 days and 1 year out-
comes were assessed. Univariate and multivariate Cox regression analyses were performed to test the independent effects. Kaplan-Meier assessment was com-
pleted 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 (un-
adjusted, 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, re-
spectively.

Conclusions: The presence of pre-TAVR moderate to severe MR is not associ-
ated 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.

P3595 | 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 Tran-
scatheter Aortic Valve Replacement (TAVR).

Methods: 50 AS patients (50% males, age 85±6 years) treated by TAVR under-
went 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 pre-
dicator 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).

Conclusions: Pre-intervention LGE extent in candidates to TAVR is an indepen-
dent predictor of longterm subsequent worse clinical outcomes. These findings should be further tested with other independent predictors in larger groups of patients.

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MYOCARDITIS

P3595 | BENCH

The myeloid 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). Myeloid derived suppressor cells (MDSC) are known to suppress the ef-
ciciency of the innate and adaptive immune response in viral infections. Previ-
ously, 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.

Methods 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 degranula-
tion 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 susceptible for chronic myocarditis compared to resistant C57BL/6 mice. Regarding the underlying mechanisms of MDSC at-
traction 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 S100A8 and S100A9 in 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 infec-
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Patients and methods: We updated our treatment registry of 162 consecutive patients with myocarditis in the clinic of University, Marburg, Germany; 2 Klinikum, Bad Hersfeld, Germany. Pentaglobin® i. v. (enriched IgG, IgA and IgM preparation, Biotest) at day 1 and every 3 days (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 knock-down was knocked-down in HL-1 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 exhibited a reduced caspase 3/7 activity and 3.4-fold (p < 0.05) lower CVB3 copy number, 1.2-fold (p < 0.05) lower L V mRNA expression of Col1a1, and 3.6-fold (p < 0.001) reduced TLR4 protein expression compared to WT CVB3 mice. 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 underlyling signalling.

Conclusion: NOD2 knock-down improves left ventricular function and attenuates pathophysiologische key mechanisms in acute CVB3-induced myocarditis mice. Modulation of NOD2 might represent a promising therapeutic strategy to treat viral myocarditis.

P3597 | BENCH
NOD2 knock down induces cardiobeneficial 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.

Conclusions: NOD2 knock down (-/-) and C57Bl/6-wild type (WT) mice. acute myocarditis was induced by intraperitoneal injection of 5x10^5 p.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 knock-down in HL-1 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 3.4-fold (p < 0.05) lower CVB3 copy number, 1.2-fold (p < 0.05) lower L V mRNA expression of Col1a1, and 3.6-fold (p < 0.001) reduced TLR4 protein expression compared to WT CVB3 mice. 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 underlyling 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.

P3598 | BENCH
Pentaglobin treatment in viral myocarditis - An update
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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 (~14 infiltrating cells/mm²) by endomyocarcial biopsy (EMB). In 102 pts parvovirus B19 (63%), in 36 pts adenoviruses (22%), in 14 pts HHV6 (9%) and in 10 pts EBV (6%) were assessed by PCR as causative viral pathogens. All virus positive patients were treated with 10 g/day Pentaglobin® i. v. (enriched IgG, IgA and IgM preparation, Biotech) at day 1 and 3. After six months all patients were reevalutated clinically, 75 patients (46%) in addition by EMB.

Results: After Pentaglobin treatment 141 pts 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%) rebioisped pts inflammation had resolved. In all rebiosied 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 rebioisped 46 pts (78%). Parvo B 19 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).

Conclusions: 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 in Parvo B19 infection.

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P3599 | BEDSIDE
Pentadise with acute myocarditis more often develop beta1-receptor autoantibodies than patients with post-infarction myocardial inflammation: first results from the prospective ETiCS-study
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Introduction: Heart failure (HF) is a main cause of mortality & morbidity in Western countries. In the last decade evidence for a key role of autoimmunity in the pathogenesis of HF has emerged; particularly, autoantibodies targeting the cardiac beta1-receptor (beta1-aabs) are thought to be able to induce HF. However, the events triggering the formation of beta1-aabs and their effects on the course of HF are unknown.

Methods: Exposure of beta1-receptors & other cardiac antigens after inflammation or necrosis might trigger formation of beta1-aabs. Therefore, 13 European centres prospectively recruit 200 pts. with 1st acute myocardial infarction (FAMI), and 180 pts. with acute biopsy-proven myocarditis (AMitis) into the ETiCS-study. At baseline (BL), after 3, 6, and 12 months pts. receive thorough clinical evaluation (incl. echo & cMRI’s at BL and 12 months) and blood sampling to follow the course of cardiac aabs. Activating beta1-aabs are assessed by a cell-based cAMP-assay that detects beta1-mediated cAMP-increases by measuring the change in fluorescence-resonance energy transfer (FRET) within a cAMP-sensor molecule.

Results and conclusion: The first 8 ETiCS-patients with complete follow-up (n=4 AMitis/4 FAMI) were assessed for beta1-aabs and corresponding LVEFs (echo). The 4 FAMI-patients did not develop aabs, but 2/4 (50%) of the AMitis-patients developed activating beta1-aabs 6 months after cardiac injury. In beta1-aab-pos.(+) patients cardiac function did not recover, whereas LVEF almost fully recovered in beta1-aab-neg.(-) AMitis (n=2/4) or FAMI-patients (n=4/4; see Figure).

FRET activity and LVEF: AMitis vs. FAMI
TLR3, TLR4, TLR7, TLR8; p < 16.83g (AUC=0.92, 95% CI 0.84–0.99; p < 0.001–0.05) and CK had a good diagnostic accuracy in identifying a LGE mass greater than rho=0.78, p < 0.0001. The expression levels of genes coding for cytokines or chemokines from MCA or control subjects.

**Results:** The expression levels of genes coding for cytokines or chemokines (CCL20, IL1B, IL6, IL10; p < 0.001–0.05) and proteins involved in the mitochondrial energy metabolism (ATP6, CYB, DHCODH, ND4; p < 0.05) were differentially expressed in 2 to 3fold range respectively. Bioinformatic analyses and correlation of the gene expression data with immunohistochemical findings provided novel information regarding the differential cellular and molecular pathomechanisms in EOM. The level of gene regulation and number of inflammatory infiltrates pronounces a possible involvement of eosinophils and macrophages in EOM.

**Conclusion:** Myocardial gene expression profiling is a novel method to predict the presence of eosinophilic myocarditis in the myocardium, even without a direct histological proof. Thereby, the risk of sampling errors in single small EMB sections is reduced. Gene profiling also facilitates the discrimination of EOM from two other frequently fatal human myocardial diseases ICMG and CS, which require immediate and tailored differential therapy.

**P3602**

**Myocardial gene expression profiling as novel diagnostic tool for eosinophilic myocarditis**

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**Background:** Eosinophilic myocarditis (EOM) is a rare condition in which inflammation of the heart results in an infiltrative cardiomyopathy that is often difficult to diagnose in the acute setting.

**Purpose:** Myocardial gene expression profiling is a novel method to predict the presence of eosinophilic myocarditis in the myocardium, even without a direct histological proof. Thereby, the risk of sampling errors in single small EMB sections is reduced. Gene profiling also facilitates the discrimination of EOM from two other frequently fatal human myocardial diseases ICMG and CS, which require immediate and tailored differential therapy.

**Methods:** Here we examined gene expression profiles in EMBs from 22 patients with histopathologically proven EOM, 18 with active myocarditis (MCA), and 80 control subjects showing no signs of inflammation by quantitative RT-QPCR. We identified distinct differential profiles that allowed for a clear discrimination of EOM from MCA or control subjects.

**Results:** The expression levels of genes coding for cytokines or chemokines (CCL20, IL1B, IL6, IL10; p < 0.05), cellular receptors (ADIPOR2, IL23R, IL6R), cytokines (CCL20, IL1B, IL6, IL10; p < 0.001–0.05), and proteins involved in the mitochondrial energy metabolism (ATP6, CYB, DHCODH, ND4; p < 0.05) were differentially expressed in 2 to 3fold range respectively. Bioinformatic analyses and correlation of the gene expression data with immunohistochemical findings provided novel information regarding the differential cellular and molecular pathomechanisms in EOM. The level of gene regulation and number of inflammatory infiltrates pronounces a possible involvement of eosinophils and macrophages in EOM.

**Conclusion:** Myocardial gene expression profiling is a novel method to predict the presence of eosinophilic myocarditis in the myocardium, even without a direct histological proof. Thereby, the risk of sampling errors in single small EMB sections is reduced. Gene profiling also facilitates the discrimination of EOM from two other frequently fatal human myocardial diseases ICMG and CS, which require immediate and tailored differential therapy.

**P3603 | BEDSIDE**

**Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis**


**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<0.0001) and baseline LVEF was lower (20% [Q1-Q3]:15–35% vs. 55,55–60%;p<0.0001). Median follow-up was 800 days (259–1667). Kaplan Meier survival curves showed a significantly lower transplant-free survival in FM than in NFAM (78%vs. 100%, log-rank p<0.0001). All but one events occurred during initial hospitalization (4 deaths, 3 heart transplantation [HTx]), one patient on LVAD underwent elective HTx within one year. No patients with NFAM died or received HTx or MCS. 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 [–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 1.6–6.1, 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.

**P3604 | BEDSIDE**

**Acute myocarditis: correlation between myocardial necrosis biomarkers and delayed enhancement mass evaluated by cardiac magnetic resonance**


**Background:** Cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) has emerged as an in vivo marker of myocardial fibrosis, and is now a gold standard for myocarditis diagnosis, with an additional role in the prediction of clinical outcomes. Troponin I (Tnl) and creatine kinase (CK) are myocardial necrosis biomarkers that are elevated in patients (pts) with acute myocarditis. However, their role in the quantification of myocardial necrosis has not been established.

**Purpose:** To evaluate the utility of the Tnl and CK assay in the quantification of myocardial necrosis acquired by LGE CMR in CMR.

**Methods:** Prospective observational study of consecutive pts with acute myocarditis confirmed by CMR (Lake Louise criteria). All pts have performed a CMR (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<0.0001) and baseline LVEF was lower (20% [Q1-Q3]:15–35% vs. 55,55–60%;p<0.0001). Median follow-up was 800 days (259–1667). Kaplan Meier survival curves showed a significantly lower transplant-free survival in FM than in NFAM (78%vs. 100%, log-rank p<0.0001). All but one events occurred during initial hospitalization (4 deaths, 3 heart transplantation [HTx]), one patient on LVAD underwent elective HTx within one year. No patients with NFAM died or received HTx or MCS. 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 [–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 1.6–6.1, 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.

**ABSTRACT WITHDRAWN**
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?**


**Introduction:** Cardiac diseases were identified. Testing some of these peptide antigens in an-

**Conclusion:** In this study, various epitopes for autoantibody binding in different diseases and structural changes in immunised mice.

We identified a peptide sequence within dystrophin that induced inflammation and structural changes in immunised mice. Histopathological evaluation of the heart and antibodies were determined within 7 days after RFCA for AF. Compared to the baseline value, LAVI decreased of more than 6mm after RFCA.

**Methods:** Peptide Array analysis (PEPperMAP) was performed against 26,364 peptide antigens present in cardiac tissue are found in these cardiac diseases.

**Results:** The mean of age was 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 prodrome 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±363ng/ml). Mean BNP C-reactive protein values at admission were 204±357 pg/ml and 86±394 mg/dl, respectively. ST segment elevation (58%) was the most frequent ECG changes. Coronary angiography performed in 38 (48%) 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 (38%) and involving 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 cardiovascular rehospitalizations or deaths were recorded. In a multi-variate 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:** 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 pathogenic epitopes in various cardiac pathologies**

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**Purpose:** Heart diseases are the leading cause of deaths worldwide. Dilated cardiomyopathy (DCM) and myocarditis are two of the most common cardiac pathologies (CP) which 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 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/JL mice (n=8) were immunised on days 0, 7, 14 with peptide sequences derived from laminin, sodium/potassium transporting ATPase and the voltage-gated potassium channel KCNQ1. Mice were immunised with peptides found in the myocarditis and DCM groups. We identified a peptide sequence within dystrophin that induced inflammation and structural changes in immunised mice.

**Conclusion:** In this study, various epitopes for autoantibody binding in different cardiac diseases were identified. Testing some of these peptide antigens in an-
Life expectancy of adults with congenital heart disease

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Background: Contemporary estimates of survival in adults with congenital heart disease (CHD) are sparse.

Methods: We performed a survival analysis for 3,345 adult survivors with CHD prospectively followed up to 25 years. There were 1,688 males and 1,656 females. Median age at first examination was 22 years (19–39). 1,346 patients had simple CHD (group I); 1,606 patients had moderate complexity (group II); and 393 patients had CHD of great complexity (group III). Our database was linked to the National Death Index of Spain. Survival was estimated by computing left-truncated Kaplan–Meier survival analysis, using age as time scale.

Results: Total follow-up was 37,934 person-years. Median follow-up time was 10.6 years (1–18). At the end of the study 328 patients had died (prevalence 9.8%; annual incidence 0.86%). Female subjects died at a median age of 77.5 years (95% CI 76–81) and male subjects at a median age of 70.8 years (67–74) (p < 0.001). The median survival in group I (77.8 years [77–83]) did not differ from reference population. However, survival of patients was severely reduced (< 60 years) in the majority of patients in group III, and moderately reduced (60–75 years) for complete transposition and patients in group II (Table).

Conclusions: Contemporary life expectancy in adults with CHD is worse in male than in female, is lower than 60 years in the majority of complex CHD, between 60 and 75 years in complete transposition and in patients with moderately complex CHD and close to that of the reference population in patients with simple CHD.

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Population health science approaches to cardiovascular disease in Marfan syndrome

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Background: Marfan syndrome is the commonest inherited connective tissue disease, and is associated with increased risk of aortic complications. The magnitude of this risk (overall, and in various age-sex groups) is not known precisely, and may have been under- or overstated by selective reporting from institutions with specialist interest in the condition. Furthermore, the risks of non-aortic cardiovascula
discos are uncertain.

Methods: Large scale datasets of routinely collected statistics of all hospital ad-
misions, and linked datasets of all registered deaths, in England 1999–2011 were used to define a cohort of 4,468 patients with Marfan syndrome. Risks of aortic dissection and of non-aortic cardiovascular complications were quantified in this cohort, and in a cohort of 10,119,152 controls, stratified for a number of baseline characteristics, including age and sex, over a mean follow-up period of 6.9 years.

Results: The relative risk of aortic dissection in the Marfan syndrome cohort compared to controls was 188 (95% CI 160–220, p < 0.0001). The relative risk was spectacularly increased (>1000-fold) in some age-sex groups. Risks of non-
median age at first examination was 22 years (19–39). 1,346 patients had simple CHD (group I); 1,606 patients had moderate complexity (group II); and 393 patients had CHD of great complexity (group III). Our database was linked to the National Death Index of Spain. Survival was estimated by computing left-truncated Kaplan–Meier survival analysis, using age as time scale.

Results: Total follow-up was 37,934 person-years. Median follow-up time was 10.6 years (1–18). At the end of the study 328 patients had died (prevalence 9.8%; annual incidence 0.86%). Female subjects died at a median age of 77.5 years (95% CI 76–81) and male subjects at a median age of 70.8 years (67–74) (p < 0.001). The median survival in group I (77.8 years [77–83]) did not differ from reference population. However, survival of patients was severely reduced (< 60 years) in the majority of patients in group III, and moderately reduced (60–75 years) for complete transposition and patients in group II (Table).

Conclusions: Contemporary life expectancy in adults with CHD is worse in male than in female, is lower than 60 years in the majority of complex CHD, between 60 and 75 years in complete transposition and in patients with moderately complex CHD and close to that of the reference population in patients with simple CHD.

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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. The aim of this study was to determine the prevalence of psychiatric disorders and to assess the quality of life in ACHD patients.

Methods: We performed a cross-sectional study in 1,000 adults with ACHD. Self-rating instruments were used to screen for depression and anxiety disorders. Quality of life was measured with the 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: 36.5–39.6). In particular mood (30.7%; CI: 24.0–38.0 vs. 10.2%; CI: 9.0–11.5) and some 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, 61 (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 dependence (p = 0.036), and NYHA class (p = 0.007). Accuracy of the HADS-D and BDI-II as screening instruments for depression in ACHD was moderate (AUROC 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-II rather underestimate this problem, therefore misdiagnosing 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.

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. Tran
catheter technique for closing the defect is nowadays available also for the el
derly 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 52.±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 hemody-
amic or anatomical reasons. There was no procedure related mortality. Major complication rate was low, 1.9% (1 stroke, 1 pulmonary embolism, 1 respiratory failure in 4.9%). Minor complications were recorded in 4.3%. 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 propor
tion of patients in NYHA I increased from 39.1% to 67.3% (p<0.001) and the proportion 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 antithrombotic therapy six months after the intervention. At follow up 81.8% still used antithrombotic 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
mendment 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: Anatomic repair (double switch operation) for congenitally corrected transposition of the great arteries (cTGA) is associated with good short-to-mid-term outcomes. An increasing number of these patients are surviving to long-term follow-up. There is a paucity of data in adults regarding late sequelae. We sought to determine the long-term outcomes in older patients who have previously undergone a double switch operation for cTGA.

Methods: A retrospective analysis of 16 patient records from 2001 to 2015 from a single institution was conducted. Median age was 23 years (range 18–56 years). Six patients had undergone a Senning arterial switch and 10 patients underwent a Rastelli-Senning procedure. Associated defects included VSD (n=13), pulmonic stenosis (n=2) and pulmonary atresia (n=13). Three patients had undergone primary pulmonary artery banding and 7 patients systemic-pulmonary artery shunting. We determined freedom from re-operation/intervention, development of systemic left ventricular (LV) dysfunction, systemic mitral regurgitation, conduction disorders and arrhythmias.

Results: Median follow-up was 19 years (18–21 years). Eleven patients required further surgery with 4 patients having undergone two subsequent operations. Following anatomic repair, median time to 1st operation was 11 years (7–13 years). Indications for re-operation included re-do RV-PA conduit in the Rastelli-Senning patients (n=8) and aortic valve replacement in the Senning-arterial group (n=3). Four patients underwent coronary artery bypass grafting. Two patients underwent aortic valve replacement. Three patients developed atrial arrhythmias, with 2 requiring ablation procedures. Six patients developed LV dysfunction. There were no deaths or need for cardiac transplantation in this series.

Conclusions: 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.

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 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 for patients who were born between January 1970 and December 1993 with a diagnosis of congenital heart disease diagnosed at birth or subsequently, without previous congestive heart disease, atrial fibrillation or myocardial infarction. Follow-up and morbidity data were collected for all patients until December 2011. Ten controls 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 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 mean follow-up was 10.8 years (1–32). There were 1,856 males, 1,346 females had a simple CHD (group I), 1,606 patients had moderate complexity 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 1.3–2.6; p<0.001) in male subjects and 1.8 (95% CI 1.2–2.1; p<0.001) in female subjects. For the patients belonging to I, the SMR

Main diagnosis | No. of cases | SMR | 95% CI | p
--- | --- | --- | --- | ---
Ventricular septal defect | 583 | 0.97 | 0.90–2.3 | 0.931
Bicuspid aortic valve | 555 | 1.12 | 0.87–1.4 | 0.314
Atrial septal defect | 383 | 1.21 | 0.89–1.6 | 0.168
Subvalvular aortic stenosis | 114 | 1.52 | 0.97–2.4 | 0.038
Eisenmenger | 75 | 1.97 | 0.87–4.5 | 0.067
Coarctation of the aorta | 355 | 2.90 | 1.8–4.5 | -0.001
Tetralogy of Fallot | 325 | 3.02 | 1.91–4.8 | -0.001
Transposition of the great arteries | 124 | 8.02 | 4.4–14.1 | -0.001
Eisenmenger syndrome | 49 | 12.5 | 7.3–21 | -0.001
Single ventricle physiology | 300 | 14.5 | 9.0–24 | -0.001

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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 10.2 (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

P3617 | BEDSIDE

Accuracy of a clinical-ultrasonographic 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-ultrasonographic 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 73% of patients. 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 curves of US-WS (88.4%, 95% CI 83.2–90.6), was significantly superior to that of WS (62.1%, 95% CI 53.5–70.7) (p<0.01).

Conclusions: A clinical-ultrasonographic score (US-WS 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 disease 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 outcome.

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 P 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 associated with PE outcome. 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.
P3619 | BEDSIDE
Time trends and case fatality rates of pulmonary embolism during 11 years of observation in a tertiary hospital setting.

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Background: Pulmonary embolism (PE) is a common and increasingly diagnosed 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 (13.8 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 in the two genders 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 68.7±14.54. The mean pulmonary artery systolic pressure (PASP) (56.5±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±0.07, 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), TAPSE (0.47±0.08 vs. 0.55±0.07, p < 0.001), S′ (9.6±2.8 vs. 15.3±2.6) were significantly increased post-TT (Table 1). No major bleeding was observed. None of the patients had stroke or intracranial 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.

P3621 | BEDSIDE
Withholding anticoagulation after negative CTPE is safe in patients with a likely clinical probability of PE

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Background: According to the 2014 ESC guideline on acute pulmonary embolism (PE), a negative multi-slice computed tomography pulmonary angiography (CTPA) alone is a controversial criterion to rule out symptomatic PE in those patients who have a likely pretest probability of PE, as assessed with a validated clinical decision rule (level B recommendation). Whether these patients should be further investigated thus remains controversial.

Aims: To determine the safety of withholding anticoagulation in patients with a likely pretest probability by the Wells score (≤ 4 points) in whom PE was excluded by negative CTPA alone, and whether this safety is modified by a history of symptomatic venous thromboembolism (VTE). We defined the upper limit of the range of VTE rate in symptomatic VTE after a negative angiogram (2.7%) as the cut-off point for the safe exclusion of PE (van Beek, Clin Radl 2001).

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 likely probability of PE 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 diagnosis (Wells score ≤ 4 points), prior VTE (3.7% (n=21; 95% CI 1.5–7.7)) and a negative non-CTPA alone is safe. It could be debated whether patients with a likely probability and a prior episode of VTE should be referred for additional diagnostic testing.

Conclusions: Withholding anticoagulation in patients with a likely probability of PE can be considered safe without a prior VTE, provided the patient has no history 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 likely probability of PE alone and with prior VTE separately.

P3622 | BEDSIDE
CTproET1 predicts survival in scleroderma-associated pulmonary hypertension

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Background: Pulmonary hypertension (PH) is one of the most frequent causes of disease in Systemic Sclerosis (SSc). N-terminal pro-brain natriuretic peptide (NT-proBNP) is the established biomarker in this setting. Many factors, including renal function, which is common in PH, affect serum levels of NT-proBNP.

Other biomarkers that may be helpful include Copeptin, midregional portion of proadrenomedullin (MR-proADM), midregional portion of pro-adrenomedullin (MR-proADM) and carboxy-terminal pro-endothelin-1 (CT-proET1).

Results: 31 consecutive patients with SSC and clinical suspicion of PH were included, median follow-up was 60 months. PH was detected by right heart catheterization (RHC) in 15 patients (RHC), in 16 patients mean PAPmean was 33±14.2 mmHg, mean pulmonary vascular resistance (PVR) was 5.3±3.7 Wood Units. Mean echocardiographic tricuspid regurgitation pressure gradient (dPmax) was 45.9±24.8 mmHg, and correlated well with PAPmean at RHC. MR-proANP, Copeptin and NT-proBNP significantly correlated with PAPmean and PVR, whereas MR-proADM did not. CT-proET1 had the highest rank correlation coefficient for PAPmean and PVR, and correlation was stronger than for Echocardiography-derived dPmax. Next, we assessed whether these biomarkers were able to differentiate between SSc patients with (PAPmean ≥ 25 mmHg) and without PH (PAPmean < 25 mmHg) by ROC analyses. CT-proET1 had the largest area under the curve (AUC) of 0.879, substantially higher than that of NT-proBNP (AUC 0.788), and of echocardiography-derived dPmax (AUC 0.834).

Partial correlation analyses controlling for glomerular filtration rate revealed that correlation between NT-proBNP and PAPmean was lost, in contrast to CT-proET1 (p=0.001).

Next, diagnostic value of the combination of biomarkers and echocardiographic dPmax to diagnose PH was evaluated. The combined assessment of CT-proET1 and MR-proANP led to an AUC of 0.919, performing better than NT-proBNP with dPmax (AUC 0.834). The highest AUC was achieved by combination of CT-proET1, MR-proANP and dPmax with an AUC of 0.931. During follow-up, 11 of 31 patients died. Cox regression analyses revealed that CT-proET1 predicted survival, and an increase of CT-proET1 levels by 10 pmol was associated with a 14.5% increase in the risk of death (p=0.048).

Conclusion: CT-proET1 predicts pulmonary hemodynamics in SSCs and provides significantly more information than NT-proBNP. Furthermore, CT-proET1 is less dependent on renal function and increased levels predict survival. The combination of CT-proET1, MR-proANP and echocardiography appears very promising to non-invasively identify SSCs-patients with PH.
P3623 | BEDSIDE
Homogarginine predicts mortality in treatment-naive 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 homogarginine), which are potentially involved in the pathophysiology of PAH.

Methods: 108 newly diagnosed, treatment-naive 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 using homogarginine median (1.38 μmol/L; p<0.01; Figure) and fully adjusted Cox proportional hazard models identified homogarginine as an independent predictor of mortality in this study (HR: 0.45, CI: 0.22–0.89). Plasma homogarginine 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 homogarginine 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 homogarginine 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 = dPAP-PAWP) <7 mmHg has recently been introduced for ‘isolated pcPH’ (ipcPH), 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 pre-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 pre-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.

CARDIOVASCULAR PREVENTION: INTERVENTIONS AND OUTCOMES

P3625 | BEDSIDE
Factors associated with operability of chronic thromboembolic pulmonary hypertension: insights of Spanish registry (REHAP)
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Introduction: The treatment of choice for chronic thromboembolic pulmonary hypertension (CTEPH) is the pulmonary endarterectomy (PE). However an important proportion of patients with CTEPH receive only medical treatment (MT) due to distal inoperable disease, comorbidities or no referral for assess operability.

Aim: To analyze the factors associated with PE in CTEPH patients in Spain.

Methods: Voluntary reporting of incident CTEPH cases from 2006 to 2013 were evaluated (n=349). PE were performed in 100 patients (29%) and 249 patients (71%) received only MT. Clinical parameters, 6-minutes walking test (6MWT) and hemodynamic variables were analyzed. Results: Patients undergoing PE were younger [55 (43–68) vs 72 (58–80) years, p<0.001], higher proportion of men (58% vs 37%, p<0.001) and a greater distance walked in the 6MWT [390 (293–468) vs 319 (194–418) meters, p<0.004] than those receiving only MT. No significant differences were found in functional class (FC), or baseline hemodynamic parameters other than mean pulmonary arterial pressure (mPAP) 49±12 vs 45±12 mmHg (p=0.004); pulmonary vascular resistance (PVR) 10.2±4.5 vs 9.9±6.2 Wood Units; cardiac index (CI) 2.2±0.6 vs 2.3±0.6 l/min·m^-2. The figure 1 shows the multivariate analysis for PE.

Conclusion: In Spain, independent factors associated with operability were having proximal lesions in angiography, a better physical status (6MWT) and an unexpectedly a higher mean pulmonary arterial pressure. While older age was an independent risk factor associated for non-operability.

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classified as 390–469 and 100 to 199, ischemic 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, linear regression was performed to estimate mortality trends for each case.

Results: During the study period there were 248,269 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 258 deaths per 100 000 inhabitants and at the end, 145 deaths per 100 thousand inhabitants, with 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 cerebrovascular diseases, a reduction of 6.4% (95% CI −8.1; −4.8) per year, from 69 to 48 deaths per 100 thousand inhabitants. The largest reductions were in 1997–2001, 3.4% (95% CI −4.9; −1.9) and from 2004 to 2010, 3.2% (95% CI −3.7; −2.6) per year. In relation to cerebrovascular disease, the mortality rate decreased from 91 to 41 deaths per 100 thousand 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 2005–2008 period.

Conclusion: There was a progressive reduction in mortality from cardiovascular diseases, ischimic heart disease and cerebrovascular diseases. However, despite this reduction, high rates of death from these diseases still exist.

P3628 | 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 prevalence of type 2 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 and 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” (STT depression/inversion or LBBB) according to Minnesota code. Prevalences were age and sex adjusted to the Mauritian 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, 3.9% (3.0–4.9) vs. 5.1% (4.2–6.1), respectively, or in women, 2.0% (1.4–2.7) and 3.2 (2.6–3.9), respectively. The prevalence of probable CHD did not increase between the surveys, 1.1% (1.0–1.1) vs. 1.1% (1.0–1.2), 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 hyper tension, 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.

Conclusion: The prevalence of self-reported CVD or ECG-changes indicative of CHD did not increase in Mauritius between 1987 and 2009 despite a pronounced increase in diabetes in this population. Both probable and possible CHD was however strongly associated with glucose intolerance and hypertension.

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 year 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 standard 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 >27.9kg/m2 [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 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 colonial class of 2005. The association between aggregate risk factors and grade 1 hypertension should also be taken into consideration in long-term preventive strategy.

Acknowledgement/Funding: This study was funded by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong [Project DOI: 09100701]
P3630 | BEDSIDE
Sub-specialization in cardiology care and outcome: should clinical services be redesigned, again?

Background: Inpatient management of cardiac patients by cardiologists results in reduced mortality and hospitalization. With increasing sub-specialization of the field due to growing 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=0.14), re-admission (p=0.26), re-hospitalization before METs (p=0.05), or reduced LOS and cardiovascular readmissions and mortality (p=0.05). This reduction in mortality was seen mainly in low risk patients (p=0.05). There was a reduction in LOS and cardiovascular readmissions in arrhythmia patients receiving subspeciality 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<0.05). 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 health-care personnel and an 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 have an increased risk for adverse outcomes, primarily in-hospital mortality.

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). Cox proportional hazard model 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 58.98±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 trial.

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 pharmacy 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). No 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 (ICD) have an improved quality of life following cardiac rehabilitation
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Background: 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%), “physical fitness” (25%). A reduction of 14.25% 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.
P3634 | BEDSIDE

Exercise in patients with stable coronary artery disease

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Purpose: To evaluate the effects of cardiovascular rehabilitation on the endothelial function, assessed through changes of circulating blood markers of endothelial function: the stable end product of Nitric oxide (NOx) and Xanthine Oxidase (XO); and on the levels of Unc Acid (UA), and its association with hypertensive response during exercise test in patients (pts) with stable coronary artery disease (CAD).

Design and methods: 90 pts with stable CAD (59.41±6.52 years, all men), admitted at residential rehabilitation center, were studied. All patients underwent a 3 weeks supervised comprehensive rehabilitation program. At baseline and after 3 weeks in all pts values of NOx, XO and UA were determined and exercise test was performed.

Results: After 3 weeks NOx increased (from 45.44±15.96 to 49.42±15.89 μmol/L, P = 0.013) with mean increase 3.97±13.21 μmol/L. Also, XO decreased (from 291.52±63.43 to 260.32±43.56 μmol/L, P = 0.005) with mean decrease 91.21±36.13 μmol/L. Exercise capacity increased from 5.64±1.43 to 6.66±2.26 METs (mean increase was 1.01±1.43 METs), and SBP per minute changes during the first exercise test were 4.75±0.75 mmHg/min. Value of mean per minute changes during the second exercise test, at the level on which the first exercise test was ended was 3.66±1.95 mmHg/min (P < 0.001, mean decrease 1.08±2.84 mmHg/min). A positive correlation was found between mean increase in NOx and mean decrease in UA (r = 0.628, p < 0.0005), as well as between mean decrease in NOx and mean increase in XO (r = 0.704, p < 0.0005). A positive correlation was also found between mean decrease in SBP per minute and mean NOx increase (r = 0.808, p < 0.0005) as well as between mean decrease in SBP per minute and mean decrease in UA levels (r = 0.564, p < 0.0005).

Conclusion: Cardiovascular rehabilitation induced improvement in endothelial function in patients with stable CAD, expressed through significant increase of NOx and significant decrease of XO; also significant decrease in UA and significant improvement in exercise capacity was achieved. Our results show an association between per minute changes during exercise test and metabolic markers of endothelial function. Beneficial changes in NOx, XO and UA may induce favorable changes in vascular tone, and hence they might contribute to endothelial function improvement and SBP regulation during exercise.

P3635 | BEDSIDE

Exercise in patients with stable coronary artery disease

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Purpose: To assess the impact of the CB-CDMP demonstrating 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.

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.

Methods: Between April 2012 and December 2014, acetylcholine provocation test (ACh) was performed in 269 patients. They were divided into 4 groups according to 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 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 CI: 2.74 [1.51–5.90]).

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.

P3636 | BEDSIDE

Exercise in patients with stable coronary artery disease

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Purpose: To assess the impact of the CB-CDMP demonstrating 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.

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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

Exercise in patients with stable coronary artery disease

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Introduction: Previous studies have suggested a higher cardiovascular risk of eastern Europeans as compared to European patients. 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 artery disease (CAD), and in-hospital outcomes of immigrants from Eastern Europe undergoing coronary angiography and compare them with patients in southern Europe. We compared 4 groups of patients from different continents, those from Eastern 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 53%. Angioplasty was performed in 88% and coronary artery by-pass 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), more often males (83 vs 69%, p = 0.005), with less hypertension (48 vs 60%, p = 0.041) and diabetes (19 ± 28.6%, p = 0.079, albel Hba1c of 7 (IQR: 5.9–8.2) vs 6.1 (5.8–6.8), p = 0.150), but higher smoking rate (62 vs 21%, p = 0.005), 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 CAD and history of hypertension. Coronary artery disease (CAD), and in-hospital outcomes were similar maybe due to their younger age. Long-term differences, remaining LVEF, or in-hospital mortality were found.

Conclusion: Immigrants from Eastern Europe in our environment present similar coronary artery 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.
CARDIOVASCULAR REHABILITATION: INTERVENTIONS AND OUTCOMES I

P3638 | 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 slow down the accelerated decline in FEV1 in long-term smokers. However, in long-term smokers who have history of smoking cessation therapy can affect respiratory function in the short term. Thus, we evaluated the short-term effects of smoking cessation therapy with varenicline 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 colleagues. In the last visit, comprising subjects who attained an 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±52.0% vs. 59±31.9% mg/dL, respectively; P<0.01); however, spirometric lung ages significantly deteriorated in the failure group (62±51.7% vs. 65±72.1% mg/dL, respectively; P<0.01). The effect sizes (Cohen’s d) of spirometric lung age in the success and failure groups 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.

P3639 | BEDSIDE
Intensive aerobic exercise training on 3 days/week compared to 5 days/week in patients with coronary artery disease: Is less more?
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Purpose: To elucidate the impact of regular physical exercise on 5 days/week in patients with coronary artery disease: Is less more?
Methods: Our study was to elucidate the impact of regular physical exercise on 5 days/week in patients with coronary artery disease and continuous training observed similar improvements in peak VO2. However, it is well established in cardiac rehabilitation programs. Studies comparing interval training up) compared to exercise training on 3 days per week (Monday-Friday) or 3 days per week (Monday-Thursday/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, intensive exercise training on 5 days per week (Monday-Friday) or 3 days per week (Monday/Thursday/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, intensive exercise training on 5 days per week (Monday-Friday) or 3 days per week (Monday/Thursday/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.
Results: Initial assessment

| Education | 504 (50.5) | 638 (74.0) |
| Follow-up | 291 (29.1) | 476 (55.5) |

P-value 0.001; from 24.7±5.1 ml/kg/min at follow-up compared to exercise training on 3 days per week (P<0.001; from 24.7±5.1 ml/kg/min at follow-up).
Conclusion: In patients with CAD, physical exercise training on 3 days/week compared to 5 days/week has significant improved aerobic exercise capacity compared to 3 days per week with one day for recovery between training sessions. In clinical practice, a more intensive exercise-based cardiac rehabilitation programs should be preferred to achieve greater beneficial effects.

P3640 | BEDSIDE
A contemporary model of cardiac rehabilitation improves accessibility and uptake
J. Smith1, T. Briffa2, A. Brenner2, J. Garton-Smith3, J. Redden4, D. Hendrie5, J. Rankin6, L. Dimers7, A. Maiorana8 on behalf of ACCES.
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Background and introduction: Following acute coronary syndrome (ACS), cardiac rehabilitation (CR) is guideline-advocated but widely underutilised and 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 conducted with staff (n pre/post=44/21) and patients (76/66) occurred, supplemented with phone interviews (11/8) and focus groups (11/8) 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>ACCES (n=862)</th>
<th>Controls (n=999)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial assessment</td>
<td>723 (72.4)</td>
<td>835 (96.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Individualised CR plan</td>
<td>543 (55.0)</td>
<td>638 (74.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Education</td>
<td>723 (72.4)</td>
<td>835 (96.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Follow-up</td>
<td>291 (29.1)</td>
<td>476 (55.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: ACCES compared with controls, engaged twice as many patients in CR, significantly improving the proportion of care provided in 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.
Acknowledgement/Funding: State Health Research Advisory Council, Government of Western Australia

P3641 | BEDSIDE
The role of the individual hospital in adherence to medical guidelines after acute myocardial infarction
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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: Nationwide Danish registers were used to examine the influence of individual hospitals in Denmark on survival 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 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: 0.20; 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; 2.01]). 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 variation 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 assure guideline adherence in individual hospitals is likely to improve appropriate treatment.
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: functional capacity, cardiac risk factors, quality of life, LV systolic and diastolic function, cardiovascular 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. Patients attended the CR twice a week for 60 minutes. Exercise intensity relied on the VO2 peak and rating of perceived exertion (RPE). The IE group performed 2 minutes of low intensity (RPE 1–13) followed by 2 minutes of moderate-high intensity (RPE 14–16), while the CE group exercised continuously at a moderate intensity (RPE 12–14).

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% vs 5% in 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 substantially but similarly. The calculated left ventricular ejection fraction (LVEF) 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 CR 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).

Conclusions: 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.

Short term inspiratory muscle training associated with combined aerobic and resistance training is benefic in patients undergoing cABG surgery in phase II cardiac rehabilitation program

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Background: Inspiratory muscle training (IMT) 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 and resistance training on respiratory muscle strength, functional capacity, and 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 t test and Chi-square test were used (p<0.05).

Results: Compared to AE+RT, IMT program associated increment in VO2peak values were significantly greater when compared to control group (PImax (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.

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), FEV1/FVC (p<0.0002), FEF (p<0.0001) and values in the training group. 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.
Home-based walking training and adherence to medical therapy in patients undergoing coronary artery bypass grafting

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Aim: To evaluate the effects of home-based walking training on adherence to antihypertensive 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 cardiac rehabilitation program (CR) (n=35), Group 2—home-based diabetics, Atrial fibrillation (AF), Heart failure (HF), CABG patients (n=36) and the comparison group (n=41). Subjects did 3 trainings per week for 3 months. Patients were examined 1 month and one year after CABG.

Methods: Echocardiography (ECHO-CO), bicycle ergometer (BE) and the assessment of adherence to medical therapy.

Results: One year after surgery the number of patients receiving β-blockers decreased from 77 to 63.4% (p=0.003), antihypertrophic therapy (from 100% to 88%, p=0.0004) and statins (from 97% to 82%, p=0.0005) decreased in Group 1 with CR. 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<0.0001), antihypertrophic therapy (97% to 82%, p=0.001) 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 also 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), antihypertrophic therapy (from 100% to 65%, p=0.0001) and statins (from 98 to 57%, p=0.00001) was observed in the comparison group. The number of patients treated with ACE inhibitors/ARBs remained at the same level (73% and 75%, p=0.07). Importantly, the number of patients in Group 1 and Group 2 taking statins (p=0.07) and p=0.02, respectively), antihypertrophic therapy (p=0.03 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 trainings have lower 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.
Background: Multivessel coronary artery disease and incomplete revascularization is one of the most serious conditions in ischaemic heart disease. Although the benefit from revascularization programmes in patients with ischaemic heart disease after an acute event is recognised, 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 in our hospital. The study population is composed of 130 patients 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 all-cause mortality (RR 0.273; 95% CI, 0.131–0.537; p<0.001) and cardiovascular mortality (RR 0.831; 95% CI 0.429–1.611; p=0.583) as well as a no significant reduction in non-fatal acute myocardial infarction (RR 0.947; 95% CI 0.576–1.556; p=0.947) 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. The obtained results indicate that the device is beneficial in the early detection of arrhythmias and other cardiac events, allowing for timely intervention and improved patient outcomes. The data also provide evidence for the potential role of remote telemetry in improving patient care and outcomes in cardiac rehabilitation settings.
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 mentally psychosocial 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 a beneficial effect on the primary endpoint VO2peak at 4 months (24.8 ml/kg/min versus 22.4 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-heat, chest pain) were 11/72 (15.3%) in the intervention group versus 3/75 (4.0%) of self-reported non-serious adverse events (e.g., musculoskeletal injuries, heart, 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 VO2peak at 4 months and increased total SSRNP scores, and cardiac-specific scores for sexual counseling, indicating that an intervention grounded in social-cognitive theory provided a feasible approach to enhance sexual counseling knowledge and practice.

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±1.1 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: 0.1–2.1, p=0.03 vs. 1.1% in ACS group: 95% CI: 0.5–1.8, p<0.002). And also, peak oxygen uptake (VO2max) 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).

Results: There was no significant difference of FMD at baseline (8.1% in angina vs. 7.7% in ACS, p<0.18) 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: 0.1–2.1, p=0.03 vs. 1.1% in ACS group: 95% CI: 0.5–1.8, p<0.002). And also, peak oxygen uptake (VO2max) 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).

Conclusion: FMD was improved after CR in patients with PCI, and this beneficial effect was noted 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

Introduction: Cardiac resynchronization therapy (CRT) has been proven to improve functional class and systolic function in heart failure patients (NYHA class III-IV ambulatory III 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±4147, p<0.001), peak VO2 (ml/kg/min.) (17.44±4.76 to 21.01±5.36, p<0.001), MET level (4.97±1.37 to 5.73±1.53, p<0.001), FMD which was measured at baseline (before implantation of CRT), after CRT and after rehabilitation respectively.

Conclusion: There were statistically significantly further improvement on the duration (seconds) of the CPET (614±166 to 743±4147, p<0.001), peak VO2 (ml/kg/min.) (17.44±4.76 to 21.01±5.36, p<0.001), MET level (4.97±1.37 to 5.73±1.53, p<0.001), oxygen pulse (9.46±3.76 to 10.58±3.36, p<0.05), VE/VCO2 (39.42±8.40 to 36.58±7.82, p<0.05) as well as 6-MWT (meters) (433±58.95 to 493.3±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 waiting list) showed significantly improved FMD at 3 months from the 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-
ficial and safe. Additional multidisciplinary intervention further improved patients’ well-being.

### P3658 | BENCH

**Loaded breathing exercise increases cardiovascular sympathetic modulation and blood pressure levels in hypertensive patients.**


**Introduction:** Inspiratory muscle training (IMT) reduces cardiac sympathetic modulation and blood pressure levels in hypertensive patients. 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 loaded breathing exercises session.

**Methods:** Hypertensive volunteers (GH) and healthy controls (GC) were recruited to perform a 30 min LBE session, at 30% of maximum inspiratory pressure (Pmax). Cardiac autonomic responses were monitored by oscillometric 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: GC: 51.51±37 vs 47.89±37.7 mmHg, p<0.05; GH: 4.42±1.61 vs 6.11±44 mmHg, p<0.01), heart rate variance (SD: GC: 51.88±17.15 vs 49.23±17.51, p<0.05; GH: 35.14±7.61 vs 41.45±7.20, p<0.005) and sympathetic peripheral modulation (L-Fabs: GC: 14.90±16.51 vs 9.71±9.32 mmHg2, p<0.04; GH: 16.00±10.01 vs 27.15±13.56, p<0.005) as well as increase of cardiac parasympathetic modulation (H-Fabs: GC: 108.99±81.28 vs 1110.61±1048.16, p<0.006; GH:667.74±547.43 vs 1079.52±1200.37, p<0.003). In addition, there was improvement of the baroreflex sensitivity (BRR: 56.5±4.9 vs 69.1±12.6, p<0.003) and changes in baroreceptor effective-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.

**Acknowledgement/Funding:** CNPq

### P3659 | BEDSIDE

**Effect of long-term home based cardiac rehabilitation programme on readmission and mortality risk after coronary revascularization.**


**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 old) were randomized: group 1 – 91 pts; group 2 – 106 CRP performed a training and secondary prevention programme over 12 months. Clinico-functional assessment and the Seattle Heart Failure Model (SHFM) prediction of survival were obtained at baseline and follow-up.

**Results:** Relhospitalization rate during 12 months period in CRP group was 2.7 times lower than in the control group (20% vs 77%) (Table). Only 2.9% and 2.2% of patients were hospitalized for other reasons, but the majority required cardiovascular readmissions. Baseline mortality prognosis at one year in non-CRP group was estimated as 6.55% vs 3.35% in CRP group, at two years 12.73% vs 7.21% and 30.11% vs 16.53% at five years. After intervention these parameters were significantly lower.

**Conclusions:** Cardiac rehabilitation participation is associated with a markedly reduced risk of readmission during first year after. 2) Partially supervised rehabilitation program improved long term estimative survival prognosis.

### P3660 | BENCH

**Implementation of Jacobson’s progressive relaxation in coronary bypass surgery patients before chest tube removal.**

M.R. Rupar, S. Kostic.

**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), who 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 1-test: 2.63±0.725 vs 3.62±0.725, p<0.001. All experimental subjects stated that the relaxahtiontechnique 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 end points (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±0.5 vs 4.0±3.4, p<0.008). AOPP levels were decreased in both groups, with higher mean AOPP decrease in no-AP group (46.7±13.5 vs 2.5±3.13, p<0.0005). Also, XO levels decreased in both groups (p<0.0005, both), with higher mean XO decrease in no-AP group (120.97±19.02 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<0.002) and XO decrease (OR 0.931, CI 0.869–0.974, p<0.002) and AOPP 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.
had higher healthcare costs both in the first year after MI and in the long-term.

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.

Acknowledgement/Funding: Sponsored by AstraZeneca

P3664 | SPOTLIGHT

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 dysfuction).

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Conclusion: An unexpected decrease in quality indicators at discharge was observed in 2012, contrasting with a regular improvement from 2008 to 2011. This change was driven by lower AP at discharge in low volume centers.

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Acknowledgement/Funding: Sponsored by AstraZeneca

P3665 | BEDSIDE

Deterioration in quality of care after acute myocardial infarction in 2012: results from 5 consecutive years of French nation-wide assessment of quality of discharge prescription after AMI

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Background: We report the results of 5 consecutive years of assessment of quality indicators (QI) at discharge after acute myocardial infarction (AMI), stratified by volume of activity.

Methods: Nationwide assessment of QI at AMI discharge was performed in France by the National Authority for Health (HAS) for 5 consecutive years (2008–2012). Participation was mandatory for all centres admitting >10 AMI per year for QI calculation in a random selection of up to 60 patient files. Centres were categorized by volume of activity (AMI per year: < 30, 30–60, 60–120, > 120). Appropriate prescription (AP) at discharge of aspirin and a P2Y12 inhibitor, beta-blockers, angiotensin conversion enzyme inhibitors (ACEI) when left ventricular ejection fraction < 40%, and statins was defined as prescription at discharge or non-prescription in case of contra indication. A composite indicator was computed (All-or-None method).

Results: We examined 61759 charts from 272 centres. From 2008 to 2011 (n=12406, 10204, 11587 and 12380), there was a gradual increase in the rate of each QI and in the national average of the Composite (62%, 70%, 76% and 83%), this trend was observed in all volume categories. In 2012 (n=15362), there was a significant decrease in the national composite (79%) driven by a decrease in AP of beta-blockers, antiplatelet and statins, whereas AP of ACEI remained stable. When stratified by volume, the decrease was observed in moderate and low volume centers; compared to 2011, AP of antiplatelets decreased by 3%, 1% for ACEI, 7% for beta-blockers and 4% for statins.

Conclusion: The benefit was similar in different socioeconomic groups. To date it is unknown whether the benefit was similar in different socioeconomic groups. AAMI: to evaluate changes in survival after AMI according to socioeconomic position (SEP) from 2002-2011 in Chile.

Methods: National hospital discharge database of the our Ministry of Health were used to identify all first cases of AMI hospitalized in public and private hospitals between 2002–2011 in Chile (ICD 10, I21-22). Link with national mortality database from 2002 to 2012 was done to identifying cardiovascular deaths using a personal unique identification number. SEP was grouped according to health insurance in: low (public insurance, patients without payment capacity), middle (public insurance, partially payment capacity) and high (private insurance). With Cox regression we evaluate the effect of the year of hospitalization in survival adjusted for age and sex; year 2002 was used as reference.

Results: 59,447 fatal and nonfatal hospitalizations for a first event of AMI with complete information were registered between 2002 and 2011; 31.1% women, average age 68.5±13.5 years, men age 61.5±13.1 years. The distribution by type of health insurance was: 62.9% low, 19.2% medium and 17.9% high. Adjusted one-year survival improved only in low SEP group by comparing years 2003–2011 with 2002 (Figure 1), however there was no change in early survival.

Conclusion: After 2005 there was an improvement in one-year survival in AMI.
Social inequalities in 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 (GNHIES98, n=4,170) and 2008–2011 (DEGS1, n=8,530), 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<0.05) among both women and men 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 for low vs. high SES 2.8 (95% CI 1.9–3.8)) and men (OR low vs. high SES 2.02 (95% CI 1.35–3.02)). Between 1998 and 2010, social inequalities in CVD prevalence remained stable among women and increased among men.

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.

Burden of cardiovascular hospitalisations following myocardial infarction among older adults

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Background: Most research on post-myocardial infarction (MI) prognosis has focused on the time to first recurrent cardiovascular disease (CVD) event. However, given the chronic nature of the disease, patients may experience repeated CVD hospitalisations. This overall burden has not been well described.

Purpose: To examine the cumulative number of CVD hospitalisations following an MI.

Methods: Individuals age 66 and older enrolled in Medicare, a government health insurance system for older adults in the United States, who were hospitalised for MI between 2000–2010 were followed for up to 10 years for CVD hospitalisations (MI, stroke, and other cardiovascular conditions) through administrative claims. The number of hospitalisations was annualised to account for variable follow-up.

Results: Among 136,153 individuals followed for 10 years after MI, 69,242 (50.8%) had ≥1 CVD hospitalisation, including 29,802 (21.9%) with ≥1 heart failure hospitalisation, 9,752 (7.2%) with ≥1 MI hospitalisation, 9,561 (7.0%) with ≥1 ischaemic stroke hospitalisation, and 938 (0.7%) with ≥1 haemorrhagic stroke hospitalisation. Of those who experienced at least one CVD hospitalisation, 63.7% had multiple CVD hospitalisations (Figure). Heart failure was associated with multiple recurrent hospitalisations; 50.5% of those experiencing a heart failure hospitalisation had multiple heart failure hospitalisations. The proportion of individuals experiencing multiple recurrent hospitalisations was 32.0%, 28.5%, and 9.8% for MI, ischaemic stroke, and haemorrhagic stroke hospitalisation, respectively.

Conclusion: Studies limited to the first recurrent CVD event following MI substantially underestimate the burden of disease on patients and healthcare systems.

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. 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 (84–625) 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.

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 PCI in 24/7. A survey was conducted during one month for four consecutive years (2011–2014) in order to characterize all patients admitted for STEMI with indication for PCI (>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; 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 lower “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 to reinforce 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.

Table 1. MetS risk factors and LVMR

<table>
<thead>
<tr>
<th>Gender</th>
<th>MetS factor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Waist circumference</td>
<td>2.795</td>
<td>1.649–4.737</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>Waist circumference</td>
<td>2.638</td>
<td>1.479–4.696</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: Among MetS factors, abnormal WC in men and high DBP in women were independent risk factors for abnormal LVMR in normal-weight individuals, and therefore might be useful for predicting diastolic heart failure during routine physical examinations.

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 in Poland following accession in 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±3.01; 48.0% boys; 63.2% urban inhabitants). The following cardiovascular risk factors were considered: physical activity, smoking, oral hygiene, alcohol 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, sex, domicile, family structure and perceived family wealth.

Results: The proportions of teenagers with unhealthy lifestyle habits are presented in the Table. The 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).

Table 1. MetS risk factors and LVMR

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<td>Waist circumference</td>
<td>2.638</td>
<td>1.479–4.696</td>
<td>&lt;0.001</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 overweight 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.
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 nonvalvar 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. Median age was 79±8.6 years, 53% women (180p) 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) (<60%). For this patients Rivaroxaban proved to be cost effective but as an Incremental Cost Effectiveness Ratio (ICER) of 105300€ for avoided ischemic stroke and 288017€ for haemorrhagic stroke. Rivaroxaban therapy did not show gain of QALY’s versus standard anticoagulant therapy.

Cost effectiveness analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Annual cost (€)</th>
<th>Incremental ICER/stroke (€/QALY)</th>
<th>Incremental ICER/major ICER/death (€/QALY)</th>
<th>Incremental ICER/death (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acenocoumarol</td>
<td>196030</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>262169</td>
<td>1714.39 Dominated</td>
<td>1053000 Dominated</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban (TTR &lt;60%)</td>
<td>167489</td>
<td>1053 1053000 Dominated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 which 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: Participants were classified according to body mass index (BMI) and metabolic status. (HUNT) using the ARCHITECT STAT High-Sensitive Troponin assay. All patients participating in the prospective observational Nord-Trøndelag Health Study (HUNT) were included in an Excel database for analysis.

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). We observed for the entire population, hs-TnI levels were significantly associated with increasing body mass index in the eumetabolic 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 with 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 excluded the patients with a history of acute coronary syndrome, advanced chronic kidney disease (eGFR <30 mL/min/1.73 m²), or a history of diabetes mellitus (HbA1c >7.8%). 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 g/L vs 16.5±7.3 g/L, 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.

<table>
<thead>
<tr>
<th>Levels of troponin I</th>
<th>BMI</th>
<th>Median hs-TnI (IQR) (g/L)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Eumetabolic (p &lt; 0.001)</td>
<td>Dysmetabolic (p &lt; 0.001)</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>3748</td>
<td>2.70 (1.90–4.00) g/L</td>
<td>4.80 (3.40–8.35) g/L</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>2870</td>
<td>3.00 (2.50–4.80) g/L</td>
<td>4.60 (3.10–6.90) g/L</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>1239</td>
<td>3.30 (2.50–4.80) g/L</td>
<td>4.30 (3.20–6.50) g/L</td>
</tr>
<tr>
<td>35.0–39.9</td>
<td>254</td>
<td>3.50 (2.50–4.80) g/L</td>
<td>4.30 (3.20–4.30) g/L</td>
</tr>
<tr>
<td>≥40.0</td>
<td>50</td>
<td>4.14 (2.00–7.10) g/L</td>
<td>4.00 (2.75–5.15) g/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.

Association of IMW and WC

Improvement of medical care in cardiovascular patients: social and economic issues / Deleterious effects of obesity and diabetes 641
Methods: From a community-based population, we enrolled 284 asymptomatic T2DM pts (71±4y, 55% men). Associations were sought between 6MW and WC, diabetes duration, HbA1c, health questionnaire (EQ5D) and echo results including global longitudinal strain (GLS). Nested multivariable linear regression models were created to assess increment value of 6MW.

Results: Tertiles of increasing WC were associated with worsening 6MW (1st:475±959m; 2nd:470±96m; 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<0.01), BMI (r=-0.42, p<0.01), 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 6MW after adjusting for other variables including BMI (model R2=0.45). The association of clinical variables (age, sex, EQ5D and BMI) was not influenced by GLS (p=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

Ankara University, Cardiology Department, Ankara, Turkey

Introduction: Contrast-induced nephropathy (CIN) is a common cause of hospital-acquired acute kidney injury (AKI). NGAL represents non-invasive, tropinin-like biomarker for the early prediction of AKI in various clinical settings. In this 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 under- going elective coronary angiography. Serum creatinine (SCr) and plasma NGAL levels were measured at baseline and after intervention (SCR at 72h and NGAL at 4h). CIN was defined as an increase in SCr of ≥25% or 0.5 mg/dl from baseline within 48-72 h after angiography.

Patients were divided into two arms based on the use of RASB: RASB+: Drugs not stopped before the procedure, RASB−: Drugs stopped 24 h before the procedure. CIN was observed more common in RASB+(+) group than in RASB(−) group, but statistically not significant (9 [19.5%] vs 4 [10.3%], p=0.33). The amount of contrast agent volume and preventive treatment were independent predictors of CIN in multivariate analysis (OR=1.007; 95% CI: 0.999-1.015; p=0.07 for contrast agent volume and OR=5.937; 95% CI: 1.460-32.965; p=0.01 for preventive treatment). Plasma NGAL levels were not elevated at 4 h post-procedure in CIN+(+) patients versus CIN(−) patients (4839±3374 pg/ml versus 4304±1814 pg/ml, p=0.68) (see table).

Comparison of NGAL and serum creatinine levels in contrast induced nephropathy (+) and (−) patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>CIN(+), n=12</th>
<th>CIN(−), n=68</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCr (mg/dl), mean±SD</td>
<td>0.96±0.24</td>
<td>0.89±0.25</td>
<td>0.35</td>
</tr>
<tr>
<td>SCR (72h, (mg/dl)</td>
<td>1.25±0.30</td>
<td>1.91±0.26</td>
<td>0.01</td>
</tr>
<tr>
<td>NGAL baseline (pg/ml), mean±SD</td>
<td>6734±6031</td>
<td>4251±3417</td>
<td>0.05</td>
</tr>
<tr>
<td>NGAL (4 Hour), (pg/ml), mean±SD</td>
<td>4839±3374</td>
<td>4304±1814</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Comparison of NGAL and serum creatinine levels in contrast induced nephropathy (+) and (−) patients

Conclusions: In diabetic patients undergoing coronary procedure, chronic usage of RAASB don’t increase the risk of CIN significantly. Plasma NGAL appears to be a powerful early biomarker of AKI, however, in our study NGAL levels didn’t increase in contrast-induced nephropathy.

P3678 | BEDSIDE
Concordance of glucose based and of 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 are dependent on presence of T2DM. In this prospective study we compared concordance of glucose and HbA1c as a standard, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the HbA1c criterion were 66.7%, 94.9%, 16.7% and 99.5%, respectively.

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±6). The diagnosis of DR was made by ophthalmoscopy and best-corrected visual acuity (BCVA) was measured in both eyes. A BCVA less than 0.8 was considered as severely impaired. C reactive protein (CRP) and Interleukin-6 (IL6) were measured as well established inflammatory markers contributing to atherosclerosis progression.

Results: Although there were no significant differences in baseline characteristics, patients with DR compared to NDR patients had increased levels of IL6 [2.24 (1.33–3.99)pg/ml vs. 1.51 (0.96–3.05)pg/ml, p=0.03] and worse BCVA [0.8 (0.92–
1/3 of 0.8 (0.5–1), p<0.001, while there was no significant difference in CRP levels (2.85 (0.91–4.41)mg/L vs. 1.25 (0.56–4.29)mg/L, p=0.12). Moreover, in diabetes mellitus subjects, BCVA was inversely correlated with IL-6 levels (r=−0.25, p<0.03). CRP levels (r=−0.26, p=0.16) glycosylated hemoglobin levels (r=0.38, p<0.001), age (r=−0.34, p=0.001) and with duration of diabetes mellitus (r=−0.41, p<0.001) and positively correlated with creatinine clearance (r=0.21, p<0.04). Interestingly, after adjustment for age, gender, body mass index, smoking habits, CRP levels, insulin treatment and the aforementioned confounders, IL-6 was independently associated with BCVA [b=−0.034 95% CI (−0.056, −0.012), p=0.004] while CRP was not a significant factor in the multivariate model. Moreover, ROC curve analysis revealed that IL-6 levels (AUC=0.70, p<0.01) have a significant diagnostically ability in detecting diabetic subjects with severely impaired BCVA. More precisely, IL-6 levels more than 1.85pg/ml has a sensitivity of 78% and a specificity of 83% for the diagnosis of severely impaired BCVA.

Conclusion: 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

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: 3380 men and 1528 women (≥18) without any clinical evidence of CVD or any other chronic disease, at baseline, living in Greece, were enrolled. In 2011–2012, the 10-year follow-up was performed in 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD was defined according to WHO-ICD-10 criteria. 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 MedScore test (OR: 1.83, 95% CI: 1.24–2.72). CRP and IL-6, and to a lesser extent uric acid, mediated the influence of MS on cardiovascular events; when examining the associations based on the NCEP ATP III definition, the CRPs for MS tended to decrease while CRP levels increased in the models (OR: 1.72 (1.13–2.61) and 1.78 (1.16–2.68), respectively). Further analyses were performed in order to better clarify these relationships, evaluating the C-statistic. The values for the models including potential confounding factors and the inflammatory or renal markers MS definitions confirmed 0.789, indicating fair to good predictive probability. Furthermore, the C-statistic for the models including CRP or IL-6 exceeded 0.80 for all three MS definitions.

Conclusion: Results of the present work better clarify the mediating role of inflammatory and renal parameters in the MS and CVD association.

Acknowledgement/Funding: Demosthenes Panagiotakos and Eikav Geogouroupolou received research grants from Coca-Cola SA.

P3682 | BEDSIDE
Decreased insulin sensitivity and abdominal obesity promote coronary atherosclerosis' extent and severity in non-diabetic patients
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Purpose: We sought to determine the metabolic profile of non-diabetic patients and its influence on severity and extent of coronary atherosclerosis, bearing in mind the role of insulin resistance in atherosclerosis.

Methods: Coronary angiograms were evaluated using number of diseased vessels and Gensini score. Insulin sensitivity (SI) was assessed by a frequency sampled intravenous glucose tolerance test with minimal model analysis (Plasma glucose concentration were determined every 5 min) in 23 patients (85% male). BMI ranged 21.3 (17.4–24.9), 23 patients included in group 2 (8 women, mean age 65±2.0 years), PCI was done 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. In order to better clarify these relationships, evaluating the C-statistic. The values for the models including potential confounding factors and the inflammatory or renal markers MS definitions confirmed 0.789, indicating fair to good predictive probability. Furthermore, the C-statistic for the models including CRP or IL-6 exceeded 0.80 for all three MS definitions.

Conclusion: Results of the present work better clarify the mediating role of inflammatory and renal parameters in the MS and CVD association.

Acknowledgement/Funding: Demosthenes Panagiotakos and Eikav Geogouroupolou received research grants from Coca-Cola SA.
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% (0.09±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±0.01% and 0.023±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 ≦6.4%, 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), CD34 + CD133 + CD45- in 40.3% (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 glycaemic control. Thus, in the subgroup of patients with T2DM with good glycaemic control (HbA1c ≤7.5%) the EPC levels were significantly higher after endovascular interventions.

P3685 | 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 65.98±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 (HbA1c ≦6.4%) and the higher group (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 is 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. Metlicous 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.
**P3680 | BEDSIDE**

Long-term clinical outcome of periprocedural myocardial injury in patients undergoing percutaneous coronary intervention for chronic total occlusion lesions

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**Purpose:** To evaluate the incidence and clinical implications of periprocedural myocardial injury (PMI) during percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) lesions.

**Methods:** Between October 2005 and December 2008, 641 consecutive patients with 711 CTO lesions underwent percutaneous coronary intervention (PCI) at our institution. Creatine kinase-myocardial band (CK-MB) fraction was measured before PCI and from 12 to 24 hours after PCI in all patients. PMI was defined as CK-MB increase ≥3 times the upper limit of normal. Cardiac death during 5-year follow-up was evaluated.

**Results:** The procedural success rate was 88.5%. PMI occurred in 30 patients (4.7%). PMI was significantly more common in the retrograde approach than in the antegrade approach alone (7.7% vs. 3.0%, P < 0.01). Clinical follow-up was completed in 85.8% of patients at 5 years. The cumulative incidence of cardiac death at 5 years was similar between PMI and no-PMI (12.0% vs. 5.6%, P = 0.157). A multivariate analysis revealed that procedural failure was an independent predictor of cardiac death (hazard ratio [HR] 3.48, 95% confidence interval [CI] 1.65 to 7.32, P < 0.01), but the retrograde approach was not (HR 0.86, 95% CI 0.42 to 1.77, P = 0.68). Kaplan–Meier curves of cardiac death event rate at 5 years are shown in the Figure.

**Conclusions:** PMI was more common with the retrograde approach, but was not associated with cardiac death during long-term follow-up. When procedural failure which causes PMI occurs, though relatively rare, target vessel revascularization may be required.

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**P3681 | BEDSIDE**

Real-world comparison between 1st and 2nd generation drug-eluting stents: Insights from the DESIRE Registry


**Background:** Despite the data from controlled trials pointing to improved clinical outcomes of periprocedural myocardial injury (PMI) for 1st and 2nd generation drug-eluting stents, a propensity score model was built to minimize the difference between the cohorts. The primary endpoint was the comparison of MACE and stent thrombosis (ST) up to 2 years of follow-up.

**Methods:** A total of 5,614 pts were enrolled in the DESIRE. After propensity score matching, 2,747 pairs were compared. The cohorts were comparable in terms of clinical profiles, with relatively high incidence of diabetics (33%) and STEMI pts (17%). Conversely, 2nd generation pts had more LM disease (1.1% vs. 2.3%, P = 0.005), ostial lesions (3.8% vs. 6.5%, P < 0.001) and bifurcations (7.2% vs. 10.3%, P < 0.001).

**Results:** The use of 2nd generation DES was associated with similar efficacy profile and improvement in safety performance, with a marked reduction in MI occurrence.

**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.

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**P3682 | 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. 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 (MACE) defined as cardiovascular death and hospitalization due to acute coronary syndrome (ACS), stroke, and coronary vascularization. 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, MACE developed in a total of 88 patients (19.9%). At baseline, there was no significant difference in the age, rate of male gender, 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 = 0.8) or high-VEGF-A (P = 0.5), was significantly associated with the risk of MACE. Furthermore, multivariate Cox proportional hazards analyses, 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 independent and independent predictor of MACCE.

**Conclusions:** A low VEGF-C value may serve as a predictive marker of atherosclerotic cardiovascular events after DES implantation.

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**P3683 | BEDSIDE**

Independent predictors of the recurrent restenosis after paclitaxel-coated balloon angioplasty for in-stent restenosis; importance of initial ballooning and ballooning position during the procedure

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**Background:** Recently, the efficacy and the safety of paclitaxel-coated balloon (PCB) angioplasty for in-stent restenotic lesions had been reported. However, some cases still repeat the in-stent restenosis (ISR) after PCB angioplasty.

**Purpose:** The aim of this study was to evaluate the predictors of the recurrent restenosis in patients who underwent PCB angioplasty for ISR.

**Methods:** From January 2011 to January 2015, we performed re-PCI to consecutive 709 ISR lesions. Lesions were divided into two groups (PCB angioplasty group and conventional angioplasty group) for the retrospective analysis of the angiographic data. Follow-up angiography was performed 6 months after the procedure.

**Results:** Incidence of the binary restenosis (≥50%) after re-PCI was significantly lower in PCB angioplasty group compared with conventional balloon angioplasty group [15.0% vs. 38.2%, P < 0.01], and target lesion revascularization was performed in 5.0% and 29.1% in each group, respectively (P < 0.01). Then, we investigated the predictor of recurrent ISR after PCB angioplasty. Multivariate analysis showed 1% diameter stenosis after initial ballooning for ISR and 2) geographic mismatch between PCB position and target re-PCI site during PCB angioplasty were independent predictors of recurrent ISR after PCB angioplasty.

**Conclusions:** Recurrent ISR occurred in 15.0% of patients who underwent PCB angioplasty. Careful positioning of the PCB to avoid the geographic mismatch and optimal expansion at the initial ballooning should be important to prevent recurrent restenosis after PCB angioplasty for ISR.
**P3692 | BEDSIDE**

**Left Ventricular Global Strain 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:** We conducted this study 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 (DTc), 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 DTc. GLS showed a significant improvement for 9 months after successful PCI (Δ-2.0±2.8%; P<0.01), whereas in failed PCI group the change did not reach significance (Δ+0.9±4.0%; P=0.48). ΔGLS is greater in successful PCI group than failed group (p<0.05). LVEF, LVESV and LVEDV 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.

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**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 has been shown in the context of provisional stenting to generate more 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 1-year follow-up MACE were similar between groups (2.1% vs 3.7%, p>ns). The overall MACE rate at 42.1 years-followup-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.

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**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-infarction (re-Inf), 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-Inf, TLR/TRV, 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 was significantly associated with lower risk of death (11% vs 14%, RR=1.282 (1.103–1.489) and p=0.001), re-Inf (10.2% vs 11.7%, RR=1.135 (0.999–1.290) and p=0.051), TLR/TRV (9.5% vs 11.1%, RR=1.335 (1.103–1.615) and p<0.001), ST 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=1.346 (0.825–2.194) and p=0.234) and MACE (RR: 1.346 (0.825–2.194) and p=0.234), re-MI (RR: 1.149 (0.520–2.534) and p=0.732), 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 (5.2%) 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 26.7 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 SYSTEI 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.
P3698 | 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 DES (UL-2nd DES; > 50 mm, 166 patients, 259 lesions), long 2nd DES (L-DES; 20–50 mm, 758 patients, 1,212 lesions), or 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 significantly higher in the UL-DES group relative to other groups due to higher TLR rates in 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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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 was 34.6 months.

Results: During the in-hospital period, MACE, the prevalence of stent thrombosis, left ventricular (LV) remodeling, and LV ejection fraction (LVEF) fall were higher in patients with higher WBV. After mean follow-up, the incidence of MACE was 1.1% higher in patients with higher WBV compared to those with lower WBV (p = 0.036). Similarly, the incidence of LVEF fall was 1.4% higher in patients with higher WBV compared to those with lower WBV (p = 0.001). The incidence of LV ejection fraction (LVEF) fall was 1.5% higher in patients with higher WBV compared to those with lower WBV (p = 0.001).

Conclusions: WBV was a powerful independent predictor of in-hospital and long-term outcomes in STEMI patient population undergoing primary PCI.

Acknowledgement/Funding: None
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 prevalence 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). In multivariate analysis, WBV at LSR (OR: 1.236 95% CI: 1.174–1.302 p < 0.001) and WBV at HSR (OR: 1.152 95% CI: 1.057–1.268 p = 0.002) were demonstrated as independent predictors of in-hospital MACE. WBV at LSR (OR: 1.243 95% CI: 1.213–1.272 p < 0.001) and WBV at HSR (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.

Conclusions: Not only as the determinant of ESS but also a contributor to establish risk factors, WBV seems to be 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.

P3701 | 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 (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. failed group = 1531.3±333.5 to 1565.3±97.5 days, P<0.001). Moreover, successful revascularization of CTO significantly decreased evident cardiac death [22/656 (3.4%) vs. 15/89 (16.9%), P<0.001], ensuing need for CABG [15/656 (2.3%) vs. 9/89 (10.1%), P<0.0001], and presentation of congestive heart failure was numerically lower in the success group [21/656 (3.2%) vs. 6/89 (6.7%), P<0.09].

Conclusions: This study suggests that the successful revascularization of CTO improves not only long-term mortality, but also quality of life of CTO 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), target-lesion revascularization (TLR) and cardiac death.

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 predictors of MACE were hemodialysis (hazard ratio [HR] 3.12, 95% confidence intervals [CI] 1.97–4.73, p<0.001) and multivessel disease (HR 2.07, 95% CI 1.38–3.24, p<0.001).

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 (<2.5mm) 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 group. 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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Purpose: Diffuse coronary lesions (length ≥21 mm) are still considered at high risk for restenosis after percutaneous intervention, even in the current drug-eluting stent era. Everolimus eluting bioresorbable vascular scaffolding (BVS) may avoid the disadvantages of long permanent metallic stents. From a total of 556 patients (680 lesions) treated with BVS, we selected for analysis 206 patients with 236 long diffuse coronary lesions (35%).

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 (n=150; 63%) without (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 patients (37%) with non compliant balloons (diameter 3.1±0.4 mm). After BVS implantation all the side branches ≥2 mm remained patent. All patients were discharged free of symptoms under dual antiplatelet therapy for at least one year. Clinical follow-up was obtained in all patients. After a mean follow up of 13±7 months the cumulative MACE was 4%; There were 2 subacute stent thrombosis (0.9%) and one of them died (0.5%). During the follow-up, one patient died (0.5%) due to late thrombosis (11 months after the procedure). A 6-month cardiac computed tomography scanner (CT) was performed in 88 patients evaluating vessel disease (40.1% vs. 68.2%, P<0.001), long lesions (>30 mm) (64.8% vs. 82.4%, P=0.002) and abrupt type (14.8% vs. 30.6%, P=0.001) were significantly higher in retrograde approach, so we performed 2:1 propensity matching. Finally, 124 lesions with antegrade approach and 62 lesions with retrograde approach were included.

Results: Two years follow-up was completed in 171 lesions (91.9%). The incidence of target lesion revascularization (TLR) was 14.5% in antegrade and 19.4% in retrograde approach (P=0.419, log-rank). Multivariate analysis showed small vessel disease (Hazard ratio 2.50, 95% CI 1.195–5.314, P=0.016) and in-stent restenosis (Hazard ratio 2.698, 95% CI 1.023–7.115, P=0.045) were predictor of TLR. Long and retrograde approach (P=0.419, log-rank). Multivariate analysis showed small vessel disease (Hazard ratio 2.501, 95% CI 1.185–5.314, P=0.016) and in-stent restenosis (Hazard ratio 2.698, 95% CI 1.023–7.115, P=0.045) were predictor of TLR.

Conclusions: After adjustment of baseline lesion complexities, there was no significant difference in TLR at 2 years between antegrade and retrograde approach for CTO.

P3707 | BEDSIDE
Predictors of early and late bleeding events after drug-eluting stent implantation
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Background: Patients who underwent drug eluting stents (DES) implantation need antiplatelet therapy and bleeding event often happen unexpectedly. Our aim in this study was to clarify the predictors of bleeding events after DES implantation.

Methods: We studied 1669 consecutive patients who underwent DES implantation in our hospital (70±10 years, 26% woman). Bleeding events were recorded as early (within 1 year) and late (more than 1 year) bleeding events. Bleeding event was defined as a composite of type 5, 3, or 2 bleeding in Bleeding Academic Research Consortium (BARC) criteria. Predictors were assessed using Cox proportional hazard model.

Results: Patients backgrounds were as follows, age=80 (17%), hypertension=81% (40%), diabetes mellitus=44%, severe renal dysfunction (defined as estimated Glomerular Filtration Rate ≤40 mL/min/1.73 m²) (12%), hemodialysis (6.2%), past history of gastrointestinal ulcer (GI) (6.2%). Percentage of warfarin use was 6.6%. Overall bleeding events happened in 82 patients (4.3%). Early and late
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 bleed- ing events (3% vs 20%, p=0.12). Warfarin use, past history of GI were inde- pendent 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 inde- pendent 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 depend- ing 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 a higher rate compared with PES group during long-term follow-up period (0.92% vs. 0.31%, p=0.02).

Method and results: Consecutive patients undergoing DES 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 (744 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 VLS, 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.

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 the true incomplete 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 DES 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 (744 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 VLS, 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.

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 treated with PCI between 2004 and 2011 at 8 tertiary cardiac centres across London, UK. Patient’s details at the time of the procedure were recorded at the time of the procedure and transferred to the relevant clinical 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 mor- tality. The primary end-point was all-cause mortality at a median follow-up of 3.0 years (IQR range: 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 PPCI 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) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p < 0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p < 0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p < 0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p < 0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, 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 in the TIMI 3 group compared to the other groups in both PPCI and NSTEMI/UA patients.

Kaplan-Meier analysis demonstrated in PPCI patients that there was a statically significant difference in mortality rates between the TIMI groups (26.3%; TIMI 0/1
Conclusion: Reduced baseline TIMI flow in moderate and high-risk patients with ACS undergoing PCI does not appear to affect survival at 1 year, in contrast to that in patients with STEMI.

P3712 | BEDSIDE
An observational study of real world clinical outcomes from 1999-2013 following percutaneous coronary intervention (PCI) among older patients in British Columbia, Canada

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Background: As the population ages, we are undertaking revascularisation procedures on older patients with more co-morbidities, the benefits of which are often debated. We examine temporal trends in clinical outcomes and procedural safety on older patients with more co-morbidities, the benefits of which are often debated.

Methods: Data from the BC cardiac registry from June 1999 to May 2013 on all PCI cases undertaken on elderly patients (age ≥ 80yrs) was linked to the Vital Statistics registry for all-cause mortality and Central Transfusion Registry for red blood cell transfusions given in the 10 days following PCI. Staged PCI and CABG within 10 days were excluded.

Results: From a total of 83,659 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; p<0.001). Further more, even within the cohort of older 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 (6.2%) 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, transfusion 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, transfusion rates decreased from 3.5% in 1999–2002 to 2.5% 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 for the elderly STEMI cohort. 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.

P3713 | BEDSIDE
Long-term angiographic outcomes of recurrent restenosis in patients with drug-eluting stent implantation for in-sent 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 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 (fuCAG) was performed in 547 (88.3%) of the 619 lesions and 20-month fuCAG was performed in 378 (85.7%) of the 441 lesions which were without target lesion revascularization (TLR) at 8-month fuCAG.

Results: In the 547 lesions after 8-month fuCAG, recurrent restenosis was documented in 138 (25.2%) lesions and TLR was performed in 106 (19.5%) lesions (acute gain, 1.79±0.6; late loss, 0.56±0.68). In the 378 lesions after 20-month fuCAG, recurrent restenosis was documented in 70 (18.5%) lesions and TLR was performed in 33 (8.7%) lesions (acute gain, 1.77±0.64; late loss, 0.4±0.88). 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 patient mortality in patients with STEMI undergoing primary PCI.

Methods: We analyzed 584 primary PCI patients from a high-volume center, from the year 2009. SS-II was calculated based on the bedside algorithm for patients undergoing primary PCI. It included SYNTAX score (SSXscore), age, sex, creatinine clearance, LVEF, left main disease, chronic obstructive pulmonary disease and peripheral vascular disease. SSXscore was determined by scoring the culprit lesion just before stent implantation. Predictive accuracy was tested with c-statistic and the Hosmer-Lemeshow test. Kaplan-Meier curves for SS-II tertiles were compared with the log-rank test.

Results: Patients were divided into the tertiles of the calculated SS-II: SS-II-Low<18.85, SS-II-MID>18.85 and SS-II-HIGH≥30.0. Overall mortality was 17.2% at the median follow-up of 4.5 years (IOR, 4.30–4.75). The mortality increased with the higher SS-II tertile: 5.6% for SS-II-LOW, 9.4% for SS-II-MID and 39.9% for SS-II-HIGH. Log-rank test showed significant difference between the cumulative mortality curves for SS-II tertiles (p<0.001; Figure, right). The ROC curve demonstrated a high accuracy of the SSXscore for predicting very long-term mortality.
P3716 | BEDSIDE
Acute coronary syndrome in octogenarians, association between percutaneous coronary intervention and long-term mortality
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Background: Evidence for improved survival after use of percutaneous coronary intervention (PCI) in elderly patients with acute coronary syndrome (ACS) is limited.

Purpose: To assess the association between PCI and long-term mortality in octogenarians with ACS.

Methods and results: 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 85.9% in the PCI and non-PCI subgroups respectively. In propensity matched cohort (n, 71+71) adjusted for baseline characteristics of these three groups neither in the MACE rate after a prolonged follow-up nor in the percentage of stent occlusion were observed, immediately after the procedure nor during follow-up. 17.3% of patients had stent occlusion (7.5% in the PCI and 20.8% in non-PCI group; p=0.03) and 5 non-cardiovascular deaths) and a TLR rate of 2.5% was observed. Two patients (7.5%) presented with stent occlusion and dissection (2.5% in the PCI and 10% in non-PCI group; p=0.03) and 5 non-cardiovascular deaths. In matched cohort: 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<0.001) and HR 0.4, 95% CI 0.2–0.5, P=0.020 respectively.

Conclusions: In octogenarians with ACS, PCI was associated with improved survival from all-cause death over five years of follow up.

P3717 | BEDSIDE
Patterns of dual anti platelet therapy cessation in left main and proximal left anterior descending artery PCI: Results from the PARIS registry
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Introduction: Drug eluting balloons currently constitute one of the therapeutic tools used in percutaneous coronary intervention (PCI) for de novo coronary lesions, mainly in bifurcations and small vessels. Nowadays, their results at a very long-term follow up are unclear.

Purpose: The main objective of this study was to evaluate the efficacy and safety of second-generation Sequent Please® paclitaxel eluting balloon (PEB) in de novo coronary lesions at 6 years.

Methods: We prospectively included 81 consecutive patients (69±12 years, 64.2% male) with 81 de novo lesions treated with PEB between March 2009 and March 2014. Additional bare metal stent (BMS) or drug-eluting stent (DES) was implanted after PEB if the result was not satisfactory because of dissection, recoil or significant residual stenosis. We evaluated the presence of major cardiac events (MACE) after a prolonged clinical follow-up (median 49 months): death, nonfatal myocardial infarction, target lesion revascularization (TLR) and thrombosis.

Results: 32.1% of patients had stable coronary artery disease and 67.9% acute coronary syndromes (48.1% Non-STEMI and 19.8% STEMI). 48.1% of patients were diabetic. 46.9% of lesions were bifurcations, 17.3% diffuse and 53.1% type B2/C. Mean vessel diameter and length were 2.43±0.35 mm and 16.2±5.7 mm, respectively. 75.3% of the lesions were treated with PEB, 21% with BMS and BMS and 3.7% with PEB and DES. There were no significant differences regarding baseline characteristics of these three groups neither in the MACE rate after a long-term follow-up (p>0.5). During follow-up, 6 patients died (1 cardiovascular and 5 non-cardiovascular deaths) and a TLR rate of 2.5% was observed. Two cases of non-fatal myocardial infarction (2.5%) and no cases of thrombosis were observed, immediately after the procedure nor during follow-up. 17.3% of patients had angiographic follow-up. We did not observe a higher need for additional stent after PEB in complex lesions such as diffuse lesions (p>0.7) and bifurcations (p=0.7).

Conclusions: Percutaneous interventions of “De Novo” coronary lesions with Sequent Please® PEB offers very favorable results at a very long-term follow-up. There was not a higher need for additional stent in cases of diffuse and bifurcated lesions.
after BMS+DCB. Therefore, an additional 2-year clinical follow-up (f/u) was attempted in addition to the invasive 6-month f/u.

**Methods:** The patient flow-chart is given in Fig. 1. f/u 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>
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<tr>
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<th>BMS+DCB (6 months / 2 years)</th>
<th>EES (6 months / 2 years)</th>
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<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%)</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>3 (5.6%) / 3 (5.6%)</td>
<td>5 (9.8%) / 6 (11.8%)</td>
</tr>
<tr>
<td>target lesion</td>
<td>1 (1.9%) / 2 (3.7%)</td>
<td>2 (3.9%) / 3 (5.9%)</td>
</tr>
<tr>
<td>target vessel</td>
<td>1 (1.9%) / 2 (3.7%)</td>
<td>2 (3.9%) / 4 (7.8%)</td>
</tr>
<tr>
<td>non target vessel</td>
<td>1 (1.9%) / 1 (1.9%)</td>
<td>3 (5.9%) / 4 (7.8%)</td>
</tr>
<tr>
<td>All MACE</td>
<td>5 (9.8%) / 6 (11.1%)</td>
<td>5 (9.8%) / 7 (13.7%)</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.

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**P3721 | BEDSIDE**

**The SYNTAX-II score predicts clinical outcomes after percutaneous coronary intervention with patients with left main and/or 3 vessel diseases**


**Background:** Currently, many risk stratification methods were established to predict clinical events after Percutaneous Coronary Intervention (PCI) in patients with complex coronary artery diseases. The anatomical Syntax score is important but has limitation because of absence of clinical variables.

**Purpose:** Our study aimed to evaluate the new SYNTAX-II score in a large cohort of patients undergoing PCI for treatment of complex coronary artery disease.

**Methods:** SYNTAX-II score is based on 8 parameters including anatomical SYNTAX score, age, creatine clearance, left ventricular ejection fraction, presence of unprotected left main coronary artery disease, peripheral vascular disease, female sex, and chronic obstructive pulmonary disease. In our study 1,262 patients with 3 Vessel (3VD) and/or left main (LM) diseases who underwent implantation of DES were analyzed. Both Syntax score and Syntax-II score were calculated. The primary endpoint was mortality of all causes at 1, 2 and 3 years after the procedure.

**Results:** Both Syntax scores (21.35±8.59) and Syntax-II score (0.09±0.11) can independently well predict the 3-year mortality (both p<0.001). When combined with clinical variables including age, sex, smoker, diabetes mellitus, hypertension, previous myocardial infarction, reduced left ventricular function, chronic pulmonary disease, higher serum creatinine, involvement of LM, peripheral vascular disease in multivariate analysis, the predictive value of SYNTAX-II score (HR 20.16, 95%-CI: 2.70–150.29, p=0.003) shows better predictive function than SYNTAX score (HR 1.02, 95%-CI: 1.00–1.04, p=0.011).

**Conclusion:** The new Syntax-II score was superior to the anatomical SYNTAX score and is an independent predictor of mortality in patients with complex coronary artery disease after PCI.

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**P3722 | BEDSIDE**

**Gender differences in 5-year clinical outcomes following percutaneous coronary intervention**


**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 1994 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. Lipid profiles were worse and LVEF was reduced in the male group. Kaplan-Meier estimation for 5-year all-cause death and acute coronary syndrome was superior to the male group (Figure 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 for confounding factors, gender was not associated with the long-term clinical outcomes. Multivariable Cox regression analysis showed that higher age and MVD was 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.
Conclusion: Late TLR and ST after DES implantation should be considered during long-term follow-up period.

P3723 | BEDSIDE
The influence of aortic root calcium volume and distribution on the risk of paravalvular regurgitation after transcatheter aortic valve replacement
N.C. Hansson1, J. Leipsic2, A. Rossi3, D. Divir4, M. Simionato2, S. Kennon5, H.R. Andersen1, J. Webb2, F. Pugliese3, B.L. Norgaard1, A. Aarhus University Hospital, Aarhus, Denmark; 2St Paul’s Hospital, Vancouver, Canada; 3London Chest Hospital, London, United Kingdom

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 predischARGE 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 Ventricle (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 predischarge PAR—mild or PD (as a surrogate for PAR—mild) was defined (PD/PAR patients).

Results: Mean age was 81.5±8.6 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). Medial (interradial) range. Upper LVOT and Overall LVOT calcium volumes were higher in PD/PAR patients compared to non-PD/PAR patients, 25 [0–56] mm3 vs. 15 [0–56] mm3 (p=0.001), 49 [0–105] mm3 vs. 31 [0–63] mm3 (p=0.03), respectively. Aortic Valve Region calcium volume did not differ between PD/PAR patients and PD/PAR patients, 498 [204–873] mm3 vs. 565 [245–1004] 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 in patients with paravalvular regurgitation size<15%, AUC (95% CI): 0.83 (0.72–0.93) vs. 0.53 (0.38–0.67) (p=0.0001).

Conclusion: PAR—mild and need for PD is best predicted by calcium volume in the Upper LVOT. Pre-TAVR planning and prosthesis valve selection may be further refined by assessing aortic root calcium distribution.

P3724 | BEDSIDE
Clopidogrel not indicated before TAVI, after TAVI with caution and under platelet reactivity assessment
K. Czerwinska, A. Witkowski, M. Dobrowski, J. Stepinska, Institute of Cardiology, Warsaw, Poland

Dual antiplatelet therapy (DAPT): aspirin (ASA) + clopidogrel (CLOP) after TAVI is recommended. Safety of DAPT has not been defined. While in ACS pts the use of Transcatheter Aortic Valve Implantation (TAVI) to treat severe aortic stenosis transthoracic echocardiography (TTE) is recommended (PD/PAR patients).

Methods: PLT-R measured by light transmittance aggregometry with VerifyNow P2Y12/Aspirin assays was performed within 24 h before and on the 6th day after. The results were expressed as P2Y12 reaction units (PRU) and reaction units (ARU). BC/VC were defined according to VARC scale. Statistical analysis: logistic regression. ROC curve with AUC (95% CI).

Results: PLT-R was performed in 99 TAVI pts. Pre-post-TAVI: 68 (68.6%) 87 (87.8%) were on ASA, 44 (44.4%) 77 (77.7%) were on CLOP.

Mean peri-TAVI PLT-R values were: ARU (473.25±65.28/462.18±61.55), PRU (87.8%) pts were on ASA, 44 (44.4%)/77 (77.7%) pts were on CLOP.

Conclusion: PAR was assessed using predischarge 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 Ventricle (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 predischarge PAR—mild or PD (as a surrogate for PAR—mild) was defined (PD/PAR patients).

Results: Mean age was 81.5±8.6 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). Medial (interradial) range. Upper LVOT and Overall LVOT calcium volumes were higher in PD/PAR patients compared to non-PD/PAR patients, 25 [0–56] mm3 vs. 0 [0–8] mm3 (p=0.001) and 49.9 [0–112] mm3 vs. 3 [0–59] mm3 (p=0.03), respectively. Aortic Valve Region calcium volume did not differ between PD/PAR patients and PD/PAR patients, 498 [204–873] mm3 vs. 565 [245–1004] 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 in patients with paravalvular regurgitation size<15%, AUC (95% CI): 0.83 (0.72–0.93) vs. 0.53 (0.38–0.67) (p=0.0001).

Conclusion: PAR—mild and need for PD is best predicted by calcium volume in the Upper LVOT. Pre-TAVR planning and prosthesis valve selection may be further refined by assessing aortic root calcium distribution.

P3725 | BEDSIDE
Pressure half-time by echocardiography in comparison with cardiac magnetic resonance for quantification of paravalvular regurgitation after transcatheter aortic valve implantation
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1RWTH University Hospital Aachen, Internal Medicine I, Cardiology, Pulmonology & Vascular Medicine, Aachen, Germany; 2St. Bonifatius Hospital Lingen, Medical Clinic, Department of Cardiology, Lingen, Germany

Background: Aortic regurgitation is common after transcatheter aortic valve implantation (TAVI) and is associated with negative impact on patient outcome. Assessment of paravalvular regurgitation severity is limited by most methods of contemporary echocardiography. Pressure half-time (PHT) is a parameter easy to assess by echocardiography in these patients but it is affected in case of left ventricular hypertrophy (LVH).

Purpose: This study sought to evaluate the accuracy of PHT with distinct cut-off values for differentiating patients without and 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 (TTE) and CMR were performed after TAVI to assess the influence of CMR on the echocardiographic assessment of paravalvular regurgitation.

Results: In 13 of 53 patients (25%) paravalvular regurgitation after TAVI was more than mild as graded by CMR analysis. LVH was present in 29 of 53 patients (55%). PHT correlated less to regurgitant fraction by CMR analysis in patients without LVH (r=0.47; p=0.49) than in patients with LVH (r=0.54; p=0.023). In patients without LVH accuracy of PHT to predict more than mild paravalvular regurgitation 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 240 ms (AUC=0.800, sensitivity 80.0%, specificity 84.2%).

Conclusion: Analysis of PHT with distinct cut-off values differentiating patients without and with LVH allows accurate identification of more than mild paravalvular regurgitation after TAVI as defined by CMR.

Acknowledgement/Funding: This study was supported by a research grant from GE Ultrasound, Horton, Norway.

P3726 | BEDSIDE
3-D Echocardiographic measurement of aortic annulus using area or circumference for TAVI. Does it make a difference?

King’s College Hospital, London, United Kingdom

Introduction: The use of Transcatheter Aortic Valve Implantation (TAVI) to treat aortic stenosis is increasing worldwide. Accurate sizing of the AV prosthesis is paramount. We present our 7-year experience using 3-D TOE and investigate if different sizing methods of the aortic annulus (AA) lead to different results.

Methods: We investigated 193 patients who underwent TAVI in our Hospital and had 3D TOE datasets of the AA. We derived the AA diameter by two different methods: a) Diameter by annulus area; DA = 2π (area-) and b) diameter by circumference; DC = circumference-/π. Using the Edwards Sapien 3 Valve-3D Sizing
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.

Number of patients in size groups by calculating the aortic annulus diameter with different methods

<table>
<thead>
<tr>
<th>Valve size by area</th>
<th>Valve size by circumference</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too small</td>
<td>Too small</td>
<td></td>
</tr>
<tr>
<td>23 mm</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>23 or 26 mm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>26 mm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>29 mm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>361</td>
</tr>
</tbody>
</table>

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.

**P3728 | BEDSIDE**  

Learning curve of percutaneous left atrial appendage closure for stroke prevention in single high volume center  

Y. Matsuo, 1 M. Sandri, 2 N. Mangner, 2 G. Schuler, 2 M. Kurabayashi, 1 Stroke prevention in single high volume center

**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 August 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:** Over all 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=0.0001). Total number of the device showed a trend forward less but stastically 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 23 physicians during the study. We conclude there was a clear learning curve in LAA closure in clinical routine at a high volume center.

**P3729 | BEDSIDE**  

Ruptured sinus of Valsalva aneurysm closure with new types PDA devices  

M. Szukutn1, R. Fischer2, J. Bialkowski1 3, Medical University of Silesia, Zabrze, Poland; 4 Silesian Center for Heart Diseases, Zabrze, Poland

**Introduction:** Ruptured sinus of Valsalva aneurysm (RSOA) is a rare short-lived lesion frequently treated percutaneously. Lately for this purposes have been used also Chinese PDA nitinol 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 RSOA 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 RSOA with nitinol wire mesh PDA occluders (produced by 3 different companies). All but two pts had congenital sinus of Valsalva aneurysm. Two pts had acquired RSOA 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 2.6–6 mm bigger than orifice of RSOA. 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 RSOA. In one pt with iatrogenic RSOA (after LVOT operation) devices have 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 RSOA. 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 RSOA 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 implantation 2 y later (during pregnancy) recanalization of SOVA occurred treated successfully by PDA occluder after delivery. In follow-up (ranged from 0.5 to 4 years) no complications were observed in any pt.

**Conclusions:** Transcatheter closure of ruptured sinus of Valsalva aneurysm with new PDA nitinol wire mesh occluders are safe and effective procedures.

**P3730 | 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 septal aneurysm (ASA) or a large right-to-left shunt (up to 40%) 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 suffer-
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 Amplatz device in both groups (85% versus 83%, p=0.84) but with a complex anatomy 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 periprocedural 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 0.33/100 patient-year, p=0.24), even after adjusting by age and device size (HR 2.52, 95% CI 0.28–22.75, p=0.41).

Conclusion: In this real-life series, we have not 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
C. Bouleti 1, D. Himbert 1, E. Brochet 1, P. Ouw 2, B. Iung 1, M. Urena 1, Y. J. Kim 3, S. H. Hur 4, I. W. Seong 5, H. Park 1, H. K. Kim 1, M. H. Jeong 1, Y. G. Ahn 1, D. S. Sim 1, S. C. Chae 2, J. G. Cho 1, Y. J. Kim 1, S. H. Hur 1, I. W. Seong 5

Purpose: Redo tricuspid surgery may be high risk or even contraindicated due to comorbidity. Transcatheter valve implantation (TVI) has been recently reported in this setting.

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 23% had previous 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 the open configuration. However, RA may raise issues due to their oval shape and open configuration.

Conclusion: Transcatheter implantation of SAPIEN XT valves in failed tricuspid BI patients in a highly-risk cohort, with good early and 1-year hemodynamic and clinical results. However, RA may raise issues due to their oval shape and open configuration.

P3732 | BEDSIDE
Clinical outcomes of the intra-aortic balloon pump for resuscitated patients with acute myocardial infarction complicated by cardiac arrest
H. Park 1, H. K. Kim 1, M. H. Jeong 1, Y. G. Ahn 1, D. S. Sim 1, S. C. Chae 2, J. G. Cho 1, Y. J. Kim 1, S. H. Hur 1, I. W. Seong 5

Methods and results: Between November 2005 and April 2014, 49,542 patients were enrolled in a prospective cohort study for AMI in Korea (KAMIR). Cardiopulmonary resuscitation (CPR) was performed in 1,700 patients with cardiac arrest. Patients were excluded from the study if they had not undergone a coronary angiogram, if extracorporeal membrane oxygenation (ECMO) or thrombolyis was performed, and if mechanical complications presented. The primary end point was 1-month all-cause mortality. A total of 883 patients in the IABP group and 476 in the control group were included. During the 1-month follow-up, all-cause mortality was 14.8% versus 9.1% (p=0.03), even after adjusting by age and device size (HR 2.52, 95% CI 0.28–22.75, p=0.41).

Conclusion: IABP use in subjects with especially high risk of death. The use of IABP did not show clinical benefits in patients with AMI complicated by severe cardiogenic shock after propensity matching analysis.

P3733 | BEDSIDE
A multi-modality intra-arterial imaging comparison of renal artery trauma induced by balloon-based and non-balloon-based renal denervation devices
A. Karanasos 1, N. Van Mieghem 1, M. Bergmann 2, E. Hartman 1, J. Ligthart 1

Methods: Twenty-five patients underwent bilateral renal denervation in two centers with 5 different systems, 2 nBD [Symplast™ (n=6), EnligHTN™ (n=3)] and 3 BD [Symplicity™ (n=6), Vessix™ (n=4) and Vessix™ (n=6)]. Analysis included quantitative angiography pre- and post-procedure, morphometric measurements by IVUS pre- and post-procedure, and assessment of vascular trauma (dissection, edema, or thrombus) by OCT after denervation.

Results: In nBD-treated vessels, there was a significant reduction of minimal lumen diameter by 0.52±0.86mm (p<0.05) by angiography, while by IVUS the minimal lumina area decreased by 3.11±4.38mm² (p<0.05) and the percent in- tima & media volume increased by 4.0±3.9% (p<0.01). Conversely, in BD-treated vessels, these differences were not significant.

By post-denervation OCT, dissection was seen in 2 vessels treated with nBD devices (13.3%) vs. 12 nBD-treated vessels (42.9%; p<0.09). Thrombus was observed in 12 nBD-treated vessels (80.0%) vs. 23 BD-treated vessels (82.1%; p=0.39). Edema was detected in 13 nBD-treated vessels (86.7%) vs. 42 BD-treated vessels (67.9%; p=0.08). Percent frames with dissection was lower in nBD-treated vessels vs. BD-treated vessels [0.1% (0–1.4%) vs. 2.8% (0.6–11.2%); p<0.05], whereas there was no difference for percent frames with thrombus [6.1% (2.9–12.6%) vs. 7.5% (4.3–12.6%); p=0.68] and percent frames with edema [14.9% (5.3–35.2%) vs. 3.7% (2.4–12.7%); p=0.13]. In BD-treated vessels, balloon-to-artery ratio had a good discriminative ability for predicting dissection by OCT [ROC: 0.81 (0.85–0.97); p<0.01], with a value > 1.18 predicting dissection with 56.3% sensitivity and 87.5% specificity.

Conclusion: A varying extent of vascular injury was observed after renal denervation. nBD systems were associated with a "spasm-like" response with reduction of lumen dimensions and increase of intimal-medial volume. BD systems were associated with higher extent of dissection, which was observed in > 40% of the cases. The occurrence of dissection in these vessels was associated with a higher balloon-to-artery ratio.
P3734 | BENCH
One-shot circumferential renal artery denervation with relative sparing of the arterial wall may be possible using a novel microwave catheter
P. Qian1, T. Barry1, S. Al Raisi1, P. Kovoora1, A. McEwan2, A. Thaigalingam1, S. Thomas1,2,1Westmead Hospital, Cardiology, Sydney, Australia; 2University of Sydney, Faculty of Electrical and Information Engineering, Sydney, Australia
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 visera 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 visera 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% CI 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.

P3735 | BEDSIDE
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 capacity of 8-10 W at 55 °C, 4-10 points for each PA, for 2 minutes per point. 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 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 to 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 RH 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 | BEDSIDE
The proximity of structural changes to the renal artery: a study to assess the potential risks of renal denervation
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Background: Limited safety data are available regarding inadvertent soft tissue injury a study to assess the potential risks of renal denervation. Method: 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 3mm in diameter (Spyral, Ves-six) and create ablation zones of up to 10mm in depth (Paradise).
Results: 53° C isotherm was taken as the lesion boundary and dimensions were assessed using serial digital photography and analysed with in-house built software. 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 RH 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.
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.

**P3738 | BEDSIDE**

**Effects of renal sympathetic denervation on cardiac sympathetic activity and function in patients with therapy resistant hypertension**

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**Background:** Renal sympathetic denervation (RSD) is currently being investigated in multiple studies of sympathetically driven cardiovascular diseases such as heart failure and arrhythmias. In the present study, our aim was to assess systemic and cardiac sympathetic effects of RSD by measurement of cardiac sympathetic activity and cardiovascular parameters.

**Methods:** A total of 21 consecutive patients with refractory hypertension (daytime ambulatory blood pressure (BP): >150/100mmHg despite the use of 3 or more antihypertensive drugs), no evidence for secondary hypertension and normal renal vascular anatomy were included. RSD was performed with the Medtronic Symplicity renal denervation catheter with an average of 4.2 (range 3–6) ablations per renal artery. 123I-mIBG cardiac scintigraphy was performed before and after RSD to assess cardiac sympathetic activity. In addition, the effect of RSD on peripheral BP and cardiac hemodynamics were assessed non-invasively in supine position and after standing.

**Results:**

- 123I-mIBG uptake before and after RSD was 1.7±0.4% vs. 1.7±0.5% at 15 min. and 1.4±0.4% vs. 1.5±0.5% after 4 hours. As a consequence, washout rate was similar before (33.7±11.7%) and after RSD (30.1±12.6%, p=0.27). In line with earlier RSD studies, a significant drop in systolic office BP (~12.2 mmHg, p<0.04) was detected. However, no changes were seen in heart rate, stroke volume or left ventricular contractility, both in supine position and after standing.

**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 the Vessix multi-electrode system.

**P3737 | BEDSIDE**

**Semiquantification of 123I-mIBG**

Semiquantification of 123I-mIBG 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.

**P3739 | 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 at 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 scores for LAAC and HAS-BLED scores were 4±2.5 and 4±2.0, 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 antiplatelet 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±5
HAS-BLED 4±2
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. Lifelong rather than short-term single antiplatelet therapy should be considered after the procedure for patients at high cardio-vascular risk.

**P3740 | BEDSIDE**

**Multi-centre European experience of left atrial appendage closure using a new generation percutaneous epicardial suture device in non-valvular atrial fibrillation**

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**Introduction:** The safety and efficacy of a modified new generation transcatheter epicardial left atrial appendage (LAAs) suture-mediated closure device to prevent thromboembolic stroke in patients with non-valvular AF has not been studied before. We present the collective multi-centre European experience with the LARIAT+ percutaneous epicardial suture device.

**Purpose:** To define the safety and efficacy of the LARIAT+ device

**Methods:** 86 consecutive patients (pts) with AF underwent LAAT ligation using the LARIAT+ device. In 84 pts pericardial access was achieved with a novel microcannula-telescopic two-piece needle; in the 2 remaining pts a conventional 18 guage
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-eight 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 micropuncture pericardial access technique effectively achieves acute LAA closure with an acceptably low risk of adverse events.

**HEART FAILURE THERAPY, VARIOUS I**

**P3742 | BEDSIDE**

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 is yet to be elucidated in furosemide-resistant heart failure (HF) with renal dysfunction.

**Methods:** The K-STAR is a multi-center, open-labelled, randomised, controlled, prospective study that enrolled 18 hospitals from December 2012 to August 2014. HF patients with fluid overload despite taking ≤15 mg/day of additive tolvaptan (TLV) group or ≤40 mg/day of oral furosemide (FUR) group for 7 days to evaluate outcome measures.

**Results:** Patients suffered from moderate HF, with the majority of patients in NYHA class II–III, and complicating renal dysfunction with 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 TLV 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, odds ratio, 0.242, 95% confidence interval, 0.068–0.792; p=0.013) was significantly lower in the TLV 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, 0.068–0.792; 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 | BEDSIDE**

Strategies for diuretic management of acute heart failure: data from a web-survey of the Italian Association of Hospital Cardiologists (ANMCO)

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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.

**Purpose:** To investigate strategies for diuretic treatment in primary AHF, we conducted a web-survey among members of a National Cardiology Society.

**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% men, age 52±11 years, 78% of clinical practice) 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. Diuretic resistance was identified through a multiple dose titration by 48%, while 24% considered as diagnostic an urine output <1000ml/24h in isolation. Sequential nephron blockade was used only in cases of loop 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 (14%) 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 | BEDSIDE**

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 of 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<0.001) from 0.95±0.08 µg/ml (mean ± SE) at baseline to 3.42±0.20 µg/ml at 6 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 non-significant between the two groups at 6 months (p=0.08). The primary endpoint (major adverse cardiovascular events) was reached by 10 patients (9%) in the CoQ10 group, as compared with 33 patients (27%) in the placebo group by intention to treat analysis (Hazard Ratio CoQ10 vs. placebo: 0.28 (95% CI: 0.13–0.58);
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: 0.15-0.86), p=0.017).

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.

P3745 | BENCH
UM206, a peptide fragment of wnt5a, attenuates post-infarct remodeling
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Introduction: Following myocardial infarction (MI), left ventricular (LV) remodeling aims to maintain cardiac function. Nevertheless, adverse remodeling results in thinning of the infarct and LV dilatation which may subsequently lead to the development of heart failure with poor prognosis. Wnt/Frizzled signaling plays a key role in cardiac remodeling following MI. We have shown previously that blockade of the wnt inhibitor Dkk1 with UM206 (peptide fragment of Wnt5a) reduced infarct expansion and prevented heart failure development in mice. This was accompanied by increased myofibroblast presence in the infarct region in treated mice. The aim of the present work was to investigate the effects of UM206 in a porcine model of repertused myocardial infarction.

Methods: Twelve Yorkshire x Landrace swine were subjected to 2 hours of myocardial ischemia by ligation of the proximal left circumflex artery, followed by reperfusion. Starting 24 hours post-MI, 6 animals were treated with continuous infusion of UM206 (0.6 µg/kg/day i.v.) for 5 weeks using a balloon pump. The 6 control swine were treated with vehicle. Another 8 swine were sham-operated. Cardiac dimensions and infarct mass (IM) were determined by echocardiography and dedicated markers, respectively. At follow-up, infarct tissue was stained for alpha-smooth muscle actin to quantify myofibroblast content of the infarct region. In addition, components of Wnt/Frizzled and TGF-β signaling were measured at follow-up with qPCR.

Results: Treatment with UM206 for 5 weeks resulted in a significant decrease in IM compared to baseline (−41±10%), whereas IM remained stable in the control group (3±17%). This was accompanied by progressive dilation of the LV in the control group between 3 and 5 weeks after MI while adverse remodeling was halted in the UM206 treated group. Myofibroblast presence was significantly lower in the UM206 treated animals (1.53±0.43% vs 3.38±0.61%). Fzd-2 mRNA was increased in the UM206 treated swine but not of control swine with MI. Fzd-2 mRNA as well as mRNA expression of the inflammatory mediators TGF-β1, TGF-β3 and the ECM protein tenasin-c were increased in remote non-infarcted myocardium as compared to sham, and their expression increased even more in MI, but was not influenced by UM206 treatment.

Conclusion: UM206 treatment in a clinically relevant swine model of repertused myocardial infarction attenuates adverse remodeling, but is not accompanied by an increased myofibroblast presence in the infarcted area 5 weeks after MI.

P3746 | BENCH
The adaption and application of ivabradine treatment along with beta blocker therapy in real life clinical practice: Results from REALITY HF Study
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Purpose: Although heart rate (HR) modulation therapy has been shown to improve clinical outcomes in patients with heart failure (HF), their application in clinical practice is less than optimal. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study data were analyzed to evaluate the adaption and application of ivabradine treatment along with beta blocker (BB) therapy in real life routine clinical care in patients with chronic HF.

Methods: REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients' clinical characteristics and the effects of cardiovascular medications on heart rate in real-life settings. The extent of heart rate abnormalities on resting heart rate (HR) and enrolled 1251 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age. 826 patients were in sinus rhythm, in whom 653 (79.1%) were receiving BB treatment. The target doses of BB treatment, as defined by ESC guidelines had only been reached in 13.9% of patients. Patients in sinus rhythm, NYHA II-IV, EF ≤35% and resting HR >70 bpm despite BB were considered eligible for ivabradine treatment based on the HF guidelines recommendations. Results: In patients with sinus rhythm, mean resting HR was found to be 76.7±14 bpm, HR was ≥70 bpm in 69.1% 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 also 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 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.

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P3747 | BENCH
High use of statins in heart failure patients also after trials that failed to show a benefit: a Danish nationwide study
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Introduction: Although the role of statins in primary and secondary prevention of cardiovascular events is well-established, their role in tertiary prevention after development of heart failure (HF) is still unresolved.

Purpose: 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 aetiology. 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 logistic 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 HF patients, initiation of statins in HF patients increased during the study period.

P3748 | BENCH
STAT3 is indispensable for cardioprotective effects of DPP-4 inhibitor on heart failure after myocardial infarction
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Background: Dipeptidyl peptidase-4 (DPP-4) inhibitors are a new class of antidiabetic drugs that block DPP-4 enzyme activity. Many basic researches reported that DPP-4 inhibitors have protective effects on various organs including pancreas, kidney, and heart. There are several papers that demonstrate the cardioprotective effects of DPP-4 inhibitors. However, the exact interaction between DPP-4 inhibitor and myocardium is not well understood. In this study, we aimed to elucidate the molecular mechanisms by which DPP-4 inhibitor has beneficial effects on heart failure after MI by using in vivo and in vitro experiments.

Methods and results: C57BL/6 mice and DPP-4 knockout (DPP-4KO) mice were subjected to left coronary artery ligation to produce acute MI. C57BL/6 mice and DPP-4 knockout (DPP-4KO) mice were then treated with vehicle or DPP-4 inhibitor. Left ventricular function, infarct size, the number of vessels, and myocardial ischemia were assessed at 5 days after MI. The treatment with DPP-4 inhibitor significantly improved cardiac function and decreased the infarct size. DPP-4 inhibitor increased the ratio of endothelial progenitor cells to cardiac progenitor cells. The extent of myocardial ischemia was significantly decreased in DPP-4 inhibitor treated group. The number of TUNEL-positive cells in the border area were significantly decreased by DPP-4 inhibitor. The level of SDF-1α, which is a substrate of DPP-4 and produces its effects through its receptor CXCR4, in myocardium was significantly decreased.

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increased by DPP-4 inhibitor. These cardioprotective effects after MI were abolished by cardiomyocyte-specific deletion of STAT3. **Conclusions:** At the doses evaluated, LCZ improved LV function and reduced pulmonary congestion versus Peri, with similar anti-remodeling effects in the heart, despite the further reduction in blood pressure observed with Peri compared to LCZ. The implications of this study support LCZ as a novel agent for treating post-MI LV dysfunction more efficiently than ACEi.

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### P3750 | BENCH

**LCZ696, the angiotensin-receptor neprilysin inhibitor, attenuates cardiac fibrosis and improves its function in the heart failure model of diabetes mellitus in mice**

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**Background:** Angiotensin-receptor neprilysin inhibitor (ARNi) has the effects of angiotensin receptor blockers (ARB) and augments natriuretic peptides (NP). Although the ARNi LCZ696 improves heart function 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 LCZ696 to 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 treat for 4 weeks with LCZ696 (60 mg/kg), valsartan (30 mg/kg), or no treatment. Cardiac function was assessed by Pressure-Volume Millar catheter. Myocardial fibrosis was determined by quantitative histology (Pi-crisoris 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 (valsalat, p < 0.05; LCZ696, p < 0.01). Treatment with LCZ696 more improved left ventricular EF (4.1±2.1% vs 10.1±2.1% in the control group (29.1±2.1%, p < 0.01; 1.7±0.9 mi/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.

### P3751 | 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 the ex vivo isolated cardiac sarcomeres from hypothermic ischemia.

**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, Nox, GPT/GOT, glucose, LDH were also measured serially. In addition, activation of pro-inflammatory mediators including INOS, COX-2, and the nuclear factor-κB (NF-κB) pathway in heart tissue were also 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%; heart rate: 33%, P < 0.05). There were also improvement of biochemical 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 LPS-induced nuclear translocation of NF-κB by blocking phosphorylation of HSC70.

**Conclusion:** Our results indicate that extracellular HSC70 has a promising role in the treatment of septic cardiomyopathy through anti-inflammatory pathways.

### P3770 | 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 hospitalized 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 inhospital WHF in patients hospitalised for AHF.

**Methods and results:** RELAX-AHF-EU is an open-label study planned in ~400 cardiologists, 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 at baseline. Main outcome measures are randomized to 2:1 receiving 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 achieve heart failure improvement by Day 5, (c) death from any cause, (d) proportion of patients that are 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-
P3753 | BENCH
Administration of eicosapentaenoic acid reduces cardiovascular and all-cause mortality in chronic hemodialysis patients

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Background: Eicosapentaenoic acid (EPA) is now recognized to have beneficial effects on cardiovascular disease (CVD). In hemodialysis (HD) patients who are at high risk for CVD, serum EPA levels have been reported to be lower compared to general population due to consumption of inadequate amounts of dietary fish. We investigated whether the EPA administration improves CVD and all-cause survival in this population.

Methods: Maintenance HD patients receiving 300mg EPA thrice daily in conjunction with HD were enrolled in this study. Serum EPA and arachidonic acid (AA) levels were measured at the beginning of the administration and after 6 months in the EPA group. 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: In the EPA group than in the control group (58.5% vs. 41.1%, p=0.016 and 24.8% vs. 13.7%, p=0.029) compared to the control group, respectively. Furthermore, in 93 propensity score-matched patients in each group, 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=0.023) 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.

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 type 1 (AT1) receptor-induced aldosterone (Ald) synthesis in human adrenocortical cells.

Methods and results: Binding affinity of valsartan + LBQ-657 (the active form of nephrilysin inhibitor pr-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 + LBQ-657 and valsartan alone. In Ang II-sensitized human adrenocortical cells, ANP or BNP alone, but not LBQ-657 or valsartan alone, significantly decreased Ald synthesis. Most important finding was that valsartan + LBQ-657 with ANP or BNP dramatically 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 GMP-dependent protein kinase. In addition, the suppression levels of Ald synthesis in valsartan+LBQ-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: These results support the view that the effects of LCZ696 in CVD may be partly due to the reduction of Ald synthesis by its nephrilysin inhibition.

P3755 | BESIDE
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 (HF). 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.

Results: Comorbidity proportion of OMT was present in 74% patients (51%). Absence of OMT was independently associated with age, higher left ventricular ejection fraction, impaired renal function, and concurrent use of calcium blockers and loop diuretics. 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.

P3756 | BESIDE
Incidence and predictors of doubling of serum creatinine during treatment of heart failure and preserved ejection fraction with spironolactone

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Background: Adherence to optimal medical treatment is associated with a reduction of all-cause mortality in ambulatory patients with heart failure

Methods: We examined the incidence of DSC in TOPCAT for both placebo- and spironolactone-assigned patients. Due to previously reported regional variation in spironolactone safety/efficacy and low rates of DSC in both treatment arms in Russia/Georgia (R/G), baseline predictors of DSC were defined in multivariable Cox proportional hazards models restricted to the Americas.

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.
Results: DSC occurred in 260 of 1767 (14.7%, 5.4 per 100 p-yr) in the Americas compared with 35 of 1678 (2.1%, 0.6 per 100 p-yr) 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-yr, 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-PEF 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 isoosprotenol-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 in promoting macrophage inflammation 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 citrux pectin, MCP) or aldosterone (potassium canrenone) on left ventricular (LV) function in a murine model of HF.

Methods: Forty-one 3 to 5-month old male mice with cardiac specific hyperaldosteronism (AS mice) underwent isoosprotenol subcutaneous injections, and were then randomized to receive placebo (n=12), MCP (n=10), canrenone (n=9) or MCP+canrenone (n=10) for 14 days.

Results: Isoosprotenol 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 canrenone (both p < 0.001 vs placebo). MCP and canrenone also reduced the extent of cardiac hypertrophy and fibrosis, as well as the expression of genes involved in fibrogenesis (Coll-I and Coll-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 canrenone. Combined use of antagonists of Gal-3 and aldosterone resulted in additive effects, compared to MCP or canrenone alone, on cardiac hypertrophy, inflammation and fibrosis. Combined treatments are consistent with the mechanisms of aldosterone-mediated myocardial damage in a HF murine model with cardiac hyperaldosteronism. Inhibition of Gal-3 and aldosterone can reverse isoosprotenol-induced LV dysfunction, by reducing myocardial inflammation and fibrogenesis. Gal-3 inhibition may represent a new promising therapeutic option in HF.

P3759 | BEDSIDE The influence of metformin on mortality and hospitalization in patients with heart failure and type 2 diabetes


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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 1030 of 1126 patients with HF representing Polish population of the Heart Failure Long Term Registry. Three hundred and forty-two patients (34.5%) were treated with metformin. Metformin treatment was associated with lower mortality rates compared to not-metformin treated group (11.0% vs. 14.9%, HR 0.74; 95% CI: 0.53 to 1.02, p = 0.072). The study concluded in 2009 in Poland among cardiologist and general practitioners. Patients diagnosed with asthma were excluded from the following analyses.

Results: Among 3557 patients with systolic HF in a sinus rhythm 431 persons were diagnosed with COPD (12%). RHR was higher in patients with vs. without COPD (77±13 vs. 75±13 beats per minute [bpm], p < 0.001) and in 79% patients with COPD RHR was > 70 bpm as compared with 68% of enrollees without COPD (p < 0.001). The percentage of patients with RHR > 70 bpm rose with HF severity in patients without COPD (NYHA class I/II/III/IV - RHR > 70 bpm: 64.8%/73.7%/87.7%/90.6%, p = 0.001) but not in subjects with this respiratory disease (NYHA class I/II/III/IV - RHR > 70 bpm: 76/78/80/78%, p = 0.9). In patients with systolic HF and COPD in the multivariable regression analysis the more advanced NYHA class, younger age, and higher systolic blood pressure were independently associated with higher RHR (all p < 0.01). Beta-blockers were administered in 93% of patients with and in 98% of patients without COPD (p < 0.001). Percentage of target daily dose of administered beta-blocker did not correlate with RHR either in all patients or in subjects with vs. without COPD, separately (all p > 0.2). The percentage of guidelines-based target daily dose of 4 major beta-blockers (bisoprolol, carvedilol, metoprolol, and nebivolol) in the whole group of patients was 46±35%, and patients with COPD were administered lower percentage of daily recommended dose as compared with those without COPD (41±36 vs. 47±35%, respectively, p = 0.003). Importantly, in all patients with systolic HF treated with beta-blockers, subjects with COPD were less often administered cardioselective agents (bisoprolol, metoprolol or nebivolol) as compared with those without COPD (62 vs. 68%, respectively, p < 0.009).

Conclusions: The presence of COPD identifies those patients with systolic HF with a higher risk of hospitalization and mortality. 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.

Acknowledgement/Funding: The DATA-HELP registry was funded by Merck Serono. All analyses were performed by the authors without any influence from the sponsor.
Abstract P3760 – Table 1

<table>
<thead>
<tr>
<th>Patients without left or right sys-HF (n=336)</th>
<th>Patients with isolated left sys-HF (n=196)</th>
<th>Patients with isolated right sys-HF (n=79)</th>
<th>Patients with combined sys-HF (n=164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TTR</td>
<td>65.4±22.5</td>
<td>61.6±27.0</td>
<td>54.6±21.1</td>
</tr>
<tr>
<td><strong>TTR &gt;65%</strong></td>
<td><strong>61.6±27.0</strong></td>
<td><strong>55.0±23.5</strong></td>
<td><strong>39.5±25.1</strong></td>
</tr>
<tr>
<td><strong>&lt; Table 1</strong></td>
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Conclusion: Right ventricular sys-HF has negative effect on TTR and effective warfarin treatment which should be taken into consideration while planning warfarin monitoring.

P3761 | BEDSIDE

Clinical efficacy and safety of tiotropium and indacaterol administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

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Purpose: To compare clinical efficacy and safety of indacaterol and tiotropium administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease.

Methods: After enrollment in this trial 143 patients (96 men and 47 women), aged 66.3±5.7 years, with CHF classes II to III (New York Heart Association) combined with moderate to severe COPD (GOLD) and with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized into three groups - tiotropium (18 µg daily, n=50), indacaterol (150 µg daily, n=45) and tiotropium+indacaterol group (18/150 µg daily, n=48). Patients of all groups received the complex CHF treatment comprising diuretics, nebivolol, losartan, cardiac glycosides (if necessary) and basic COPD therapy (inhaled corticosteroids). Echocardiography, exercise tolerance (6-min walk distance), 24-hour electrocardiography and blood pressure monitoring were assessed at baseline and after 6 months of treatment, respectively. Towards the end of the observation period, in all groups there was a significant and authentic increase of forced expiratory volume during 1st second (FEV1) which made 5.8%, 7.4%, and 10.2% accordingly, 6-min walk distance increased by 18.0%, 23.5% and 26.2% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (14.1%, 18.5%, 24.5%) and MYHFQ score (25.6%, 27.4%, 32.0%), significant improvements in MMRC dyspnea grade (20.5%, 23.2%, 24.6% respectively). All treatments were well tolerated and side effects of therapy and the number of deaths in all groups was comparable.

Conclusions: The tiotropium and indacaterol inclusion in the structure of complex therapy in patients with CHF combined with COPD raises efficiency of treatment, improves quality of life, basic parameters of central hemodynamics and pulmonary function. Efficacy and safety of tiotropium and indacaterol in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the therapy.

P3762 | BEDSIDE

Comparative temporal effects of nitrate-centred and diuretic-centred treatment of acute decompensated heart failure on congestion and renal function injury as well as tubular damage biomarkers

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Background: 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-dosed nitrate plus short intermittent nitrate infusion (“diuretic-centered strategy” – DC) on congestion markers (CVP and NT-pro-BNP) and renal function injury (eGFR – creatinin level, duration of warfarin administration in patient with chronic heart failure due to coronary artery disease)

Methods: To compare clinical efficacy and safety of indacaterol and tiotropium administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

Aims: To identify the prevalence and characteristics of recently hospitalised patients with chronic heart failure in community care after hospitalisation: a potential role for Ivabradine

C.C. Lang, M. Mohan, L. Cochrane, H. Charles, D.H. Elder. Ninewells Hospital and Medical School, Centre for Cardiovascular and Lung Biology, Dundee, United Kingdom

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 with ADHF, subsequent referral to the THFNLS, data for 18.5%, 24.5%) and MYHFQ score (25.6%, 27.4%, 32.0%), significant improvement in MMRC dyspnea grade (20.5%, 23.2%, 24.6% respectively). All treatments were well tolerated and side effects of therapy and the number of deaths in all groups was comparable.

Conclusions: The tiotropium and indacaterol inclusion in the structure of complex therapy in patients with CHF combined with COPD raises efficiency of treatment, improves quality of life, basic parameters of central hemodynamics and pulmonary function. Efficacy and safety of tiotropium and indacaterol in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the therapy.

P3763 | BEDSIDE

Characterising patients with chronic heart failure in community care after hospitalisation: a potential role for Ivabradine

C.C. Lang, M. Mohan, L. Cochrane, H. Charles, D.H. Elder. Ninewells Hospital and Medical School, Centre for Cardiovascular and Lung Biology, Dundee, United Kingdom

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 with ADHF, 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

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Abstract P3762 – Table 1

<table>
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<th>Groups</th>
<th>NT-pro-BNP, Msm mg/ml</th>
<th>eGFR, Msm ml/min per 1.73 m²</th>
<th>Cystatin C, Msm mg/ml</th>
<th>NGAL, Msm mg/ml</th>
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<tr>
<td>NT-pro-BNP</td>
<td>D1</td>
<td>D4–6</td>
<td>Disc</td>
<td>E</td>
</tr>
<tr>
<td>NC</td>
<td>3292±625</td>
<td>3503±608</td>
<td>0,05</td>
<td>2732±461</td>
</tr>
<tr>
<td>DC</td>
<td>132±21</td>
<td>132±21</td>
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<td>347±56</td>
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</table>
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 these “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 (AHF) 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 reducing 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=86), 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 46.2±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. However, AIx normalized from 25.9 [9.9; 30.9] to 33.5 [24.7; 38.7] in group 1 (p < 0.05) and from 21.1 [7.1; 29.9] to 29.1 [15.9; 31.1], p < 0.01, but not in group 2. 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.

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.

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 >75 bpm, being on standard therapy and being stable on therapy for 4 week.

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 (7/516=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>Standard treatment</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB + ACEI/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.

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 (AIX) increased from 25.9 [9.9; 30.9] to 33.5 [24.7; 38.7] in group 1 (p <0.05) and from 24.1 [11.2; 22.9] to 30.9 [20.7; 38.1] in group 2 (p <0.05). However, AIX normalized for HR of 75 bpm was significantly elevated in pts with HF treated with bisoprolol up-titration therapy – from 21.1 [7.1; 29.9] to 29.1 [15.9; 31.1], p <0.01, but not in pts receiving a combination of bisoprolol and ivabradine – from 20.1 [11.7; 25.2] to 21.1 [11.7; 28.9]. Moreover, up-titration of bisoprolol resulted in a reduction of time to return reflected wave (Tr) from 140.4±2.6 ms to 134.7±3.1 ms, while bisoprolol + ivabradine combination was characterized by an increase in Tr from 140.4±2.6 ms to 134.7±3.1 ms.

Conclusion: In pts with HF of ischemic etiology, tight heart rate control with bisoprolol up-titration, but not with a bisoprolol 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 1000 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 data 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.

**P3768 | BEDSIDE**

Impact of digoxin use in patients with atrial fibrillation and heart failure: data from the Korean Heart Failure (KorHF) Registry

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**Background:** There are conflicting data about the effect of digoxin in patients with atrial fibrillation and heart failure (HF). We aimed to evaluate the clinical impact of digoxin use in Korean patients with atrial fibrillation and HF, using large HF database.

**Method and result:** We analyzed the data from patients with atrial fibrillation and acute HF that were enrolled in the Korean Heart Failure Registry (n=708). The primary endpoint was a composite of all-cause mortality and rehospitalization during the follow up period (median: 404 days; interquartile range: 98–933 days). Among study patients, 263 patients (37%) took digoxin during hospitalization during the follow up period (median: 404 days; interquartile range: 98–933 days). During study patients, 263 patients (37%) took digoxin during hospitalization. In multivariate Cox-proportional hazard model, low pH in arterial blood gas analysis, prior myocardial infarction, on treatment of cardiac arrhythmia, chronic kidney disease, and use of dobutamine were independently associated with increased risk of primary endpoint. Use of digoxin during hospitalization showed independently decreased primary endpoint during follow-up period (hazard ratio 0.993; 95% confidence interval 0.386–0.911; p=0.017). When analyzed according to ejection fraction, beneficial effect of digoxin was shown only in patients with HF with reduced ejection fraction.

**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 beta1-adrenergic stimulation

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**Background:** Chronic stimulation of the β1-adrenergic pathway, as in mice over-expressing the beta1-adrenergic receptor (β1-1OE), 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+/Ca2+ on cardiac hypertrophy and dysfunction.

**Methods:** Single left ventricular (LV) myocytes were isolated from young (8–12 weeks) male β1-1OE (n=4) and wild-type controls (WT, n=6). The late component of the Na+ current (INa,L) was measured as end of pulse current sensitive to 30 μM tetrodotoxin, normalized to cell capacitance. Moreover 6 weeks old male β1-1OE mice were treated with 30 mg/kg body weight BW/day per os ranolazine (+RAN, n=18) or vehicle (CTRL, n=15) both for 6 weeks. Baseline clinical variables were comparable between the groups. 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 compared to WT CTRL (N=15)). Pressure volume measurements and echocardiography were performed at the end of the chronic treatment period. After sacrifice, organ morphomery, LV hypertrophy, and LV cardiomyocyte function were determined.

**Results:** In young β1-1OE mice, INa,L was significantly increased (−0.063±0.018 pA/μF in WT, n=9 vs. −0.149±0.034 pA/μF in β1-1OE, n=10; p<0.05) as well as the integrated current (85±17 pC/μF in WT, n=9 vs 138±17 pC/μF in β1-1OE, n=10; p<0.05). In 6 month old mice, heart weight/BW (HW/BW), LV mass and lung weights (LW/BW) were significantly increased in β1-1OE 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 TAU) were increased. Chronic ranolazine treatment significantly attenuated HW/BW, LV mass as well as LW/BW in β1-1OE, significantly decreased LVEDP. IVRc TAU and improved dP/dtmax and dP/dtmin. Cardiomyocytes from 6 months β1-1OE mice showed significantly elevated Ca2+ transient amplitudes (CaT) at 1 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 β1-1OE cardiomyocytes.

**Conclusion:** Early elevated cytosolic Ca2+ was related to increased Na+ influx via INa,L. Chronic treatment with ranolazine improves cardiomyocyte Ca2+ transients, adverse remodeling and cardiac function in this heart failure model.

**P3770 | BEDSIDE**

Efficacy of long-term ivabradine therapy on prognosis, and left and right heart functional parameters in patients with chronic heart failure and preserved left ventricular systolic function

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The aim of study was to assess the efficacy of long-term ivabradine (l, 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 NYHA III IVF patients, with preserved LV ejection fraction (PEF).

**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 in-hibitors, beta-blockers and diuretics. Deceleration time of transmural (DTm) and transmural systolic (DTs) E waves, E/A ratio of transmural flow (E/Am), RV fractional area change (FAC), tricuspid annulus plane systolic excursion (TAPE), pulmonary artery (PA) ejection (ET) time, RA and LA fractional contribution (FC), functional index (FI), relation of pulmonary vein (PV) systolic and diastolic fraction (S/D), systolic contribution (SC), difference between duration of reversal atrial flow (Ar) and late (A) transmural 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 45.1% 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%, TAPE at 42.1%, DT at 32.1%, PA ET at 17.9%, RA and LA FI at 48.8% and 46.7%, FC at 28.2% and 29.3%, PV S/D at 35.2%, SC at 39.9%, E/A at 51.1%, decreased Ar-A at 82.7% and 72.4% and DTm at 32.5%, RA and LA FI, PV S/D at 50%, RA and LA FC, RV FAC, DT, PAET at ≥25% and Ar-A and DTm at ≥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 Ar-A and DTr −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 0.35, 0.34, 0.35 and 0.33, p < 0.001. Events Death at 6 (12) months (%) 0.7 (0.9) 0.1 (0.2)

Results: Across studies, 337 pts received ZS-9 Ig 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 48 h 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., Coppeell TX, USA.

P3774 | BEDSIDE

Safety and efficacy of G-CSF and autologous bone marrow-derived cells in ischaemic cardiomyopathy: Results of the REGENERATE-HD 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 intra-myocardial (IC) or intramyocardial (IM) injection of autologous bone marrow-derived cells (BMC) improves cardiac function.

Methods and results: 90 patients with symptomatic ischaemic cardiomyopathy and no further treatment options were enrolled in the randomised, placebo

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., Coppeell 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 primary aim 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 Optimet™ 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 MLWHFQ, Peak VO2, NYHA, 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, 31.25min 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.
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, apart from 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 left ventricular ejection fraction (LVEF) at 1 year assessed by cardiac MRI. 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-proBNP at 6 months. None of the other groups showed a significant change in LVEF.

Conclusion: We have shown that G-CSF alone has no effect in patients with ischaemic 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, 16% 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 (normal: >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±6 μV, p=0.026). Figure shows typical QRIS-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

P3776 | BEDSIDE
Effects of beta blocker therapy on resting heart rate in real life clinical practice in patients with chronic heart failure and reduced ejection fraction: results from real life HF study

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Purpose: Heart rate (HR) reduction in chronic heart failure (HF) is associated with improved outcomes. Although, the achievement of target dose of beta-blocker (BB) treatment in systolic HF is strongly recommended by HF guidelines, recent meta-analysis showed that the magnitude of HR reduction may be more important than the recommended target doses, REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dys-function) study data were analyzed to evaluate the effects of BB treatment on resting HR in real life clinical practice in chronic HF patients.

Methods: REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients’ clinical characteristics and the effects of current treatment modalities on resting heart rate (HR) and enrolled 1251 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age. 826 patients in sinus rhythm were included in this analysis, in whom 653 (79.1%) were receiving BB treatment and 173 (20.9%) were not. In patients receiving BB therapy, 6.3% of those were using bisoprolol, 42.4%- carvedilol, 49.1% -metoprolol succinate and 3.2%- nebivolol. The target doses of BB treatment had only been reached in 13.9% of patients.

Results: In patients with sinus rhythm, HR was found to be 76.7±14 bpm and 69.1% of patients had a resting HR <70 bpm. HR was significantly lower in patients receiving BB therapy than those not receiving BB (75.8±15 bpm vs 80.4±15 bpm respectively, p<0.001). Although patients receiving BB had lower resting HR, 65.8% patients receiving BB and 75% patients not receiving BB therapy had a resting HR >70 bpm (p=0.028). Mean HR were 71.5±10, 78.6±13, 74.5±13 and 73.8±12 bpm with bisoprolol, carvedilol, metoprolol succinate and nebivolol respectively (p<0.01). Patients with a resting HR >70 bpm were 59.4%, 72.7%, 60.4% and 67.4% in bisoprolol, carvedilol, metoprolol succinate and nebivolol groups, respectively (p<0.022). However, 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).

Conclusions: The results of this study show that despite the highly prevalent use of BB therapy in patients with systolic HF in real life clinical practice and despite the significant reduction in resting HR by BB, most patients still have a resting HR >70 bpm and there was no significant additional effect of target doses of BB treatment on resting HR.

Acknowledgement/Funding: This study is supported by Servier

HEART FAILURE THERAPY, VARIOUS IV

P3777 | BEDSIDE
Tolvaptan in patients with acute decompenesated 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 decompenesated heart failure (ADHF). Tolvaptan is known to induce diuresis and prevent volume overload. 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- tide), B group: Conventional therapy with 14 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, e-GFR, 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 higer 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 (*AB), P=0.03 (*AB+C) by Paired T test).

Conclusions: Additional treatment with tolvaptan could prevent WRF in patients with ADHF.
P3780 | BEDSIDE
Clinical characteristics of responders to treatment with tolvaptan in patients with acute decompensated heart failure: importance of preserved kidney size

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Background: Recent clinical trials have demonstrated the efficacy of short-term treatment with tolvaptan, an oral vasopressin V2 receptor antagonist, in patients with heart failure. However, the response to tolvaptan varies among patients. The aim of this study was to determine factors associated with response to tolvaptan in patients with acute decompensated heart failure (ADHF).

Methods: We enrolled consecutive ADHF patients treated with tolvaptan and they were divided into two groups: responders and non-responders. Responders were defined as subjects who met all of the following three conditions: (1) increasing urine volume during a 24-hour period after the start of tolvaptan treatment, (2) improvement in NYHA functional class and (3) decrease in cardiothoracic ratio assessed by chest X-ray on day 3 of tolvaptan administration.

Results: Among the 114 patients, treatment with tolvaptan improved three conditions of heart failure (increase in urine volume, improvement in NYHA functional class and decrease in cardiothoracic ratio) in more than half of the patients with ADHF (number of responders versus non-responders: 71 (62%) versus 43 (38%)). As for baseline characteristics, estimated glomerular filtration rate, urine osmolality, and kidney size were significantly greater in responders than in non-responders. Multivariable logistic analysis revealed that kidney size was independently associated with responders.

Conclusions: The main clinical characteristic of responders to treatment with tolvaptan is that kidney size is preserved.

P3779 | BEDSIDE
Long-term advantages of HR control with ivabradin-bisoprolol combination versus bisoprolol up titration on exercise capacity, chronotropic reserve and pulsatile arterial hemodynamics in CAD patients

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Purpose: To compare long-term effects of equivalent heart rate (HR) control at rest with ivabradine (IV) and bisoprolol (BS) combination and that of BS up titration on exercise tolerance, its chronotropic support, LV function, pulsatile arterial hemodynamics assessed by pulse wave analysis (PWA) in CAD patients with mild depression of LV ejection fraction.

Materials and methods: In single-blind, parallel-group study 85 pts aged ≤ 60 years (53±7,7) in sinus rhythm ≥ 70 bpm with CAD (stable angina CCS class I-II), documented MI ≤ 3 months, mild hypertension and EF of 38–45%, treated with ACE inhibitors and BS 2.5 mg od or BB naive, were randomized into 2 groups. In Group 1 (n=40 per protocol, 9 women) BS was uptitrated to 5mg pd and IV was added (5mg bid uptitrated to 7.5 mg bid, 12,7±0,37 mg pd, in Group 2 (n=45 per protocol, 11 women) BS was uptitrated to 10 mg od (9,3±0,37 mg). At baseline (M0) and 6 months (M6), symptom-limited treadmill test (Bruce protocol) was performed, heart rate control at rest with long-term IV plus BS therapy, but not BS uptitration, produced exercise tolerance improvement, associated with major increase of chronotropic reserve, and to lesser extent - with resting mitral E/E' reduction accompanied by arterial pulsatile unloading assessed by PWA.

Conclusions: 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.

P3778 | BEDSIDE
Effects on beta-blockers on heart failure with preserved ejection fraction; from the Korean Acute Heart Failure (KorAHF) registry

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Purpose: To investigate the hypothesis that beta-blockers are associated with reduced adverse events in patients with HFpEF.

Methods: The KorAHF 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 weighing (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], 0.51–1.04) (Figure A). However, beta-blocker significantly reduced rehospitalization (HR, 0.74; 95% CI, 0.62–0.89), and a composite outcome (HR, 0.75; 95% CI, 0.59–0.89). In the propensity-score matching, beta-blockers were not associated with reduced all-cause death (HR, 0.76; 95% CI, 0.57–1.03) 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 and metformin 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 exerts better cardioprotection than enalapril in attenuating adverse LV remodeling.

P3782 | BENCH
Fedex-3 promotes transcription activity of FoxO3a via its nuclear localization.

1 The Sakakibara Heart Institute of Okayama, Department of Cardiology, Okayama, Japan; 2 Kameda Medical Center, Kamogawa, Japan; 3 Kawasaki Medical School, Division of Cardiology, Kurashiki, Japan.

Introduction: Vasodilators play an important role in management of acute heart failure syndrome (AHFS). However, it remains to be elucidated which subgroups of patients should be treated with vasodilators.

Purpose: The aim of this study was to identify the characteristics of patients receiving benefit from vasodilators.

Methods and results: We retrospectively reviewed 763 patients (382 males, 77.6±12.9 years old) hospitalized due to AHFS. Vasodilators were used within 48 hours from admission in 329 (43.1%) patients. After propensity score matching, 546 well-balanced patients with or without vasodilators (273 patients in each group) were endpointed. The primary endpoint of this study was the composite of all cause death and re-hospitalization due to heart failure. During the follow-up period (median 228 days, interquartile range 55–1031 days), the primary endpoint was observed in 150 patients (28.6%). Cox regression analysis revealed that vasodilators did not reduce the primary endpoint in all cohort (hazard ratio [HR] 0.79, 95% confidence interval [CI] 0.57–1.09, p=0.15). However, in subgroup analysis, the prognosis was significantly improved with vasodilators in female (HR 0.54, 95% CI: 0.34–0.85), but not in male gender (HR 1.23, 95% CI: 0.77–2.96). P value for interaction between male and female groups was significant (P=0.048).

Conclusions: The efficacy of vasodilators in AHFS differs between male and female. Vasodilator therapy may be preferred as initial treatment strategy for female patients with AHFS.

P3783 | BEDSIDE
Furosemide dose response curve after hypersaline in heart failure patients.

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1 University of Palermo, Department of Internal Medicine and Specialty, Palermo, Italy; 2University of Palermo, Dipartimento Biopatologia e Biotecnologie Mediche e Forensi (DIBM4EF), Palermo, Italy; 3GF Ingrassia Hospital, Cardiology Division, Palermo, Italy; 4Stony Brook University, Cardiology Division, New York, United States of America.

Aims: Loop diuretics remains a mainstay of heart failure (HF) therapy. The chief indicator to evaluate diuretic responsiveness is the urine production per unit dose of diuretic rather than the absolute urine output or diuretic dose. In many patients, sodium and water excretion plateau over time before adequate fluid elimination, especially in chronic heart failure (CHF). This phenomenon is termed as diuretic resistance, which may be overcome by the administration of hypertonic saline solution (HSS) plus high dose furosemide (Furo).

Methods: Urine sample of 36 consecutive patients hospitalized for acute HF were collected at 30, 60, and 90 minutes and 3,4,5,6,8 and 24 hours after infusion of

P3784 | BEDSIDE
Difference in efficacy of vasodilators for acute heart failure syndrome between female and male.

1 The Sakakibara Heart Institute of Okayama, Department of Cardiology, Okayama, Japan; 2 Kameda Medical Center, Kamogawa, Japan; 3 Kawasaki Medical School, Division of Cardiology, Kurashiki, Japan.

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Conclusions: The efficacy of vasodilators in AHFS differs between male and female. Vasodilator therapy may be preferred as initial treatment strategy for female patients with AHFS.
furfur 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 concentration were evaluated for each collected urine sample.

**Results:** HS5 addition to Fur significantly increased urine output, diuresis, 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 decrease significantly (<0.0001). Furosemide concentration increases over time and was observed to rise into urine at all different doses when diluted in HS5. In 31 pts (86%), curves fit with sigmoid function (ALLFIT) confirming that HS5 addition to fur have positive effects on diuresis and natriuresis.

**Conclusion:** This study demonstrates that addition of HS5 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.

**P3786 | BENCH**

**Head to head comparison of therapeutic efficacy among three iron chelators on cardiac function in iron-overloaded rats**

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**Background:** Iron overload cardiomyopathy is an important complication and responsible for high mortality rate in ß-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 deferiprone (DFP), and deferasirox (DFX) are used to prevent iron-overloaded complications. Despite their effective chelating effects, there are no reports on the head-to-head comparison regarding the efficacy of these 3 iron chelators on the heart in iron overload cardiomyopathy.

**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 vehicle, and continued feeding with HFe diet 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 NSTDA Research Chair Grant (NC), the Thailand Research Fund RTA5680006 (NC), BRG5780016 (SC), Chiang Mai University Center of Excellence Award (NC)

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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 etiology**

J.Y. Cho1, K.H. Kim1, Y. Ahn1, E.S. Jeon1, J.J. Kim2, S.C. Chae3, S.H. Baek4, S.M. Kang4, M.C. Cho1, B.H. Oh1 on behalf of KorAHF investigators. 1 Chonnam National University Hospital, Cardiology, Gwangju, Korea, Republic of; 2 Samsung Medical Center, Seoul, Korea, Republic of; 3 Asan Medical Center, Seoul, Korea, Republic of; 4 Kyungpook National University Hospital, Daegu, Korea, Republic of; 5 Seoul St Mary’s Hospital, Seoul, Korea, Republic of; 6 Yonsei Cardiovascular Center, Seoul, Korea, Republic of; 7 Chungbuk National University Hospital, Cheongju, Korea, Republic of; 8 Seoul National University Hospital, Seoul, Korea, Republic of.

**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, 2252 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=n.s.). 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.

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**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 differentially modulates skeletal muscle proteins in rats with aortic stenosis-induced heart failure.

**Figure 3789**

**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 etiology**

J.Y. Cho1, K.H. Kim1, Y. Ahn1, E.S. Jeon1, J.J. Kim2, S.C. Chae3, S.H. Baek4, S.M. Kang4, M.C. Cho1, B.H. Oh1 on behalf of KorAHF investigators. 1 Chonnam National University Hospital, Cardiology, Gwangju, Korea, Republic of; 2 Samsung Medical Center, Seoul, Korea, Republic of; 3 Asan Medical Center, Seoul, Korea, Republic of; 4 Kyungpook National University Hospital, Daegu, Korea, Republic of; 5 Seoul St Mary’s Hospital, Seoul, Korea, Republic of; 6 Yonsei Cardiovascular Center, Seoul, Korea, Republic of; 7 Chungbuk National University Hospital, Cheongju, Korea, Republic of; 8 Seoul National University Hospital, Seoul, Korea, Republic of.

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**P3788 | BENCH**

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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. Tropotiy was analyzed in soleus 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 groups presented similar echocardiographic parameters. GH 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 atrin-1 were higher in AS and AS-GH groups. GH attenuated MyoD increase. Immunofluorescence staining showed that staining with anti-neural cell adhesion molecule (NCAM) and anti-neonatal myosin heavy chain isoform was statistically more intense in AS-GH than AS and Sham. In soleus, GH activated IGF-1 and P38K 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 trophicity. 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 predominately oxidative muscles (soleus), GH activates IGF-1 and P38K 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 (>500 ng/l)] and 109 (10%) did not fit into 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, larger left atrial volumes and IVC diameter, more impaired right ventricular function and higher systolic pulmonary artery pressure], lower LVEF, worse renal function, more anaemia and hyponatraemia. During a median follow-up of 934 days (IQR: 513–1425 days), 450 patients were hospitalized for HF or died. Compared to patients with cardiac dysfunction not taking loop diuretics, those treated with higher doses of loop diuretics (Furosemide or equivalent >80 mg/day) had a 3.5-fold greater risk of an adverse event (HR: 3.50, 95% CI: 2.49–4.93). However, in multi-variable models clinical, biochemical and echocardiographic phenotyping of patients with congestive heart failure, 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 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 (n=402) 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% vs 14%; p<0.009). After treatment, the mean change in weight loss (~3.8±1.9 kg vs. 2.7±2.5 kg, p<0.01) and the mean urine output (25/±730 ml vs. 225±451 ml, p=0.04) were higher in the Civ respect to 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 respect 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<0.01). 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></td>
<td>RR (95% CI of RR)</td>
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<tr>
<td>BNP AT*</td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>Creatinine AT*</td>
<td>3.17 (1.98–5.08)</td>
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<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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</tbody>
</table>

Conclusions: In AHDF, 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 (51.2±2.1 vs 34.4±1.1% in group A (p<0.001); 45.3±1.9 vs 34.1±2.1% in group B (p<0.01)). End FS and mid FS also increased at the end of the study [41.8±1.1 vs 24.5±1.2% and 25.1±0.5 vs 13.3±0.3%, respectively in group A (p<0.001); 35.3±1.2 vs 24.8±1.3% and 20.4±0.6 vs 13.6±0.5%, respectively in group B (p<0.01)].

Conclusions: 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) from a phase 3 study

Background: Renin-angiotensin-aldosterone system inhibitors (RAASI) increase risk of hyperkalaemia (HK; serum K+ ≥5.0 mmol/L), often leading to suboptimal dosing or discontinuation of these agents, despite proven cardioprotective benefits in heart failure (HF) patients (pts). Sodium zirconium cyclosilicate (ZS-9) is a first-in-class, highly selective, non-absorbed cation exchanger designed to trap K+ in the GI tract. In the Phase 3 HARMONIZE trial, ZS-9 rapidly achieved and maintained normal serum K+ for 28 days in HF pts.

Methods: HARMONIZE was a multicenter, randomized, double-blind, placebo (PBO)-controlled trial which evaluated efficacy and safety of ZS-9 in pts with HFrEF (N=258). All pts received ZS-9 10g TID for 48h (open-label phase). Pts achieving PBO-controlled trial which evaluated efficacy and safety of ZS-9 in pts with HK without modification of RAASI therapy in high-risk pts with HF and HK.

Results: In HF pts on RAASI (n=258), mean age was 69; 79% had eGFR <60. Within 48h, mean K+ declined from 5.6 to 4.4 mmol/L, with a median time to normalization of 20h; 91% and 98% of pts achieved normal K+ by 24h and 48h, respectively. During the randomized phase, pts in the 5, 10, and 15 mg ZS-9 groups maintained significantly lower K+ at 4.6, 4.5, and 4.4 mmol/L, respectively, vs. 5.3 mmol/L in the PBO group (p<0.05 for all doses; Figure). ZS-9 was well tolerated with GI adverse events similar to PBO.

Conclusions: ZS-9 rapidly normalized K+ within hours of the first dose, maintained normal K+ for up to 28 days, and was well tolerated in HF pts on RAASI. These results suggest that ZS-9 may enable optimization of cardioprotective RAASI therapy in high-risk pts with HF and HK.

Acknowledgement/Funding: Supported by ZS Pharma, Inc., Coppell TX, USA.

P3794 | BEDSIDE
Right ventricular function is associated with survival in patients undergoing surgical left ventricular reconstruction

Introduction: Left ventricular reconstructive surgery (LVR) in heart failure patients has shown to yield beneficial effects on functional status and quality of life. Several LV parameters have been associated with prognosis in patients treated with LVR but little is known about the prognostic implications of RV function.

Purpose: The aim of the present study was to evaluate the association between RV systolic function and outcome in patients treated with LVR.

Methods: 134 consecutive patients (age 62±10 years, 79% male) underwent LVR between 2006 and 2012 according to the technique described by Dor. Echocardiographic biventricular performance was assessed before surgery. Mortality during the first two years after surgery was registered. Multivariate cox regression analysis was performed separately for each RV parameter.

Results: Survival two years after LVR was 75%. Left ventricular ejection fraction (LVEF; 28±7 vs 25±6%, p<0.01) right ventricular fractional area change (RVFAC; 44±9 vs 39±9%, p<0.01) and tricuspid annular plane systolic excursion (TAPSE; 18±3 vs 17±3 mm, p<0.07) were better in survivors compared to non-survivors. RVFAC >35% remained independently associated with mortality (HR 2.9, p<0.01) after adjusting for age at operation, sex and LVEF.

Conclusion: Impaired pre-operative right ventricular function is associated with decreased survival in patients undergoing LVR.

P3795 | BEDSIDE
Impact of pulmonary hypertension on mortality in patients treated with nitric oxide for failure to wean following cardiothoracic surgery
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Background: Patients with pulmonary hypertension (PH) are at greater risk for perioperative complications and mortality with cardiovascular surgery (CTS). It is unknown whether administration of inhaled nitric oxide (iNO) post-operatively reduces this risk.

Methods: From a single-institution database of 177 patients receiving iNO for failure to ventilate 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) ≥50 mmHg. In-hospital mortality was compared based upon the presence of PH at discharge.

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 and ESH guidelines. Tight blood pressure control down to a mean office blood pressure of 135/75 mmHg reduced cardiovascular mortality by 18% compared to placebo (140/75 mmHg) in the ADVANCE trial. It is not known how these target blood pressure values, as assessed by office readings, correspond to the respective values of ambulatory-24-h blood pressure measurements (ABPM). Furthermore we investigated classification of blood pressure as assessed by the two different blood pressure measurement techniques.

Design and methods: A total of 919 ABPM recordings of patients with type 2 diabetes (age 64.4±12.3 years) with treated hypertension were obtained using validated recorders. Corresponding values of office and day-time-ABPM values were analysed 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 134 patients showed nocturnal hypertension. Masked nocturnal hypertension was more common (14%) than white-coat hypertension (8%). As assessed by office blood pressure isolated systolic hypertensive (ISH) was more common than combined systolic/diastolic hypertensive. 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 of 140/85 mmHg corresponds to an ABPM day-time value of 134/81, an office blood pressure of 135/75 mmHg corresponds to an ABPM day-time value of 129/71 mmHg.

Conclusions: Interestingly the predominant form of hypertension was combined systolic/diastolic hypertension as assessed by ABPM. In hypertensive patients with type 2 diabetes misclassification (white-coat, masked) of normotension/hypertension on the basis of office readings was observed in 22% of the patients. As long outcome-driven analogue values for ABPM are lacking, corresponding target values for ABPM readings may be used preliminarily to stage severity of hypertension.

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 purpose 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 percutaneous coronary intervention. Patients with an inability to perform VVUS 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 by IB-IVUS.

Results: The mean night-time systolic BP SD and RHI were 11.1±1.9 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 SD compared to those with the normal RHI (r=0.167) (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 indicated 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 (ABP) among women with obesity and normal weight of different ages.

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, glucose, ESH guidelines (IMT), carotid-foemoral pulse wave velocity (PWW), LV mass index (LVM) and arterial stiffness (GFR, EPI) were measured.

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 (PPI), SBP variability and rates of high night SBP (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 (DLP) than obese girls without HT (p<0.01).

Conclusion: Adolescent girls with obesity represents an important group for screening of nocturnal HT. Adolescents 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 for ambulatory blood pressure monitoring in adolescents with obesity.

Methods: Total 266 patients who were diagnosed as hypertension by DBPM, were enrolled from 4 university hospitals. AOBP (WatchBP Home, Microlife, Switzerland) of both arms was measured 3 times on every 3 days visits 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. 132.6±12.5 mmHg, p<0.001) and HBPM (132.1±12.5 mmHg, p<0.001). 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, showing 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 was −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 ABP under controlled circumstances by a well-trained healthcare personnel is easy and comparable to HBPM compared with ABPM.
Abstract P3799 – Figure 1

**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. Hyper-tension 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 cholesterol, triglycerides (TG), and parathyroid hormone (PTH) were associated with WMH volumes. The presence of hypertension in women with a history of hypertension in pregnancy was significantly associated with cerebral white matter lesions.

**Conclusions:** Our results suggest that vitamin D deficiency and PTH excess have positive correlation with non-dipping and increased BP parameters on ABPM in newly diagnosed HT.

**Table 1. Levels of vitamin D and PTH**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n=34)</th>
<th>Non-dipper (n=33)</th>
<th>Dipper (n=33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.8±10.8</td>
<td>53.4±9.6</td>
<td>56.7±9.7</td>
<td>0.134</td>
</tr>
<tr>
<td>Male [%]</td>
<td>45 (45.0)</td>
<td>15 (44.1)</td>
<td>12 (36.4)</td>
<td>18 (54.5)</td>
</tr>
<tr>
<td>Female (n)</td>
<td>55 (55.0)</td>
<td>19 (54.9)</td>
<td>21 (63.6)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Log(PTH) (pg/ml)</td>
<td>1.0±0.4</td>
<td>1.1±0.2</td>
<td>1.0±0.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>Log(VitD) (nmol/l)</td>
<td>1.80±0.11</td>
<td>1.70±0.11</td>
<td>1.70±0.11</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*Difference is significant at the 0.05 level, †difference showing group (adjusted for menopause post-hoc test: p<0.05).*

**Conclusion:** Our results suggest that vitamin D deficiency and PTH excess have positive correlation with non-dipping and increased BP parameters on ABPM in newly diagnosed HT.

**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 complications 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.

Results: Among women with vitamin D level was significantly low in non-dippers than that of dipper and control groups (1.9±0.3 pg/dl, 1.7±0.2 pg/dl; p=0.001). Vitamin D levels were negatively correlated with 24-h systolic and diastolic BP (r=−0.366, p=0.003), (r=−0.295, p=0.018), and 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.

**Conclusion:** Our results suggest that vitamin D deficiency and PTH excess have positive correlation with non-dipping and increased BP parameters on ABPM in newly diagnosed HT.
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 wave-pulse 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±5.2 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 (4.63±0.5 vs 4.64±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=0.003). However, serum cystatin-C levels were higher in INH subjects compared to normotensive controls (82±34.7 vs 73±13.5 ng/ml, p=0.004) but the two groups did not differ with respect to BNP levels (22.6±13.8 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.

Conclusions: 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 Transhyretin familial amyloid polyneuropathy (TTR-FAP) V30M have changes in blood pressure (BP) profile due to disturbances in autonomic control. Liver transplantation (LT) has been used to attenuate the progression of the disease. However there is little information about its impact on the progression of the autonomic dysfunction.

Purpose: To evaluate the impact of LT in the dysfunction of the autonomic nervous system (ANS) by assessing circadian variation of BP.

Methods: Prospective study of consecutive pts with V30M TTR-FAP evaluated annually and performing a 24-hour ambulatory blood pressure monitoring (ABPM) record. Pressure profile of pts undergoing transplant was compared with that of non-transplanted pts. For that purpose, we conducted a nested case-control analysis with patient matching according to neurophysiological score measured prior to transplantation (~5% difference).

Results: From a total population of 284 TTR-FAP pts, 88 (44 transplanted, 44 non-transplanted), with a mean age of 47±15 years, 52% male, with identical mean neurophysiological and clinical scores, 25 (IQ 7.85–51.25) and 24 (IQ 12–34), respectively, were selected for analysis. During follow-up of 4 years (range 0.5–6 years), 208 ABPM records were performed. At initial evaluation, the transplanted group exhibited higher values of systolic BP (SBP) in 24 hours (121±15 vs. 113±10 mmHg, p=0.003), daytime (122±14 vs. 116±10 mmHg, p=0.013) and nocturnal (115±15 vs. 106±12 mmHg, p=0.008), daytime systolic load [6 (0–30) vs. 0 (0–3), p=0.003], daytime diastolic load [15 (0–70) vs. 0 (0–1), p=0.013] and nocturnal (115±15 vs. 106±12 mmHg, p=0.008), daytime SBP (at 48 months: 120±18 vs. 114±16 mmHg, p=0.032) and increased PP (at 24 hours: 102±25 vs. 90±18 mmHg, p=0.019) at baseline in the combination therapy group showed a direct correlation with delta PWVe r=0.256, p=0.019 at baseline and delta PWVe r=0.387, p=0.019 at baseline in the combination therapy group showed a direct correlation with delta PWVe r=0.256, p=0.019 at baseline and delta PWVe r=0.387, p=0.019 at baseline in the combination therapy group showed a direct correlation with delta PWVe.

Conclusions: Liver transplantation (LT) has been used to attenuate the progression of the disease. However there is little information about its impact on the progression of the autonomic dysfunction. LT improved blood pressure control in the long term. This may be due to the following factors: as more rigorous follow-up in these group or progression of the disease.

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 in two examinations over a 2-year period (mean follow-up 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). Based on these measurements the annual absolute changes were calculated.

Results: Treatment with angiotensin receptor blockers was associated with slower progression of arterial stiffening after adjustment for relevant confounders [0.03/m/s/year (95% CI: −0.12 to 0.18) vs. 0.23/m/s/year (95% CI: 0.15 to 0.30), P=0.032]. Angiotensin converting enzyme inhibitors did not attenuate the hypertension-related progression of arterial stiffening [0.33/m/s/year (95% CI: 0.15 to 0.50) under treatment vs. 0.15/m/s/year (95% CI: 0.09 to 0.22), P=0.08]. Neither beta-blockers [0.24/m/s/year (95% CI: 0.08 to 0.41) under treatment vs. 0.17/m/s/year (95% CI: 0.10 to 0.23), P=0.42], calcium channel blockers [0.11/m/s/year (95% CI: −0.04 to 0.27) under treatment vs. 0.20/m/s/year (95% CI: 0.13 to 0.27), P=0.35] or thiazide diuretics [0.31/m/s/year (95% CI: 0.12 to 0.49) under treatment vs. 0.16/m/s/year (95% CI: 0.09 to 0.23), P=0.16] showed beneficial effect on reversing progression of arterial stiffening.

Conclusions: 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 and methods: 240 healthy treated patients who underwent 6 month follow-up time were randomized to 6 months therapy with: quinapril, amlodipine, hydrochlorothiazide, losartan or bisoprolol. Each therapeutic group consisted of 59 patients (N=19). Before and then after 1, 3 and 6 months of treatment carotid-femoral waves were performed. Blood pressure, monitoring variability and arterial stiffness were tightened by an elastic type before treatment, the higher was the CBP before treatment in combination therapy. CBP at the end of treatment as monotherapy group correlated with office SBP after r=0.570, p=0.0001, office delta SBP r=0.410, p=0.014 and inversely with the delta office HR r=-0.436, p=0.009. The greater was the reduction in office heart rate, the less CBP decreased at the end of treatment. CBP at the end of treatment in combination therapy correlated with delta PWVe r=−0.371, p=0.002, PWVe before treatment r=0.286, p=0.02 and Aix after treatment r=0.443, p=0.001, Delta Aix r=0.251, p=0.041 and inversely correlated with ED after treatment r=−0.273, p=0.026.

Conclusions: CBP after treatment in the combination therapy group lercanidipine with diltiazem had more correlation with indicators elastic properties of arteries. Higher levels TIM and cholesterol at baseline was led to less reduced CBP in combination therapy. The greater was the reduction PWVe, the greater was the reduction CBP in combination therapy.

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**Conclusion:** Irrespective of chosen drug we observed similar effect for PWV.

**Methods:** Potentially overlapping inflammatory mechanisms. We therefore investigated the psoriasis with IRR 1.35 (95% confidence interval [CI] 1.19–1.52) and IRR 1.89 corresponding adjusted IRRs for AAA were markedly increased in patients with mild psoriasis (272 cases), and severe psoriasis (55 cases), respectively. The period we identified 60,477 patients with mild psoriasis and 12,285 patients with severe psoriasis.

**Background:** Atherosclerosis is a chronic inflammatory disease characterized by a 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 as T helper 1 (Th1), induced regulatory T-cells (Treg), T helper 17 (Th17) and T helper 2 (Th2).

**Conclusion:** Oxidized LDL induce tissue factor expression in CD3+ T-lymphocytes: a possible link between immunity, inflammation and thrombosis.

**Purpose:** Abdominal aortic aneurysm (AAA) is a complex multifactorial disease associated with a high morbidity and mortality. Increased inflammation including comorbidity, concomitant medication, 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 incident 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.

**3942 | BEDSIDE**

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 comorbidity, concomitant medication, 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 incident 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 might express TF protein.

**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 a 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 as T helper 1 (Th1), induced regulatory T-cells (Treg), 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 (Treg).

**Purpose:** We aimed to characterize the expression and activity of IDO in monoocytes derived (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, kyurenine, 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 Treg.

**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 patients (1112±226.0, mean ± SEM) (P<0.05) and controls (1203±224.9, mean ± SEM) (P=0.04). Furthermore, the concentration of kyurenine, 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 allogeneic naïve T-cells, the ratio between the percentage of generated Th1 and Treg from MLR was higher in ACS (2.08±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: Macrophage grade decreased significantly in both groups, and the percent decrease in macrophage grade was significantly greater in the group receiving 20 mg/day of atorvastatin compared with the group receiving 5 mg/day of atorvastatin (-38% [IQR -44 to -31%] vs. -24% [IQR -33 to 0%], p < 0.001). The percent change in macrophage grade 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 macrophage grade was negatively correlated with the percent change in fibrinogen cap thickness (R = -0.415, p = 0.003).

Conclusions: Therapy with 20 mg/day of atorvastatin provided greater decrease of macrophage accumulation in coronary plaques compared with 5 mg/day of atorvastatin. The decrease of macrophage 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
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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 without non-collagen disease. The primary endpoint was major adverse cardiac events (MACE), which was defined as cardiovascular death, myocardial infarction (MI), non-collagen disease. The primary endpoint was major adverse cardiac events (MACE), which was defined as cardiovascular death, myocardial infarction (MI), cerebrovascular accident (CVA), and revascularization. The secondary endpoints were cardiovascular death and non-fatal MI. The patients were divided into the following two groups: non-collagen disease: 42.6%, collagen disease: 57.4%. The primary endpoint was MACE, which was defined as cardiovascular death, MI, non-collagen disease (24.2% vs. 10.1%, p = 0.036). Kaplan-Meier analysis demonstrated that there was a significant difference in MACE (p = 0.036). Multivariable analysis demonstrated that collagen disease was an 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
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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. Pre-cise 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 how 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.

**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.


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**Background:** Myocardial infarction (MI) induces an exaggerated inflammatory response that results in infarct expansion and progression to 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:** Th17 female landrace pigs were subjected to 75 minute transhumal balloon occlusion of the left anterior descending artery. Post-MI, pigs received daily intravenous infusion of either a high dose of MCC950 (8mg/kg), a low dose of MCC950 (3mg/kg) or placebo. After 7 days, cardiac function was assessed using real-time three-dimensional transesophageal echocardiography. Infarct size and area at risk were determined using Evans blue/tetratolamine chloride double staining. All analyses were performed in a blinded fashion.

**Results:** Mortality was similar in all groups. 7 days post-MI, animals treated with MCC950 had a significantly higher left ventricular ejection fraction compared to both untreated (median age 3.9 years (min 0.4 – max 12.5)), 53 ART-treated HIV infected, 5.2 years (0.6–12.2), median ART duration 2.4 years (0.1–9.9), and 48 healthy children, 6.4 years (2.4–14.0). The ART-naive HIV infected had thicker cIMT (difference 70.4 μm, 95% CI 32.1 to 108.7, p < 0.001), adjusted for age, sex, socioeconomic status, parental smoking, body mass index, systolic and diastolic blood pressure, LDL-cholesterol, and HbA1c. hs-CRP level did not alter this (71.6 μm, 31.9 to 111.2, p=0.001). The ART-treated HIV infected had similar cIMT to healthy children. In terms of distensibility and elastic modulus, there were no statistically significant differences between HIV infected, either ART-naive or treated, and healthy children.

**Conclusions:** 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.

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**COMPUTED TOMOGRAPHY AND CORONARY RISK**

**3995 | BESIDE**

Can cardiac CT angiography identify asymptomatic type 2 diabetics at high risk for adverse coronary events? A prospective 7 years outcomes study.

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**Background:** Asymptomatic type 2 diabetics (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. MACE (CV death/M/unstable angina) were assessed over 6.5±1.0 yr.

**Results:** Coronary plaque was present in most (500, 79.4%) pts. MACE occurred in 41 (6.3%). A standard risk score (UK Prospective Diabetes Study, UKPDS) predicted future coronary risk, CAC score, extent of plaque on CTA and mild, grade 2–5, calcification were independent outcome predictors and successively improved discrimination on ROC analysis (Table). A multivariate model including UKPDS, total plaque length and plaque characterization had good prediction and discrimination (Table) and reclassification for MACE (Overall net reclassification improvement). Baseline C-statistic was 0.545 and increased to 0.608.

**Outcome predictors**

<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>Univariate Hazard ratio p</th>
<th>Multivariate Hazard ratio p</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS*</td>
<td>1.4 (1.3–1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Log (coronary artery calcium+1)</td>
<td>2.3 (1.6–3.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total plaque length</td>
<td>2.2 (2.4–2.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mild (grade 2–5) plaque calcification</td>
<td>1.2 (1.0–1.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>UKPDS + log(CAC+1) combined</td>
<td>1.6 (1.4–1.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>UKPDS + plaque length</td>
<td>0.7 (0.5–1.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>UKPDS + plaque length + mild calcification</td>
<td>0.6 (0.4–0.8)</td>
<td>0.105</td>
</tr>
</tbody>
</table>

*UK Prospective Diabetic Diabetic Study Risk Score. †Per 10 year risk. ‡Per quartile. †P < 0.01 vs UKPDS + log(CAC+1).
considered obstructive. Lesion-specific ischemia was defined by FFR.

**Results:** In 484 vessels, mean volumes of 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 CPA > 50% was 6.8 (3.9–12.0; p < 0.001). In multivariate analysis NCP (p < 0.001), LD-NCP (p < 0.001), and CPA (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**

**Conclusions:** The combined presence of high PC and PRU yields an additive effect on ischemic and bleeding risk in patients undergoing PCI with DES: Insights from the ADAPT-DES registry.

**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. ROC Curves for 5 year ACM and MACE

**Results:** 8,535 patients were included in the study cohort. There were no significant differences in the prevalence of HPR across platelet 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, with no 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.
effect on risk for ST. While PCI was not associated with bleeding risk, both low and high PC independently correlated with long-term mortality. PCI 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

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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 ST-segment Elevation Myocardial Infarction: PRImary PCI in MULTIvessel Disease, investigates whether complete revascularization can improve outcome in 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) for acute coronary syndromes (ACS). 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 multivessel 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 disease STEMI patient population receiving contemporary treatment with novel platelet inhibitors and bivalirudin.

Methods: We included patients with acute onset symptoms of <12 hours duration and ST-segment elevation undergoing successful primary PCI, who had >1 angiographic diameter stenosis of >50% in a coronary artery >2 mm not related to the IRA. Patients were randomized 1:1 to either optimal medical treatment after primary PCI of the IRA or fractional flow reserve (FFR) (≤0.80) guided complete revascularization during a staged procedure before discharge. Bleeding episodes were assessed based on BARC and TIMI criteria.

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, whereas the coronary angiography + 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 in-hospital, 30-days and 1-year bleeding episodes as well as short- and long-term mortality and will be ready for presentation at the ESC meeting.

Conclusion: In CHAMPION-PHONIX, 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

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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 mean IMRcorr was 16.6U (IQR 12.4–23.0U). 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 of 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 ischaemic FFR values. Integration of IMR and FFR measurements may improve the stratification of patients without evidence of MI.
Effects of prasugrel versus clopidogrel on coronary microvascular function in patients undergoing elective percutaneous coronary intervention: a randomized double-blind study

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Background: Microvascular impairment has been reported in patients on clopidogrel undergoing elective percutaneous coronary intervention (PCI); prasugrel provides more potent platelet inhibition than clopidogrel, though it is unknown whether this might prevent PCI-related microvascular damage.

Purpose: We compared the effects of prasugrel and clopidogrel on coronary microvascular function in patients undergoing elective PCI.

Methods and results: Forty-thiopentol-prone 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 diphosphase (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±14.1 in clopidogrel group, p=0.148). Post-PCI IMR was significantly lower in the prasugrel as compared with clopidogrel group (17.3±8.3 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 both at baseline (16.0±8.3 vs. 33.9±18.0 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 those treated with clopidogrel (17.3±8.3 vs. 26.1±11.0, p=0.007).

Conclusions: Unlike with clopidogrel, prasugrel pretreatment prevents from PCI-related microvascular impairment and myocardial damage in patients with stable coronary artery disease.

The comparative clinical utility of the index of microvascular resistance (IMR) for coronary flow reserve for acute risk assessment in repurposed STElevation myocardial infarction patients

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Background: Invasive assessment of coronary physiology provides prognostic insights in STElevation myocardial infarction (STEMI), but it is unclear which is the most clinically useful physiological parameter is.

Purpose: To assess the clinical utility of the index of microvascular resistance (IMR) for coronary flow reserve for acute risk assessment in repurposed STEMI survivors.

Methods: We performed a single centre cohort study in near-consecutive repurposed STEMI patients. IMR and CFR were measured at the time of primary percutaneous coronary intervention (PPCI) in a large unselected cohort of repurposed STEMI survivors.

Results: Adverse remodeling 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]) than in patients without IMH (17 [12–33]), including those that had MVO in the absence of IMH (17 [13–30]; p<0.0001). 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).

Conclusions: In patients with STEMI, both 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 stronger prognostic importance and greater potential clinical utility for risk assessment post-STEMI.
ventricular dysfunction in early or preclinical stages. Hs-cTnT at three months after starting a potentially cardiotoxic drug 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, c-TnI, NT-proBNP and Galectin-3 were measured.

**Methods:** GECAHE study (Grupo de Estudio de Cardiotoxicidad por Medicamento) is an uncenteric 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.

**Conclusion:** ALVSD was prevalent in LS after auto-HCT. However, exercise capacity was preserved and comparable to LS without ALVSD.

**Acknowledgement/Funding:** Extrastiftelsen

**4049 | BEDSIDE**

High-sensitivity T troponin 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 Medicamento) is an uncenteric 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, c-TnI, 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 c-TnI (27 ng/L CV: 7%) assays for Gal-3 (27.5 mg/L) and NT-proBNP (125 LCV: 75,75 years).

**Results:** 222 consecutive patients were included. The mean age was 58,8±14,3 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 55,5±14,3 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 55,5±14,3 years.

**Conclusion:** ALVSD was prevalent in LS after auto-HCT. However, exercise capacity was preserved and comparable to LS without ALVSD.

**Acknowledgement/Funding:** Extrastiftelsen

**4051 | BEDSIDE**

Computed tomography coronary angiography versus stress cardiac magnetic resonance for the management of symptomatic revascularized patients: a cost-effectiveness study

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**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 tests has taken in 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 a functional strategy (stress-CMR) in revascularized symptomatic patients for chest pain.

**Method and materials:** Four hundred revascularized symptomatic patients for chest pain were addressed to CTCA (n=200, mean age 68±10 years, mean 168) or stress-CMR (n=200, mean age 66±9 years, 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.
Methods: We enrolled 69 (controls: 33, intervention: 36) overweight and obese patients (57 vs. 62% female) in a 12-month randomized parallel trial 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.

Results: (Table) Structural changes between groups were independent of body surface area. No significant changes were observed in ventricular volumes between the groups.

Conclusions: 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 epicardial and pericardial fat deposition - a cardiac MRI study

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Introduction: Epicardial and pericardial fat is a common finding in cardiac imaging. Cardiac fat seems to have unfavorable local effects, which might result in an adverse patient outcome. Previous data have shown that cardiac fat is associated with metabolic syndrome and obesity. Steroids are known to induce some of the effects of the metabolic syndrome. Consequently, the aim of our study was to evaluate the impact of long-term steroid therapy on epicardial and pericardial fat distribution.

Methods: Sixty-one consecutive patients with different rheumatic disorders and long-term steroid medication (participants of the Rheum-MAR study) underwent CMR for evaluation of cardiac fat deposition. Medical history was reviewed carefully regarding dosage and duration of steroid therapy. CMR scans included cine images (to determine cardiac function and morphology) in short and long axes. Areas of epicardial and pericardial fat were measured in the patients’ 4-chamber view and compared to an age, sex and Body-Mass-index (BMI)-matched control group without steroid medication. Patients with steroid intake were divided into two groups: A high-dose steroid group (>7.5 mg of prednisone per day for at least 6 months) and a low-dose steroid group (≤7.5 mg prednisone per day for at least 6 months).

Results: Patients on steroid therapy showed increased epicardial fat (mean 6.4±4.3 cm2/20.2±22.0 cm2) compared to controls (mean 4.5±4.4 cm2/11.7±12.7 cm2, p=0.07, p<0.01, respectively). Patients on high-dose steroid therapy had significantly more epicardial fat compared to patients on low-dose steroid therapy (p=0.001 each) and to matched controls (p=0.01 and p=0.05). Although showing higher amounts of cardiac fat, epicardial and pericardial fat of patients in the low-dose steroid group did not differ significantly to the control group. Epicardial and pericardial fat correlated with BMI in patients who received long-term steroid therapy. Interestingly, no correlation of BMI and epicardial and pericardial fat deposition could be detected in the control group.

Conclusion: Long-term steroid therapy above 7.5mg per day is associated with an increase in epicardial and pericardial fat. In comparison to matched controls, patients on steroid therapy showed a correlation of cardiac fat and BMI. Beside steroid use, increased cardiac fat might be an additional or reinforcing factor for adverse cardiac outcome in this high-risk population.

4055 | BEDSIDE
Myocardial haemorrhage after acute reperfused STElevation myocardial infarction: temporal evolution, relation to microvascular obstruction and prognostic significance

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Background: The success of emergency coronary reperfusion therapy in ST-elevation myocardial infarction (STEMI) is commonly limited by failed tissue perfusion.

Purpose: To perform a longitudinal clinical study of myocardial haemorrhage in a large cohort of reperfused STEMI survivors and assess the temporal relationship between intramyocardial haemorrhage (IMH) versus microvascular obstruction (MVO) early after reperfusion in a serial cardiac magnetic resonance (CMR) sub-study.

Methods: We performed a prospective single centre cohort study in reperfused 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, 6 days and 6–7 months post reperfusion. Adverse remodeling was defined as an increase in left ventricular end-diastolic volume (LVEDV) >20% at 6 months.

Results: 245 STEMI patients had evaluable T2* data and 101 (41%) patients had IMH. In multivariable regression, IMH was independently associated with initial TIMI TIMI coronary flow grade, ECG evidence of reperfusion injury and Killip class (all p<0.03). 62% of patients who had MVO. IMH was multivariably associated with adverse remodeling, independent of baseline LVEDV odds ratio (95% CI): 2.64 (1.07, 6.49); p=0.035. IMH was also multivariably associated with cardiovascular (CV) death or heart failure hospitalisation post-discharge (hazard ratio (95% CI): 12.9 (1.6, 100.8); p=0.015). In the serial imaging subgroup, IMH occurred in 7 (23%), 13 (43%), 11 (33%), and 4 (13%) patients at 4–12 hours, 3 days, 10 days and 6 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 (25%) 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 21 post-MI. IMH is a biomarker with potential to reflect the efficacy of therapeutic interventions in STEMI patients.

4056 | BEDSIDE
Comparison of transthoracic echocardiography versus cardiac magnetic imaging for the detection of implantable cardioverter defibrillator therapy in primary prevention strategy dilated cardiomyopathy patients

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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 fraction (LVEF) <35%. This ICD threshold is largely based on studies using trans-thoracic echocardiography (TTE). Cardiac magnetic resonance (CMR) 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, mean 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 tachyarrhythmia, 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 m²/m²) and LVEDV (57±21 vs. 93±40 m²/m²) and a higher LVEF (35±10 vs. 31±9%) as compared to CMR (p<0.0001). MACE occurred in 68 patients (25%). Patients experienced MACE showed a higher LVEDV-TTE (94±28 vs. 84±22 m²/m², p=0.01), LVEF-TTE (64±27 vs. 55±23 m²/m², p=0.003), LVEDV-CMR (141±43 vs. 128±41 m²/m², p=0.01), and LVEF-CMR (105±42 vs. 90±39 m²/m², p=0.003), lower LVEF-VTTE (64±27 vs. 55±23 m²/m², p=0.003).
A total of 55 ICM and 62 DCM patients were included with a mean fol-
nov ICD-therapy. A semi-automatic quantitative algorithm was used to evaluate
benefit from ICD, as no arrhythmia occurs. The heterogeneous late gadolinium
Background:
Institutions, Division of Cardiology, Department of Medicine, Baltimore, United
Purpose:
prove cardiac function.
cardiosphere-derived cell (CDC) therapy may reduce substantial fibrosis to im-
liations may present myocardial fibrosis by cardiac magnetic resonance imag-
Background:
Cardiac progenitor cell therapy reduces myocardial fibrosis and
stiffness to improve cardiac function in patients with univentricular heart
disease
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Background: With single ventricular physiology undergoing staged pal-
prognostic value of peri-infarct tissue heterogeneity in reperfused
CMR for clinical diagnosis and prognostication

4057 | BEDSIDE
Cardiac magnetic resonance can predict appropriate primary prevention
patients undergoing late gadolinium enhancement heterogeneity
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Background: Patients at risk for malignant ventricular arrhythmias receive pri-
mary prophylactic implantable cardioverter defibrillators (ICD), but not all patients
benefit from ICD, as no arrhythmia occurs. The heterogeneous late gadolinium
enhancement (LGE) borderzone measured by cardiac MRI (CMR) has been pro-
posed as an independent predictor of ventricular arrhythmias.
Purpose: The purpose was to determine if the extent and heterogeneity of LGE
areas predicts appropriate ICD-therapy in ischemic and dilated cardiomyopathy
patients, and if a newly developed borderzone algorithm has similar predictive
value with respect to heterogeneous fibrosis.
Methods: Ischemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM)
patients who underwent LGE-CMR prior to primary prevention ICD implantation
were retrospectively included and divided into two groups (i) patients with appro-
priate ICD-therapy (anti-tachycardia pacing, shock or both) and (ii) patients with
no ICD-therapy. A semi-automatic quantitative algorithm was used to evaluate the
LGE borderzone and compared against a modified full-width half-maximum
(FWHM) and a threshold-based algorithm.
Results: A total of 55 ICM and 62 DCM patients were included with a mean fol-
low up time of 46±12 months. Kaplan-Meier analysis showed that patients with larger (≥ median) compared to smaller borderzone extents had higher rates of
ICD-therapy in ICM and DCM patients pooled together using the novel algorithm
(n=10 vs. n=3 with therapy, P=0.02) and the modified FWHM algorithm (n=10
vs. n=3 patients with therapy, P=0.02) and in LGE positive ICM patients alone
(n=5 vs. n=1, P=0.03 and n=6 vs. n=0, P=0.01 for respective algorithm) at similar
follow-up times (P ns). Total LGE burden was similar between groups with and
without ICD-therapy in both ICM (P=0.5) and DCM patients (P=0.3). The mean
borderzone was larger in the group with appropriate ICD-therapy compared to the
group without ICD-therapy in patients using the novel algorithm (38±12%
vs. 30±7%, P=0.004) and the modified FWHM algorithm (46±14% vs. 35±11%,
P=0.03), but the threshold algorithm did not separate the groups (115±5%
vs. 14±5%, P=ns). Borderzone presence was seen in 82% in DCM patients.
Conclusion: A large LGE borderzone predicted appropriate ICD-therapy in a
pooled cohort of ICM and DCM patients and in the subgroup of ICM patients. Borderzone quantification using both a novel and a modified FWHM algorithm were predictive. Thus, borderzone size may be a marker for risk stratifying pa-
tients eligible for primary prevention ICD-therapy.

4058 | BEDSIDE
Cardiac progenitor cell therapy reduces myocardial fibrosis and
stiffness to improve cardiac function in patients with univentricular heart
disease
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Background: Patients with single ventricular physiology undergoing staged pal-
lations may present myocardial fibrosis by cardiac magnetic resonance imag-
ing (CMR), a technique with late gadolinium enhancement (LGE). Recent studies suggest that
cardiosphere-derived cell (CDC) therapy may reduce substantial fibrosis to im-
prove cardiac function.
Purpose: The aim of this study is to investigate whether intracoronary CDC infu-
sion is related to the focal fibrotic area to functional myocardium by reduction of
ventricular strain and myocardial stiffness.
Methods: Thirty-eight patients (age: 2.8±1.2 years) were evaluated by CMRI dur-
ing enrollment and randomized to treat by staged shunt procedure with or without
intracoronary CDC infusion. After 1 month of follow-up, the predictive value of
CMRI had LGE during initial screening by CMRI (LGE+) and remaining 30 patients were
classified as LGE- group. Area of focal fibrosis was quantitated by two standard
deviation method. Speckle-tracking echocardiography and feature-tracking cMRI
were performed to evaluate ventricular strain and strain rate before enrollment
and during the 4 months of follow-up.
Results: Baseline examination revealed that patients with LGE showed reduced
ejection fraction (P<0.01), increased cardiac volume (P<0.03), and reduced cir-
 cumferential strain (base: P<0.02, mid: P<0.02, apex: P<0.0005) compared with
(CMR) with arrhythmic events and prognosis in patients with ischemic cardiomi-
opathy. However, it is unknown if this association can be transferred to patients
with acute ST-segment elevation myocardial infarction (STEMI) treated by pri-
mary percutaneous coronary intervention (PCI). Therefore, aim of this study was to
investigate the occurrence of future major cardiac ischaemic events. These impair-
ments may be related to remodeling in the myocardial extracellular matrix.
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 collaterals specificity.
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-
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
cardiomyocardial segments within the perfusion territory of a CTO. The function
of collateral vessels was assessed using the Rentrop classification as the reference
standard.
Results: The mean ECV of remote myocardium was significantly higher in CTO than
in normal subjects (26.6±5.6% vs. 23.3±2.0%, P<0.05). Other factors associ-
ated with 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 well-developed collaterals (r=0.61, P<0.001). Global EF significantly cor-
related 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 discriminator of collagenal formation with overall diagnostic accuracy
of 74.4%.
Conclusions: In patients with CTO, diffuse myocardial fibrosis and collagenal function
can be non-invasively assessed by ECV measurements. ECV measured by
cardiac MR may serve as a useful alternative for risk stratification and mon-
toring target treatment.

4060 | BENCH
Prognostic value of peri-infarct tissue heterogeneity in reperfused
STEMI
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Purpose: Single-center studies suggest an association of infarct tissue het-
erogeneity assessed by late gadolinium enhanced magnetic cardiac resonance
(CMR) with arrhythmic events and prognosis in patients with ischemic cardiomi-
opathy. Although latent heart failure could be predicted in these patients after palliations, adjunctive CDC therapy may have a potential to reduce cardiac dysfunction by direct conversion of the extent and
severity of myocardial fibrosis.

CMR (29±10 vs. 32±9%, p=0.0002) and a higher LGE prevalence (67 vs. 44%, p=
0.0009) as compared to patients without MACE. At multivariate analysis, LVEF-
CMR [HR: 2.3 (1.6−3.01)] and presence of LGE [HR: 4.08 (2.15−6.02)] were inde-
pendently associated with MACE (p<0.001). In the subset of patients with LVEF-
TTE<35%, the addition of LVEF-CMR and LGE provides a net reclassification
improvement (NRI) of 42% and 26%, respectively, in terms of outcomes.

Conclusions: LVEF and LGE estimation by CMR might provide additional prog-
nostic stratification as compared to TTE that could define a subset of subjects in
whom ICD implantation is still indicated despite LVEF-TTE<35%.
infarction using a standardized protocol. Analysis of tissue heterogeneity of peri-
infarct zones was performed using commercially available CMR post-processing
software (CMR42, Circle Inc, 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% IV (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 non-clinical 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 stratifi-
cation of the postinfarction patient. Further studies are warranted to determine potential early ICD indications.

Atrial Fibrillation in Real World

P4061 | BEDSIDE
Female sex, age, and time delay to cardioversion as risk factors in the cardioversion of acute atrial fibrillation. The FinCV Study

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Background: Female gender is a risk factor for thromboembolic complications (TEC) in atrial fibrillation (AF). It is also associated with an increased risk for complications such as bradycardia and TEC after cardioversion of acute AF.

Purpose: The aim of this study was to compare clinical presentation, comorbid-
ties and complications during a 30 day follow-up in women and men with electrical cardioversion of acute AF (<48 hours) performed without anticoagulation.

Methods: A total of 4715 scheduled electrical cardioversions without peripro-
dural or postprocedural anticoagulation were performed in 2313 patients with AF,
lasting <48 hours. The outcomes were failure of cardioversion, bradyarrhythmic complications, AF recurrence and TEC after cardioversion (30-day follow-up) and their combination – the net harm - was calculated. Finally, the interaction of age, sex and delay to cardioversion on the risk of TEC was assessed.

Results: Women with acute AF were older, had more comorbidities and higher heart rate (117±23 bpm for women vs. 107 ± 27 bpm for men, p < 0.001). The failure of electrical cardioversion was higher (6.7% vs. 4.0%, p < 0.001) and bradyarrhythmic complications were more common in women (1.9% vs. 0.4%, p < 0.001). AF recurrence occurred more often (30-peri-follow-up) (13.7% vs. 11.7%, p < 0.05). Female sex was also associated with an increased risk of TEC (OR 2.12, CI 1.09-4.11, p=0.03). The net harm was higher in women than in men (21.9% vs. 16.0%, p < 0.001). Older age (p=0.001), time delay from the onset of AF to cardioversion, and vascular disease (p=0.03) were the other significant predictors of TEC. The risk of TEC increased from 0.3% (p=1.0) in men <65 years and cardiovascular delay <12 hours to 2.7% (p=0.004) in women >75 years and delay >12 hours.

Conclusion: Older women 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.

P4062 | BENCH
Atrial fibrillation and hypertrophic cardiomyopathy: a propensity score analysis from a multicenter Portuguese study

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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 symptoms 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=0.68). Duration of the 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-
tory of disorganized cardiac output was similar but AF patients 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 asso-
ciated with mortality in HCM patients.

P4063 | BENCH
Atrial fibrillation in patients admitted to coronary care units in western Sweden. Focus on obesity and lipotoxicity

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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 a lipotoxic phenotype in atrial muscle, and that AF was predicts mor-
tality 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 Heart Care Admissions (RIKS-HIA) from hospitals in western Sweden. All consecutive patients between 2006–2011 ad-
mittied 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-
itative and quantitative analysis of lipid species including triacylglycerides (TAG), ce-
ramides (CER), phosphatidylcholine (PC), lysophosphatidylcholine (LPC), phos-
phatidyl ethanolamine (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) were independent predictors of AF and the odds ratio for AF increased for every one unit increase in BMI. In patients with diabetes (OR 2.12, 95% CI 1.92–2.35, P <0.001) the risk of AF was 2.12 times higher. The presence of AF was independently predicted by an old age and large left atrium (>40 mm). AF was associated with increased one-year mortality in this CCU population.

Conclusions: In addition to age and AH, obesity and diabetes were associated with increased one-year mortality in this CCU population. AF was associated with increased one-year mortality in this CCU population and AF was associated with increased mortality in this CCU population.
Methods: LLC, Titusville, United States of America

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 100 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 77.8 (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 common in the MB group, including any heart failure on discharge (24.1% versus 8.67%), coronary heart disease (60.8% versus 31.4%), and heart failure (47.0% versus 19.7%), respectively. Mean (SD) CHADS2-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.

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, 10 (20%, P=0.80) with apixaban, and 13 (18.8%, P=0.81) with warfarin. The rivaroxaban plasma concentration determined by LC-MS/MS correlated with aPTT or prothrombin time (r²=0.94) and peak (r²=0.91) samples. Between LC-MS/MS and the anti-FXa-assay was found (p<0.01, n=30). There were no significant correlations between gender, creatinine value to measure rivaroxaban in certain situations. Interestingly the POC assay for rivaroxaban plasma concentration determined by LC-MS/MS showed a pronounced variation in both trough (median 33.3; 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-FXa-assay was found (p<0.001) for both trough (r²=0.94) and peak (r²=0.91) 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.

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


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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±8 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 33.3; 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-FXa-assay was found (p<0.001) for both trough (r²=0.94) and peak (r²=0.91) 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.

Conclusion: In a cohort of ‘real-life’ AF-patients treated with rivaroxaban, we observed a pronounced variability in plasma concentrations both at trough and peak measured by LC-MS/MS. The anti-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...
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 via electronic 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 selective 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 CCL activation than prehospital CCL activation alone.

**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 21 “Code STEMI” 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 transferred ECG were false positive. A false activation was defined as any positive ECG or biomarker evidence of STEMI in the presence of a normal angiography or lack of ECG or biomarker evidence of STEMI. ECG findings in false activations were compared between the two groups.

**Conclusions:** Prehospital STEMI diagnosis by ECG transmission was associated with significantly lower rates of false positive ECG activation compared with paramedic ECG interpretation. False activations in patients with normal ECGs occurred significantly more in the prehospital activated group. **P4069 | BEDSIDE**

**Prehospital 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” Transfer (W-ECG) network. This enables swift Pre-hospital identification of STEMI and transfer of patients directly to the PPCI facility in Heart (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 patient arrives, and avoids delays in Emergency rooms.

**Methods:** Patients who had Primary PCI for STEMI, 605 (55%) were transferred directly to the Heart (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 to Balloon Time (DBT) goal of 90 min for those transferred to PPCI facility (HH), versus 120 min for those going to OH, per guidelines.

**Results:** Age was similar 49 vs 50 years and there was no Ethnic difference (73% Asians and 25% Arabs) in both groups. The DBT was 56±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 (279±375 min) than similar group going to OH (426 min), thus saving 89 vital minutes in the whole process from symptoms to balloon. 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 (2.4%) 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=0.005.

**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 1208 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 Patientsen 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**: None

**P4071 | BEDSIDE**

Feasibility of pre-hospital chest pain triage in the ambulance by paramedics using a the heart score based upon a single high-sensitive troponin T analysis. Results from phase 1 of the FAMOUS triage

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**Purpose:** Triage of patients with chest pain after an Emergency Medical System (EMS) call normally occurs in the hospital emergency room (ER) for which the HEART-score offers a simple and quick risk-stratifying tool. Additionally, the “high-sensitive” cardiac Troponin T (hs-cTnT) provides a great diagnostic accuracy in the detection of Acute Myocardial Infarction (AMI). This study investigates whether pre-hospital chest pain triage is feasible in ruling out an AMI in the ambulance by paramedics using a single hs-cTnT measurement.

**Methods:** Patients with acute onset chest pain (excluding STEMI) who called the Medical Contact (FMC) by ambulance paramedics including hs-cTnT assessment. Using “T” as the hs-cTnT value, the modified-HEART score was established for triage of patients with chest pain. Patients with acute chest pain (excluding STEMI) who called the EMS, from June 2012 till December 2014 were prospectively evaluated at First Medical Contact (FMC) by ambulance paramedics including hs-cTnT assessment. All patients were transported to ER and managed by emergency physicians according to the standard care blinded to the hs-cTnT result taken by the ambulance crew. Using “T” as the hs-cTnT value, the modified-HEART score was established using medical records. Follow-up was performed at 30 days in terms of MACE. Discharge diagnoses were evaluated in case AMI was ruled out. Clinical Trial Number 42055 (NL Trial Register).

**Results:** From a total of 1426 patients screened, 1127 (79%) patients were included. The hs-cTnT values were negative (-0.014 ng/mL) in 814 patients (72%) and the modified-HEART score was 3 or less in 402 patients (35.7%) as shown in the table. The discharge diagnoses of patients with a score of 3 or less were among, non-cardiac chest pain in 389 patients (97%), a suspicion of supraventricular arrhythmia in 8 patients (2%) and a pulmonary embolism in 1 patient (0%)

**Conclusion:** Using the modified-HEART score, a large number of patients (35.7%) with symptoms suspicious of AMI presenting to EMS could be identified as being low risk already in the ambulance. This score provides an excellent tool
in identifying low risk patients prior to presentation and might help in optimizing logistics and cost-effectiveness, as addressed in the next phases of the trial.

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 bystander 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 home locations. Bystander defibrillation was associated with markedly improved survival irrespective of location of arrest. These results underscore the need for improving bystander defibrillation in residential areas.

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 enrollment 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.

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 (n=1208/610), 413 (22.7%) had an acute MI; Patients with MI had significantly higher GDF-15 compared with non-ACS patients (967.1 pg/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.
compared to a 1.94-fold (1.45–2.60, p < 0.001) and a 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 parameters allows to predict cardiac events in patients
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**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 335 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. Everyday transmissions were 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 IAT was max. heart rate during atrial fibrillation (HR 1.03, 95% CI 1.01–1.04, p=0.004).

**Conclusions:** 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.

**P4077 | BEDSIDE**
The Utilization and Clinical Feasibility of 24-Hour Hand-Carry Remote ECG Recording Device in Cardiac Arrhythmias and Atrial Fibrillation: A Pilot Study

**Background:** Remote cardiac rhythm monitor and diagnosis has been well incorporated in Telehealth service model. The prevalence and incidence of abnormal ventricular beats by utilizing symptom-driven portable remote ECG device remains less well explored.

**Methods:** We consecutively studied 339 study participants, including 192 enrolled via symptom-driven protocol from out-patient clinics; 147 participated heart rhythm screening program. All participants are open for 24-hours data transfer using hand-carry portable ECG device (DailyCare Biomedical Inc) with automatic ECG wavelet data extraction (InstantCheck ver 4.0).

**Results:** Among a total of 1,152 data transferred (98.4% successful rate), we noticed 32.5% study subjects had evidence of cardiac arrhythmias, with AF (either permanent or paroxysmal) 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: 1.55 to 5.90), and cardiovascular disease (OR: 3.71, 95% CI: 1.69 to 5.49), cardiovascular disease (OR: 3.71, 95% CI: 2.05 to 6.7) had higher AF risk. Both populations showed age-related increase of atrial fibrillation (AF), even in multi-variate models (OR: 1.72, 95% CI: 1.31 to 2.24 per decade, Table 1).

**Conclusions:** In patients with symptoms suggestive of AMI, the QRS-T angle automatically derived from the 12-lead ECG was elevated in patients with AMI. The area under the ROC curve for the diagnosis of AMI was 0.68. Overall, 3-year survival rate was 91%. A greater QRS-T angle was significantly associated with a worse prognosis after 3 years (Survival rates 95%, 88%, 76% for patients with a QRS-T angle <50°, 50–100° and >100°; p<0.001).

**Model 1**
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<tr>
<td>Age, + per decade</td>
<td>1.72</td>
<td>1.36 to 2.17</td>
<td>1.42</td>
<td>1.09 to 1.86</td>
<td>2.59</td>
<td>1.54 to 4.35</td>
</tr>
</tbody>
</table>

**Model 2**

**Model 3**

**Conclusion:** Hand-carry ECG device shows clinical feasibility with high rate for AF detection, with a similar trend toward higher prevalence with aging from different settings. These data suggested that portable ECG device via remote care system may aid in clinical diagnosis of AF, and may facilitate therapeutic interventions or patient referral.

**P4078 | BEDSIDE**
Diagnostic accuracy of 12 lead ECG Q-waves as a marker of myocardial scar and as a predictor of infarcted artery: validation with CMR
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**Background:** Traditionally, the presence of Q-waves on 12 lead ECG is considered a marker of a large 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 all clinicians often have to make assumptions on myocardial scarred bases 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.

**Table 1. Uni- and Multivariate models for age in predicting all AF identification by hand-carry ECG device**

<table>
<thead>
<tr>
<th>Age, + per decade</th>
<th>AF all (all participants)</th>
<th>AF all (symptom-driven)</th>
<th>AF all (screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio</td>
<td>95% CI</td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Univariate model</td>
<td>1.72</td>
<td>1.36 to 2.17</td>
<td>1.42</td>
</tr>
<tr>
<td>Multivariate model</td>
<td>Model 1</td>
<td>1.73</td>
<td>1.37 to 2.19</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.61</td>
<td>1.25 to 2.06</td>
<td>1.39</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.39</td>
<td>1.31 to 2.24</td>
<td>1.39</td>
</tr>
</tbody>
</table>

**Table 2. Univariate models for age in predicting all AF identification by hand-carry ECG device**

**Table 3. Multivariate models for age in predicting all AF identification by hand-carry ECG device**
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 ms in width and > 2 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 Q waves, 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 LGE 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.

Table 1

<table>
<thead>
<tr>
<th>Q-waves vs Transmural MI</th>
<th>Q-waves vs any MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Q-waves</td>
<td>36.3</td>
</tr>
<tr>
<td>Q-waves</td>
<td>32.8</td>
</tr>
</tbody>
</table>

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 during the 2nd after MI. The primary endpoint was all-cause mortality. DC was calculated using previously established technologies. In addition to DC following 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 ms for DC, <35% for LVEF, >-0.47 for GRACE, ≤70m/s for mean HR, ≤0.47 for SDNN, and >25 ms for QTVI. For each risk factor and corresponding cut-off values, 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 was significantly lower in non-survivors compared with survivors (3.06 vs. 5.29, p<0.001). DC <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).

Conclusions: 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 33nGy/pulse.

Material and methods: The new program (8nGy/pulse) was installed on an AX-IO M Artis biplane system in August 2014. 214 patients (Group A) treated with the new program from 08/2014 to 11/2014 were compared to 195 patients (Group B) treated with the 23 nGy/pulse program 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 usual EBT. Furthermore we divided EBT and fluoroscopy time and fluoroscopy time between lead five procedures (Atrial fibrillation (Afib), Atrial flutter (Aflutter), 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 cm² (in Group B) vs 3.66 Gy cm² (in Group A), p<0.001, student-t). The two groups BMI (27.6±5.4 (B) vs 27.9±4.7 (A), p<0.05, age (56.0±18.4 (B) vs 57.1±17.3 (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 (365±35 min (B) vs 70±17 min (A); p=0.91) and AVNRT (15±4 min (B) vs 12±2 min (A); p=0.28) was remarketed. A significant difference in age (56±18 (B) vs 63±9 (A); p=0.02) and AVRT and AVNRT (142±24 min (B) vs 102±252 min (A); p<0.1) was not affected by the dose reduction. No difference between acute success rates (98% (210/214) A) vs 97% (199/205) B) was found. Procedure duration was significantly affected (p<0.05).

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).
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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1King’s College London, James Black Centre, London, United Kingdom; 2Hannover Medical School, Hannover, Germany; 3St George’s Hospital Medical School, London, United Kingdom; 4University of Strasbourg, Strasbourg, France

Background: Using proteomics, we characterize the glycoproteins of human hearts to study extracellular matrix (ECM) remodelling in the context of atrial fibrillation 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, fibrillin-2, latent TGFβ-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 with peptide-specific antibodies. Decorin expression and processing was different in ventricles compared to atria and altered upon DISEASE (i.e. congestive heart failure or atrial fibrillation). We identified a cleavage site at position S495-L50 of decorin that produces peptides containing a myostatin-binding domain. Myostatin is involved in the regulation of cardiomyocyte growth and metabolism.

When cardiomyocytes were treated with myostatin, synthetic peptides matching the myostatin-binding region of decorin were sufficient to re-activate a hypoxic response stimulated with isoproterenol and phenylephrine. The same peptide inhibited downstream myostatin signalling pathways in a dose-dependent manner. In decorin−/− mice, myostatin expression was decreased. Based on nucleotide analysis and expression data, a second cleavage site at the C-terminus (F330-S331) of decorin produces a C-terminal peptide was observed in atria but not in ventricles, suggesting a novel mechanism for the regional regulation of cardiac fibrosis.

Conclusion: This is the first proteomics study to characterize the ECM in human hearts. The presence of decorin cleavage products may regulate the local biomechanics in a dosedependent manner. In decorin−/− mice, myostatin expression was decreased. Based on nucleotide analysis and expression data, a second cleavage site at the C-terminus (F330-S331) of decorin produces a C-terminal peptide was observed in atria but not in ventricles, suggesting a novel mechanism for the regional regulation of cardiac fibrosis.

P4083 | BENCH

Inhibition of Myofibroblast Differentiation by FOXO3a - Implications for acute myocardial infarction and cardiac Remodeling

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Background: Transdifferentiation of cardiac fibroblasts into myofibroblasts regulated by TGFβ-SMAD3 signaling is a major mechanism of scar formation and adverse remodelling following myocardial infarction.

FOXO3a has recently been shown to inhibit cardiac hypertrophy by different stressors. We hypothesized that the transcription factor FOXO3a, a key regulator of cell differentiation, cyclic stretching or stress, might inhibit matricellular remodelling following myocardial infarction by regulating transdifferentiation of fibroblasts into myofibroblasts.

Methods: Acute myocardial infarction was induced in FOXO3a−/− and WT mice (FVB background) by permanent LAD ligation. Myofibroblast transdifferentiation was assessed by immunohistochemistry. FOXO3a−/− and WT cardiac fibroblasts were investigated in transdifferentiation assays ex vivo. FOXO3a gene transfer was performed with gain of function adenoviral vectors. IP/IF and Western blotting were used to test for a direct interaction between FOXO3a and SMAD3.

Results: FOXO3a−/− mice had significantly higher survival rates compared to WT littermates. Rates of ventricle perforation, however, were not different between both groups. Myocardial injury as determined by cardiac Troponin T and necrosis score were similar at day 3 post-MI. Myocardial expression of alpha smooth muscle actin (ASMA) and Collagen I (Col1A1) was significantly enhanced in FOXO3a−/− mice 14 days post infarction. Moreover, FOXO3a−/− mice showed larger fibrotic areas following MI. In line with these results, cardiac fibroblasts isolated from FOXO3a−/− mice showed significantly enhanced expression levels of ASMA and Col1A1 and were significantly transdifferentiated in 24 hours following stretch or TGF-β stimulation when compared to WT cells in vitro. Moreover, supernatants of FOXO3a−/− fibroblasts showed significantly higher protein expression of Col1A1 in p<0.01) while FOXO3a gene-transfer dose-dependent downregulated Col1A1. Immunofluorescence staining for ASMA protein was significantly attenuated following FOXO3a gene transfer in cardiac fibroblasts. Mechanistically, immunoprecipitation showed direct interaction of FOXO3a with SMAD3 that was enhanced following activation of the transcription factor leading to diminished SMAD3 downstream gene expression.

Conclusion: Our results identify FOXO3a as a direct inhibitor of TGF-β regulated matrix remodeling via FOXO3a-SMAD3 interaction. FOXO3a collectively regulates hypertrophy as well as fibrosis and scar formation following myocardial infarction and thus targeting the FOXO3a-SMAD3 axis might be of therapeutic interest.

P4084 | BENCH

Targeting the nuclear receptor PPARdelta as novel strategy to prevent in-stent restenosis and stent thrombosis

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Background: Drug-eluting stents (DES) reduce restenosis and late lumen loss compared to BMS. However, DES delay vascular healing and increase the risk of late stent thrombosis.

Results: A rabbit model of experimental atherosclerosis was employed to assess the effect of DES on PPARdelta expression. We found that PPARdelta ligands strongly reduce the development of neointima compared to BMS. We demonstrate that PPARdelta agonist GW7042 inhibits proliferation and migration of VSMCs through a receptor dependent mechanism as no effect was observed in PPARdelta−/− VSMCs. As VCMO proliferation and migration is associated with higher energy requirements, we examined the effect of GW7042 on both glycolytic flux (ECAR, extracellular acidification rate) as well as mitochondrial oxygen consumption (OCR, oxygen consumption rate) using extracellular flux technology. VSMCs were incubated with GW7042 and changes in glycolysis in response to both acute and chronic PDGF-BB (24 h) treatment were analyzed. PDGF addition increased ECAR, which was significantly reduced in GW7042 pretreated VSMCs. Oligomycin was used to eliminate mitochondrial ATP production, thus inducing maximal glycolytic response. GW7042 significantly attenuated oligomycin induced increase in glycolysis. Moreover, treatment with GW7042 significantly decreased the maximal respiratory capacity without PDGF-BB. ATP-linked respiration was maintained during PDGF-BB treatment and compromised by GW7042 in the absence of PDGF-BB. As GW7042 increased mitochondrial proton leak respiration, the reserve respiratory capacity was almost abolished upon GW7042 treatment without PDGF-BB to maintain ATP production. Using PPARdelta−/− and PPARdelta−/− VSMCs we demonstrate that GW7042 inhibits cytokine induced IL-6, MCP-1 and VCMARNA expression in a receptor dependent manner. Our data show that, while PPARdelta ligand coating delays neointima formation it also abolishes a transcriptional dissociation of the transcriptional repressor Bcl-6 from PPARdelta and subsequent binding within the IL-6, MCP-1 and VCMAM gene promoter, thus inhibiting corresponding gene expression. Ex vivo perfusion of stents in a closed-loop system showed the intact platelet rich plasma revealed that GW7042 coating inhibits both thrombocyte aggregation and activation. Treatment ECs with GW7042 increased both proliferation and chemotaxis as well as adhesion and spreading compared to vehicle treated cells.

Conclusion: In contrast to currently used DES, PPARdelta ligand coated stents not only inhibit inflammatory response and proliferation of VSMCs but also prevent thrombocyte activation and support vessel re-endothelialization.

P4085 | BENCH

Role of Rac1 GTPase for the mineralocorticoid receptor mediated structural remodelling in atrial fibrillation

D. Lavall, N. Jacobs, P. Schuster, M. Boehm, U. Laufs. Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany

Background: This study aimed to investigate the molecular mechanisms of pro-fibrotic remodelling. Human left atrial myocardium during atrial fibrillation is characterized by hypertrophy and increased expression of the mineralocorticoid receptor (MR).

Methods and results: Transgenic mice with cardiac specific overexpression of constitutively active V12Rac1 (RacET) develop an age-dependent phenotype. These mice showed larger fibrotic areas following MI. In line with these results, cardiac fibroblasts isolated from RacET mice showed significantly enhanced expression levels of COL1A1 (r=0.7169, p<0.05) and ASTMA (r=0.692, p<0.05) compared to BMS. However, DES delay vascular healing and increase the risk of thrombocyte activation and support vessel re-endothelialization.
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) treatment (174±47%, p<0.05), an inhibitor of glutathione synthesis increasing reactive oxygen species and Rac1 activity. NSC-23766, a selective Rac1 inhibitor, decreased 11β-HSD2 expression (2127%, 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<0.01). The translocation was prevented by the tubulin targeting compound (0.298±0.030 vs. aldosterone + atorvastatin) as well as by spironolactone (0.239±0.026, p<0.01 vs. aldosterone alone). NSC-23766 prevented the aldosterone induced CTGF up-regulation in cardiac fibroblasts (183±55% vs. 39±5%, p<0.01). CTGF increased fibronecin 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<0.01 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 fibrillogenic 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 protection from the occurrence of atherosclerotic complications, such as abdominal aortic aneurysm/disseension, in patients and experimenta-

Introduction: We used osmotic pumps to continuously infuse IL-1Ra−/− (n=18) and wild type mice (n=18) with angiotensin II (Ang II) for 2 weeks to study the role of IL-1Ra in angiotensin II-induced hypertension and organ damage. The propensity matched-scoring was based on age, sex, cardiovascular risk factors, and the development of aortic aneurysm after Ang II infusion. Furthermore, we also show that IL-1Ra deficiency in mice led to increased inflammation and the development of aortic aneurysm after Ang II infusion.

Conclusions: 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 (rs18007905) may represent an 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 aspects of 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 dilation (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 GG 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, compared to GG homozygotes, had significantly higher serum levels of IL-6 (3.09±1.4 vs 1.3±0.7), TNF-α (5.3±2.4 vs 2.5±1.8) and hsCRP (2.9±0.9 vs 1.05±0.69) (p<0.01 for all) in smokers as well as in non smokers (IL-6: 2.62±1.2 vs 1.64±0.89, TNF-α: 3.57±1.67 vs 4.43±2.31, hsCRP: 1.84±0.82 vs 1.62±0.77, p<0.01 for all). Importantly, the C allele carriers compared to GG ho-
motozygotes, enhanced the expression of fibrinogen (488±315 vs 318±55.611 p<0.001) and D-dimers (513±313.4 vs 355.1±218.4, p=0.025) in smokers, while it down-regulated the expression of fibrinogen in non-smokers (351.9±84.5 vs 479.4±126.8, p<0.001), while no effect was observed among non-smokers (4.8±2.9% vs 5.0±2.6%, p=0.64).

Conclusions: The C allele carriers of rs1800795 exerts a synergistic effect on smoking leading to a significantly increased risk for CAD. This action is mediated by inflammatory and thrombotic mechanisms as well as by the impairment of endothelial function.

AORTIC STENOSIS – FROM BASICS TO PROGNOSIS
P4087 | BENCH
Calcification of aortic valve and coronary atherosclerosis: differences in bicuspid and tricuspid valves
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Background: Calcific aortic valve stenosis and atherosclerosis share some underly-
dering pathophysiological processes. Although statins slow the progression of coronary atherosclerosis, this therapy has been shown to have no effect on the pro-
tension of calcific aortic stenosis suggesting important differences in the patho-
physiology of coronary artery disease and calcific aortic stenosis. Bicuspid aortic valves (BAV) develop calcific stenosis decades earlier than tricuspid aortic valves (TAV) and this process may occur in these patients inde-
dependent of coronary artery disease.

Purpose: In a propensity-score matched population, the calcification burden of the aortic valve and coronary artery stenosis were analyzed with multi-detector computed tomography (MDCT) and compared between patients with BAV versus patients with TAV. The presence of coronary artery disease (CAD) was also determined.

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 cal-
cal fibroinflammatory and thrombotic processes in coronary artery disease patients
G. Hatzis, N. Papageorgiou, G. Siason, E. Okonomou, S. Papaianou, A. Miliou, A. Kalampogias, A. Antonopoulous, B. Schieffer, D. Tousoulis. University of Athens Medical School, 1st Cardiology Department, ”Hippokration” Hospital, Athens, Greece
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 (rs18007905) may represent an 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 aspects of 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 dilation (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 GG 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, compared to GG homozygotes, had significantly higher serum levels of IL-6 (3.09±1.4 vs 1.3±0.7), TNF-α (5.3±2.4 vs 2.5±1.8) and hsCRP (2.9±0.9 vs 1.05±0.69) (p<0.01 for all) in smokers as well as in non smokers (IL-6: 2.62±1.2 vs 1.64±0.89, TNF-α: 3.57±1.67 vs 4.43±2.31, hsCRP: 1.84±0.82 vs 1.62±0.77, p<0.01 for all). Importantly, the C allele carriers compared to GG ho-
motozygotes, enhanced the expression of fibrinogen (488±315 vs 318±55.611 p<0.001) and D-dimers (513±313.4 vs 355.1±218.4, p=0.025) in smokers, while it down-regulated the expression of fibrinogen in non-smokers (351.9±84.5 vs 479.4±126.8, p<0.001), while no effect was observed among non-smokers (4.8±2.9% vs 5.0±2.6%, p=0.64).

Conclusions: The C allele carriers of rs1800795 exerts a synergistic effect on smoking leading to a significantly increased risk for CAD. This action is mediated by inflammatory and thrombotic mechanisms as well as by the impairment of endothelial function.
Aortic stenosis – from basics to prognosis

p=0.673) and the presence of significant CAS (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.

**Methods:** 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 CAS 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 (6.4)</td>
<td>68.6 (6.4)</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 (4.9)</td>
<td>28.9 (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 (6.2)</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**

Combining tumor marker carbohydrate antigen 125 and the logistic EuroSCORE improves risk stratification in patients undergoing transcatheter aortic valve implantation

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**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. We investigated the additional value of CA125 to that of the EuroSCORE alone.

**Purpose:** We investigated the additional value of CA125 to that of the EuroSCORE for predicting long-term outcome after TAVI.

**Methods:** CA125 was determined in 422 patients undergoing TAVI for severe aortic stenosis. Elevated levels of CA125 were regarded according to the manufacturer recommendations and as previously published (>30 U/ml) while elevated EuroScore was regarded as > median. 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), GLSrE (r=-0.7; p=0.005), SLS (r=0.6; p=0.01), SL-Sr (r=-0.5; p=0.03), SL-Er (r=0.5; p=0.04) and PAAPs (r=0.66; p=0.004). Plasma miRNA-21 was associated to MF (r=0.5; p=0.02) and septal 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.
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 bpline 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).

Time-varying Cox analyses

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard ratio [95% CI], p for new-onset low MWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major CV events</td>
<td>1.45 [1.15–1.83], p&lt;0.002</td>
</tr>
<tr>
<td>Aortic valve events</td>
<td>1.49 [1.17–1.90], p&lt;0.001</td>
</tr>
<tr>
<td>Heart failure or CV death</td>
<td>2.07 [1.67–2.67], p=0.013</td>
</tr>
</tbody>
</table>

Adjustment for age, gender, study treatment, hypertension, and time-varying EF, severity of AS by energy loss index, and abnormal LV geometry.

Conclusions: In asymptomatic patients with AS and normal EF at baseline, new-onset low MWS was associated with increased CV morbidity and mortality during 4-year follow-up.

P4093 | BEDSIDE

Prognostic value of new-onset low LV midwall shortening in patients with asymptomatic aortic stenosis

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Background: Left atrial (LA) strain analysis by 2D speckle tracking echocardiography (STE) represents an easy and reproducible way to estimate LA function. The aims of the present study are to assess the LA reservoir function in patients with severe aortic stenosis (AS) and to evaluate its impact on the recurrence of major adverse cardiac events (MACEs).

Methods: 128 patients (mean age 79±9 years) with severe AS underwent standard echocardiography to evaluate the left ventricular (LV) and right ventricular function. LA size, aortic valve morphology and gradients. Global peak LA strain (PLAS) is measured by 2D STE during LV systole and represents the LA reservoir function. Overall death, hospitalization for cardiac cause, and worsening heart failure were defined as major adverse cardiac events (MACEs).

Results: The mean PLAS (18.4±7.9%) was significantly reduced in AS with respect to the mean values reported in the general population. According to the multivariate linear regression analysis, LV global longitudinal strain, mitral E/e’ ratio and systolic pulmonary arterial pressure (sPAP) were the best correlates to PLAS. During follow-up, the predefined MACEs occurred in 39 patients. According to the multivariate Cox regression analysis, a PLAS <21% was a significant predictor of MACEs (HR 2.86, p=0.04), as was CAD (HR 2.68, p=0.004) and the NYHA functional class (HR 2.08, p=0.03).

Conclusion: Low LA reservoir function is a strong independent predictor of 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 urokinase plasminogen activator receptor (suPAR) is an inflammatory marker associated with cardiovascular events. Whether suPAR is a strong independent predictor of prognosis in patients with severe aortic stenosis remains unknown.

Methods: Serum suPAR levels were measured in 1,504 patients aged 28–86 years (mean age 67.7), 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).

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 mild-moderate AS, suPAR is a strong independent predictor for adverse cardiovascular events and mortality.
DIFFERENTIATING PHYSIOLOGICAL ADAPTATION FROM CARDIAC PATHOLOGY IN ATHLETES

P4096 | BEDSIDE
Athletic cardiac adaptation is secondary to increased myocyte mass
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Background: Cardiac remodelling occurs in response to regular athletic training, and the degree of remodelling is associated with fitness. Understanding the myoc-ardial structural 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±2, 85±6 ml/kg/min. LVEDVI (p<0.01 by definition). Indexed LV end diastolic volume (LVEDVI) and mass (LVM) correlated with VO2max (r=0.455, p=0.01; r=0.34, P=0.05). CMR derived measures of tissue composition (T1, ECV) differ- ently significantly by VO2max tertile. VO2max, r=0.34, P=0.05 respectively, and were signific-antly 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±1±4; 30±1±5; 29±2±4 g/m2) in AH was similar between tertiles though intra-cellular mass increased with VO2max tertile (83±17±6; 101±3±2; 110±7±18 ±0.01).

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 estab-lished risk factors for atrial fibrillation (AF). The impact of exaggerated blood pres-sure response on cardiac remodelling 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: Amateur athletes who participated in the Grand Prix of Bern, a pop-u lar 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 fe-males) 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/min/kg, respectively, p=0.698). Mean sys-tolic 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±12/96±12 vs. 170±13 mmHg/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±1.6 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 sig-nificant 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
Differentialization of arrhythmogenic right ventricular cardiomyopathy and athlete’s heart using cardiac magnetic resonance imaging
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The physiological mechanisms behind exercise-induced myocardial hypertrophy are not clearly characterized and subject to intense research. Matrix metallopro-teases (MMP) and their tissue inhibitors (TIMP) are promising biomarkers of nu-merous cardiac diseases including pathological left ventricular hypertrophies. Our aim was to assess the correlations between the physiological hypertrophy of athlete’s heart and the serum levels of MMPs and TIMPs.

Our study included elite athletes competing in waterpolo, kayaking, canoeing or rowing (EA; n=75, age: 26±8 years, 77% male) compared to age- and gender-matched healthy sedentary volunteers (CTL; n=33). The left (LV) and right ventric-ular (RV) end-diastolic volume (EDVI) and mass (MI) indexed to body surface area were measured by cardiac magnetic resonance imaging (CMR, 1.5T, QMSS 7.1 software). Serum concentrations of the enzymes (MMP-2, MMP-9, TIMP-1, TIMP-2) were determined by enzyme-linked immunosorbent assay (R&D Systems, Quantikine).

Not surprisingly, the LV and RV volumes and masses were markedly increased in the athletes compared to the control group (EA vs. CTL: LVEDVI: 119±14 vs. 93±13 ml/m2; RVEDVI: 124±17 vs. 95±15 ml/m2; LVMI: 84±18 vs. 59±12 g/m2; RVMI: 31±6 vs. 24±4 g/m2, all p<0.001). Despite the notable cardiac remodelling, we did not find significant differences in the serum levels of the measured enzymes between the two groups. In athletes, significant negative correlations were found between MMP-2 and LV and also RV mass indices (LVMI: r=−0.35, p=0.002; RVMI: r=−0.35, p=0.009) and end-diastolic volume indices (LVEDVI: r=−0.23, p=0.048; RVEDVI: r=−0.25, p=0.029). A similar inverse relationship was observed between TIMP-2 and LVMI and also RVEDVI (LVMI: r=−0.38, p=0.001; RVEDVI: 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.

Arrhythmogenic right ventricular hypertrophies, serum levels of MMP-2 showed an in-verse 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 clin-ical practice to distinguish between physiological and pathological hypertrophies and to recognize overlapping cardiac diseases.
Differentiating physiological adaptation from cardiac pathology in athletes / Prediction models in clinical practice

Method: 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 calculated.

Results: We detected 17,765 abnormal ECGs (6.47%). The largest abnormality subgroup identified was “pathologic Q waves” (59,947.21%) followed by the groups “ST segment depression (3,080.12%), “Left axis deviation (2,850.102%), “Left atrial enlargement” (1,709.052%), “Atrial tachyarrhythmias” (1,193.043%), “Right ventricular hypertrophy pattern” (991.036%), “Preme-}

Conclusions: The 6.47% of automatically detected abnormal ECGs correspond to abnormal male individuals per year which would warrant a more profound clinical, and/or electrophysiological and genetic investigation to confirm or exclude the presence of an acquired or familial cardiac disease.

P4102 | BEDSIDE
Exercise stress testing in 73,000 patients: safety with abnormalities of serum potassium

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Purpose: Guidelines recommend that performing exercise stress testing in the setting of abnormal serum potassium concentrations is relatively contraindicated; however, data supporting these guidelines are limited.

Methods: We reviewed a consecutive series of patients who had serum potassium within 48 hours of undergoing treadmill exercise stress testing (n=73,612) between 2003 and 2013. Hemolysed samples were not included in the analysis. Normal serum potassium range for our laboratory is 3.6–5.2 mEq/L. The association of potassium levels with the development of supraventricular and ventricular arrhythmias was assessed.

Results: The overall incidence of supraventricular and ventricular arrhythmia was low and the incidence of severe, clinically significant arrhythmias was very low, demonstrating the overall safety of exercise stress testing (table). 4,019 (5.5%) of patients had serum potassium abnormalities at the time of exercise stress testing. Most of these were within the mildly abnormal hypokalemic (3.1–3.6) or hyperkalemic (5.2–5.9) range. There was no significant association between potassium abnormalities and arrhythmia. The association of abnormal potassium levels with the frequency of supraventricular and ventricular arrhythmia is shown in the table (number, percentage).

Table 1. Incidence of arrhythmias

<table>
<thead>
<tr>
<th>Potassium, mEq/dL</th>
<th>n</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.1</td>
<td>3.1–3.6</td>
<td>3.6–5.2</td>
</tr>
<tr>
<td>97</td>
<td>196</td>
<td>6959</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
<td>0.001</td>
</tr>
<tr>
<td>910</td>
<td>109</td>
<td>161</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
<td>0.001</td>
</tr>
<tr>
<td>VT/VF</td>
<td>30 sec</td>
<td>0.01</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: The data confirms that the incidence of arrhythmia 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

P4103 | BEDSIDE
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 (PAD).

Methods and findings: We evaluated 1000 consecutive PAD patients treated at our institution from 2005 to 2007. Clinical symptoms, comorbidities, and concomitant medication were documented. We calculated odds ratios (OR) in a bivariate regression model and calculated possible risk factors for CLI. In a second step a total of 1124 PAD patients treated at our institution between 2007 and 2011 were included to verify the score. In the first patient group the strongest risk factors for CLI were age>75 years (OR
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 intermitted 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 elevated PLR group (n=60) as compared to low PLR group (n=71) (31.6% vs 20.7%, p<0.001, respectively). Univariate analysis (2.04±1.03 vs 2.00±1.08°C, p=0.69 and 2.46±1.12 vs 2.39±1.18°C, 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: The definition of PCI-MI may have important implications for trial outcomes. These results illustrate the importance of a careful assessment of PCI-related MI.

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 1) ultrasound echo-color Doppler (US-ECD) study and 2) 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 ΔTs 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, 305 (85%) were men and 54 (15%) were women. Women had similar ΔTmax compared to men in both vessel- and patient-based analysis (2.04±1.03 vs 2.00±1.08°C, p=0.69 and 2.46±1.12 vs 2.39±1.18°C, 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.
P4107 | BEDSIDE
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%; P<0.001), peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (0.025 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.

Acknowledgement/Funding: Canadian Institutes of Health Research

P4108 | BEDSIDE
Ankle brachial index predicts two year mortality in sub-Saharan older adults
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Purpose: To examine the rate of change in radial artery diameter (dD/dt) after 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.

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), peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (0.025 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.

Acknowledgement/Funding: Canadian Institutes of Health Research

P4109 | BEDSIDE
Protein energy wasting is associated with poor outcome after lower extremity revascularization in chronic haemodialysis patients with peripheral artery disease
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Background: Although lower extremity revascularization, regardless of surgical or percutaneous procedures, has been commonly performed in chronic haemodialysis (HD) patients with peripheral artery disease (PAD), poorer prognosis still remains major problems in such population. Recently, protein-energy wasting (PEW) or malnutrition, frequently observed in HD patients, was considered to be strongly associated with chronic inflammation and advanced atherosclerosis. We investigated whether geriatric nutritional risk index (GNI), developing as a marker of the PEW, could predict clinical outcome after lower extremity revascularization in HD patients.

Methods: We enrolled a total of 862 HD patients (age 67±10 years, diabetes 62.9%, critical limb ischemia 53.5%) who successfully underwent lower extremity revascularization (552 with endovascular therapy and 310 with bypass surgery).

The GNI was calculated from pre-procedural tests, as follows; GNI = (14.89 × albumin) + (41.7 × (body weight/body weight at BMI of 22)) were followed up for up to 10 years. Amputation-free survival (AFS), defined as freedom from major amputation or all-cause death, was primarily evaluated.

Results: During follow-up period, 63 (7.3%) patients needed major amputation and 202 (23.4%) patients died, Cox multivariate analysis identified GNI (adjusted hazard ratio (HR) 0.97, 95% confidence interval (CI) 0.96–0.99, p=0.0022), male gender (HR 1.73, 95% CI 1.25–2.39, p=0.0011), age (HR 1.02, 95% CI 1.00–1.04, p=0.018), ulcer/gangrene (HR 1.91, 95% CI 1.32–2.75, p=0.0006) as independent predictors for composite endpoint with major amputation or all-cause death. When cut-off level of the GNI was defined as median value of 92.3, Kaplan-Meier estimated AFS for 10-year was significantly lower in the low GNI group than in the high GNI group (44.9% vs. 62.6%, adjusted HR 1.74, 95% CI 1.25–2.45, p=0.0011). Similar results were obtained for freedom from major amputation (82.4% vs. 94.1%, adjusted HR 2.85, 95% CI 1.38–6.32, p=0.0044) and from all-cause death (50.4% vs. 65.9%, adjusted HR 1.69, 95% CI 1.21–2.43, p=0.0039), respectively.

Conclusion: Declined GNI which reflect PEW or malnutrition state strongly predicted worsen clinical outcome such as amputation and mortality after lower extremity revascularization in chronic HD patients. More attention should be paid to pre-procedural PEW or malnutrition condition in this high-risk population.

HEART FAILURE: DIVERSITY OF PHENOTYPING

P4110 | BEDSIDE
The relationship between hemoconcentration 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: Hemoconcentration (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 5,860 AHFS pts (3,019 males, 68±14 years of age: 73.8±6.8 years), 161 presented an ABI ≤0.90 and 26 an ABI >1.40. After two years, vital status was known for all the subjects. Death was recorded in 101 (9.8%) cases. According to final multivariate regression model, subjects with low ABI (≤0.90) at including time were associated to high mortality risk (odds Ratio [OR]: 1.86, 95% CI: 1.04–3.30; p=0.034). Similarly, age (per 5 year increase) (OR: 1.37, 95% CI: 1.13–1.65; p=0.001) and cognitive disorders (OR: 1.61, 95% CI: 1.08–2.41; p=0.002) were associated independently to an increased mortality. No or moderate alcohol consumption (OR: 0.50; 95% CI: 0.28–0.86; p=0.014) and sex (female vs male) (OR: 0.36; 95% CI: 0.22–0.76; p<0.001) were protective against mortality.

Conclusion: In a SSA older community, asymptomatic PAD detected by the ABI presents a prognostic value to predict mortality during the 2 years following the screening. ABI may represent a useful, simple, economic and non invasive tool to identify subjects with high mortality risk in SSA low-income countries.

Acknowledgement/Funding: Axa Research Fund
old, 37.4% ischemic origin, left ventricular ejection fraction 38±5±16.1%) from Koran Acute Heart Failure (KorAHF) 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 (4.8%). Mean hemoglobin lev- els at admission and discharge were 12.4±2.3 and 12.0±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), respecti- vely. The AHFS group with HC had significantly lower RFV compared to those without HC (0.33±0.36 vs. 0.39±0.58, p=0.003). 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 creatinine protein (r=0.116, p<0.001). In multivariate logistic regression analysis for in-hospital mortality in HC and RFV was independent prognostic marker after adjusting other risk fac- tors including baseline BUN, creatinine level and hemocoencentration (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.

P4112 | BEDSIDE

PCR proof of parvovirus B19 genomes in endomyocardial biopsies of patients presenting with myocarditis or dilated cardiomyopathy - Meta-Analysis confirms a possible bioprotein

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Introduction: Diverse viral infections have been associated with myocarditis (MC) and dilated cardiomyopathy (DCM). Whereas disease specificity of en- terovirus has been confirmed in this setting by meta-analysis, this relationship is not established for parvovirus B19 (B19V) genomes, yet. In this meta-analysis, we systematically reviewed the published results on the association of B19V genomes with human MC/DCM versus controls.

Methods: n=197 publications referring to B19V and MC or DCM were retrieved using multiple PubMed search modes. Out of these, n=29 publications with met the inclusion criteria with data from prospective analyses on n=10 unselected pa- tients presenting with MC or DCM (dataset: MA01). Data retrieved simultaneously both from controls and MC/DCM patients were available from n=4 from these publications (dataset: MA02).

Results: The demographic data of the n=3,595 patients of the dataset MA01 were as follows: mean age: 47±1.3 years; males: n=1,920 (53.3%). Mean LVEF by echocardiography was 38±12.8%, and the mean LVEDD was 55.5±16.7 mm. B19V genomes were detected in 42.6±17.9% of the EMB in this cohort by PCR. The dataset MA02 comprised n=634 subjects (mean age: 46.7±6.7 years; men: n=291/45.9%). The MC/DCM patients (n=500) had not significantly different demographic data compared to controls (n=134). LVEF was significantly higher in controls (mean: 62.8±8.8%) versus MC/DCM patients: 35.4±9.5%; p=0.0056.

However, the rate of B19V positivity in myocardial tissues was not statistically dif- ferent in controls (mean: 38±24.1%) versus the MC/DCM patients (45.5±24.3%; p=0.5881).

Conclusions: This meta-analysis reveals that the mean detection rate of B19V genomes in MC/DCM-patients does not differ significantly from the findings in controls. These data imply biologically irrelevant latency of B19V genomes in a substantial proportion of myocardial tissues, both in MC- /DCM-patients and in controls. It is therefore concluded that this "bioprotein" phenomenon, known for B19V in other human tissues, may equally apply to myo- cardial tissues. This may be a key factor for the failure of antiviral interferon treatment in B19V associated MC/DCM, which was merely based on PCR de- tectability of B19V genomes in endomyocardial biopsies. Further characteristics of B19V infections, such as B19V replication, and the differentiation of active anti- B19V humoral and cellular responses versus biologically irrelevant latent persis- tence of B19V genomes, may be pertinent to achieve a meaningful differentiation of biologically relevant myocardial B19V infections.

P4113 | 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 ma- trix (ECM) in human cardiomyopathy has yet to be 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 retrospec- tively analyzed. Collagen turnover was measured by testing collagen I (ICTP) and procollagen type III (PIIINP) were measured as turnover markers. Patients with highest ICTP tertiles showed a worse outcome (log rank p<0.001).

Conclusions: 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.
ing 15-min were evaluated (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


**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 are involved in cardiac fibrosis formation. However, the potential of these miRs as a quantitative and prognostic biomarker has not yet been established.

**Aim:** The aim is to examine cardiac expression of 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 (col1A1 and col1A2, and col3A1 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). 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. MI-R-133a is decreased in surgery (sham 0.35% ± 0.03 vs TAC 2.56% ± 1.07; p<0.001). VF were classified into 3 patterns; continuous flow, discontinuous flow with double peaks, and single peak. 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 un planned HF hospitalizations).

**Results:** RT showed significant correlations with estimated glomerular filtration rate (eGFR, r=−0.39, p<0.001) and central venous pressure (CVP, r=0.67, p<0.01). VF were classified into 3 patterns; continuous flow, discontinuous flow with double peaks, and single peak. 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 un planned HF hospitalizations). Discontinuous VF pattern was associated with the endpoints independendtly of ejection fraction, BNP, eGFR, and RI (Figure).

**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.

**HYPERTENSION PATHOPHYSIOLOGY II**

**P4117 | BEDSIDE**

Hemodynamic correlates of abnormal aortic root dimension in an adult population: the strong heart study

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**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.

**Results:** ARD correlated with: 1) diastolic BP (DBP, steady stress imposed on ARD); 2) stroke volume (SV, associated with 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.

**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**

Renal congestion assessed by intra-renal Doppler profile associates with the clinical courses in congestive heart failure

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**Background:** Renal congestion (RC) is a key pathophysiology of cardio-renal syndrome in congestive heart failure (CHF). However, intra-renal hemodynamics has not been well studied in assessing RC. We hypothesized that intra-renal Doppler (IRD) ultrasound could evaluate intra-renal hemodynamic abnormalities associated with RC.

**Purpose:** To reveal the determinant factors of IRD profiles and assess the associations of IRD profiles with prognosis in CHF.

**Methods:** First, we performed catheter and IRD studies in 98 patients with CHF. In IRD studies, resistance index (RI) of interlobar arteries and interlobar venous flow (VF) pressure were assessed. As the secondary cohort, 139 inpatients with CHF were enrolled to investigate the associations between IRD profiles at pre-discharge and prognosis. The primary end-points were defined as deaths for cardiovascular diseases and unplanned HF hospitalizations.

**Results:** RT showed significant correlations with estimated glomerular filtration rate (eGFR, r=−0.39, p<0.001) and central venous pressure (CVP, r=0.67, p<0.001). VF were classified into 3 patterns; continuous flow, discontinuous flow with double peaks, and single peak. 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 HF 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.
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 (fingerprint), and mean arterial pressure 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 haemodynamics in hypertensive men**

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**Methods:** We studied 70 non-diabetic, hypertensive men (mean age = 60 years old). Office brachial systolic (bSBP) and diastolic (bDBP) blood pressures were measured 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 enzymimmunoassay.

**Results:** The mean value of TT in the whole population was 4.6 ng/ml (hypo- and normo-androgenic was defined as TT<3.4 ng/ml). Plasma TT was inversely and significantly related to aoSBP (r=-0.26, p<0.03), aoPP (r=-0.30, p<0.01) and AIx75 (r=-0.31, p<0.01) but only marginally related to bSBP (r=-0.22, p<0.07) and bPP (r=-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 (r=-0.29, p<0.03), aoPP (r=-0.31, p<0.02) and AIx75 (r=-0.30, p<0.03) were independently associated with TT but the relationship of TT with bSBP (r=-0.25, p<0.06) and bPP (r=-0.23, p<0.07) remained weak.

**Conclusions:** In hypertensive men, plasma TT is independently associated with 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 24-hour blood pressure, and blood pressure variability**

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**Background and aims:** The relation between blood pressure (BP) and cognitive function has received 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 minimental examination, performed in 2001–2002 and again in 2010 using as reference cognitive data collected at the 1st PAMELA examination carried out 10 years before. 471 subjects participated at this sub-study. Measurements included clinic and 24-hour BP (Spacevels 90207). BP variability was obtained by calculating the SD of 24-hour, day, and night mean values, 2) the day/night BP difference and 3) the recent blood pressure variability (48-hour variability).

**Results:** Mean age of the subjects enrolled was 63.0±5.7 yrs (mean±SD) at the 1st examination. At the 2nd evaluation performed 10 yrs later 26 subjects had a minimental score >23, indicative of a cognitive dysfunction (CD), the remaining 446 subjects had no cognitive impairment (C). During the follow-up period (C 24–30). Both major coronary events and hospitalization for heart failure but there was no evidence of overtreatment and the incidence of adverse events such as stroke/SE, major bleeding and all-cause death.

**P4120 | BEDSIDE**

**Non-invasive central systolic blood pressure not peripheral systolic blood pressure associated with kidney function decline in a Chinese community-based population**

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**Background and introduction:** As a direct reflection of the blood flow load, central blood pressure is increasingly recognized as a stronger risk factor for cardiovascular disease (CVD) compared with peripheral blood pressure. Chronic kidney disease (CKD) is an important public health problem with a substantially increased risk of CVD. However, the association between central blood pressure and longitudinal kidney function decline, especially in individuals without CKD, is not well established.

**Purpose:** This study investigated the association of non-invasive central blood pressure with rapid kidney function decline and incident CKD in a Chinese community-based population with normal kidney function (estimated GFR≥60mL/min/1.73m2) at baseline.

**Methods:** A total of 3152 Chinese subjects from an atherosclerosis cohort were included in our analysis. Baseline central systolic blood pressure (cSBP) was obtained using HEM-9000AI (Omron Healthcare Co., Ltd.). eGFR of both baseline and follow-up were calculated using CKD-EPI formula. Outcomes were rapid kidney function decline (a drop in GFR category accompanied by a 25% or a sustained decline in eGFR of more than 5 ml/min/1.73 m2/ year) and incident CKD (eGFR<60 min/1.73 m2 at follow-up). Multivariate regression models were used to evaluate associations of cSBP and each outcome.
Results: Subjects were 56.6±8.5 years old. 36% were male and 49.3% had hypertension. Mean (SD) baseline eGFR was 101.2±16.0 mln/min/1.73 m². Mean (SD) baseline cSBP was 133.1±18.5 mmHg. After 2.3 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 (odds ratio [OR] 1.02, 95% confidence interval [CI] 1.01–1.03) and incident CKD (OR, 95% CI, 1.01–1.06) even after further 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) 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.

P4123 | BESIDE
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 such as hypertension (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±4.3) and 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 diameters (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: 9.3±1.0 mg/dl vs group B: 5.2±0.9 mg/dl vs control group: 4.8±1 mg/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 10 mg and 10 mm increase in the LVM and LA respectively, an 0.4 and 0.6 mg/dl decrease of SUA levels are significantly associated with LVM (p<0.001). Furthermore the ANOVA regression analysis revealed that SUA levels and LA, implicating that hyperuricamia might be a possible risk factor for HTN and AF (p<0.001). The relationship remained when adjusting for confounders including cSBP.

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 hyperuricamia might be a possible risk factor for LA and LV remodelling and finally for the development of atrial fibrillation.

KILLING THE HEART
4149 | BESIDE
Can we predict which patients are at risk of fluoropyrimidines cardiotoxicity?
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The fluoropyrimidines (FP) 5-Fluorouracil (5FU) and its oral prodrug Capecitabine (CAPE) are widely used in chemotherapy (CT) for several cancers. FP may cause cardiotoxicity (TOX), mostly myocardial ischaemia, ventricular arrhythmias (VA), left ventricular dysfunction (LVD) at echocardiogram (ECHOC), TOX may be asymptomatic (detected at ECG or ECHO), and triggered by physical effort. Many patients (pts) with ischaemic heart disease (IHD) or multiple cardiovascular risk factors (CVRF) have been excluded from CT assuming that they are at increased risk of TOX, but the literature data are conflicting.

Aim: To assess the individual clinical factors predictive of TOX in a cohort of cancer pts treated with FP.

Methods: We used the data of a group of patients prospectively examined during CT with 5FU continuous infusion (c.i.) or oral CAPE. All the patients had a clinical examination, ECHO and ECG before CT. A treadmill or bicycle stress test was planned before CT in pts with IHD (n=15) or with multiple CVRF, and after >48 hours of c.i. or >10 days of CAPE in the others (excluding those with severe rest TOX). We considered possible signs of TOX the appearance, during FP CT, of: typical angina; LVD at ECHO; significant ECG changes: diffuse negative T waves at rest, >2 mm ST segment elevation in >3 ECG leads (at rest or after 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 cardiological 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 after 10 days of CAPE in the others (excluding those with severe rest TOX).

Results: We examined 372 pts: 42 cases and 330 controls. Age, obesity, smoking habit, diabetes, dyslipidemia, hypertension, number of CVRF, number of cardiovascular vessels 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 dyspnea) 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 FP TOX 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.

4150 | BESIDE
Trimetizidine prevents doxorubicin cardiotoxicity: echo and biomarker study
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Background: Anthracyclines are highly effective for treatment of breast cancer but associated with irreversible cardiotoxicity. Trimetizidine is a metabolic agent proved to be effective in stable angina and heart failure.

Objective: Of the study was to assess the efficacy of primary prevention of anthracycline cardiotoxicity with trimetizidine in patients with breast cancer.

Methods: 41 breast cancer patients with indications to anthracyline therapy and without history of cardiovascular disease or previous exposure to anticancer treatment were prospectively evaluated with echocardiography within one week before first treatment and 6 months after inclusion. Ejection fraction (EF) was calculated from biplane method of discs and peak global longitudinal systolic strain (S) was calculated from apical views with Echopac, GE software. Biomarkers of myocardial injury and fibrosis were additionally tested before chemotherapy and 6 months after the treatment (high sensitive troponin T (hsT), Roche; myoperoxydase (MPO), Hycult biotech; Galectin-3 (Gal3), eBioscience; ST2, Critical diagnostics. Patients were randomized to receive trimetizidine 35 mg bid (20 patients) or standard chemotherapy only (21 patients – control group).

Results: None of the patients developed symptoms of heart failure. No significant decrease of EF was observed 6 months after chemotherapy in control (61.4±3.0 vs 60.1±2.7, p=0.08) and trimetizidine group (61.8±3.6 vs 61.2±3.5, p=0.28). At the same time 19% (4 patients) experienced decrease of EF. 5% from baseline significantly and positively associated with the incidence of hypertension and atrial fibrillation (p<0.001). Furthermore the ANOVA regression analysis revealed that SUA levels and LA, implicating that hyperuricamia might be a novel risk factor for the LA and LV remodelling and finally for the development of atrial fibrillation.

4151 | BENCH
Folic acid reduces doxorubicin-induced cardiomyopathy by modulating endothelial nitric oxide synthase and mitochondrial integrity
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Purpose: Endothelial nitric oxide synthase (eNOS) plays an important role in the pathogenesis of doxorubicin (DOXO)-induced cardiomyopathy. Here we tested the hypothesis that folic acid (FA), as an eNOS modulator, attenuates DOXO-induced cardiomyopathy and mitochondrial damage.

Methods: Male C57BL/6J mice (n=265) received DOXO (1x 20 mg/kg, ip or saline) (sham). (FA 10 mg/d po) or placebo was administered from 7d before DOXO administration until the end of the experiment (10d). Left ventricular (LV)
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 micro-}

**Results:** DOXO produced 70% mortality (P<0.01 vs sham), while mice receiving DOXO and FA (DOXOFA) had significantly lower mortality (45%; P<0.01). FA attenuated mitochondrial dysfunction and morphological changes. Furthermore, FA attenuated mitochondrial dysfunction and morphological changes.

**Conclusions:** Targeting eNOS with FA might be a new and immediate therapeutic approach to reduce DOXO-induced cardiomyopathy.

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**Background:** Long-term therapy with doxorubicin is associated with a high incidence of a cumulative and irreversible dilated cardiomyopathy, despite of its broad anti-neoplastic effectiveness. Seapolynol (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 seapolynol against doxorubicin-induced cardiotoxicity in an animal rat 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) DOXO (20 mg/kg; n=15); iii) DOXO + TRZ (20 mg/kg; 10 mg/kg, n=15); iv) NACA+DOXO (250 mg/kg; n=15); v) NACA+DOXO + TRZ (n=15) and were followed for 10 days. In vivo cardiac function was measured 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 DOXO+TRZ, left ventricular ejection fraction (LVEF) on improving the overall survival in women with breast cancer, the risk of developing heart failure cannot be ignored. Amongst the potential mechanisms of DOX+TRZ mediated cardiotoxicity, increased oxidative stress (OS) and apoptosis has gained recent attention.

**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, echocardiographic and biomarker (Troponin I, NT-proBNP and Galectin-3 (Gal3)) evaluations were performed before and 1, 3, 6, 9 and 12 months after CT. The echocardiographic assessment included measurement of left ventricular ejection fraction (EF) and myocardial deformation analysis (EF) and myocardial deformation analysis (EF) and myocardial deformation analysis (EF) and myocardial deformation analysis (EF) and myocardial deformation analysis (EF) by speckle tracking. CTX was defined as a decline in initial EF of at least 5% to an absolute value <55%.

**Results:** 92 women, 53±13 years, undergoing potentially cardiotoxic therapy were studied. 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. −19.4±2.7; P=0.009) and this parameter showed high accuracy in predicting the end-point (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. 13.8±5.5 ng/mL; P=0.023). This biomarker was an accurate predictor of CTX (AUC 0.84; P<0.027 — figure). The cut-off value of 17.8ng/mL showed the best specificity (9.3%: 0.82%). The risk of development of CTX was significantly higher in pts with Ga3 above 17.8 ng/mL (OR 13.3; CI 95% 1.2—147.5; P=0.035).

**Conclusions:** Our data showed that high dose seapolynol had cardioprotective effects against doxorubicin-induced cardiotoxicity in an animal rat model with the evidence of electron microscopic finding in addition to echocardiographic results.
### 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 7.1±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.

**Conclusion:** Prior chemotherapy is a significantly associated with reduced GLS, late after treatment. This effect is analogous to that of other SAHF risk factors.

**Acknowledgement/Funding:** Heart Foundation Health Professional Scholarship

### 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.

**Purpose:** 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. We used a healthy control group matched for age, gender, systolic blood pressure and body surface area, for comparison. A single investigator (J.C.) blinded to the participants’ status, measured GLS off-line in all participants with semi-automatic software (EchoPAC v. 112, GE Healthcare).

**Results:** The survivors were examined mean 18.5±5.3 years after diagnosis. Pre-diagnosis chemotherapy included anthracyclines in 57 (92%). The survivors and controls were well matched (Table). Survivors had lower mean GLS (Table). In 13 patients developed cardiotoxicity (group I), recovered 2 years after therapy. This effect is analogous to that of other SAHF risk factors. Global longitudinal strain has been recommended for screening of cardiotoxicity in cancer survivors. Moreover, it 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.

**Conclusion:** Prior chemotherapy is a significantly associated with reduced GLS, late after treatment. This effect is analogous to that of other SAHF risk factors.

**Acknowledgement/Funding:** Heart Foundation Health Professional Scholarship

### 4157 | BEDSIDE
**New mechanisms of taxanes-related cardiotoxicity in women with breast cancer**

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**Data about mechanisms of taxanes-related cardiotoxicity, frequently detected in breast cancer, is lacking.**

**Aim:** To describe the mechanisms and the outcome of taxanes-related LV dysfunction.

**Methods:** 35 women with HER2-breast cancer (45±7 years) 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); p index for arterial stiffness; oxidative stress from carbonyl concentration into the plasma proteins (CCP); and genetic variation from genotypes rs2837175, 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: 11.6±4 vs 8.1±3). CCP: 0.542±0.120 vs 0.320±0.099 nmol/ml, both p<0.01. Homozygote of genotype rs1056836 was related to the decrease of LVEF (r=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.

**Conclusion:** 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 right and ventricular dysfunction in patients treated with anthracyclines**

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**Introduction:** Cardiotoxicity can be a side effect of chemotherapy (CT) with anthracyclines and 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 51.2±12.4 years, forty (78.4%) females. A significant and progressive decrease of global longitudinal strain (GLS) was noticed, throughout and after CT. T0: −25.2±4%, T1: −19.9±3%, T2: −22.8±9%, T3: −17.3±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±4.6% at T4, p=0.017 vs T0 but p=NS to T1). A reduction of −10% decrease of LVEF between T0 and T3 (AUROC: 0.98; p=0.002, T3−T0: −10% decrease of LVEF between T0 and T4 (AUROC: 0.85; p=0.002). 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.

**Conclusions:** 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).

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Conclusions: Anthracyclines provoke a significant and progressive decrease of left ventricular function, during and after CT. GLS is a sensitive and early marker of myocaridal 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 elevated troponin (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 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 selectivity of 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 within 24 hours after diagnosis, if NT-proBNP was <500ng/L; they were admitted to the hospital if NT-proBNP was >=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 0.2–3.2%) 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 3-month prognosis. It changes the reality in the mortality risk of patients. It is concluded that additional BNP testing is not needed after applying the Hestia decision rule.

4176 | BEDSIDE
Effectiveness of 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 results from 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 acute PE. The PE severity was stratified using the sPESI rule, based on the patient’s presenting characteristics and their sPESI score, RVD (by either echocardiography or computed tomography) and troponin level (intermediate-low ESC group), and 10 (1.1%; 95% CI 0.2–3.2%) 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 3-month prognosis. It changes the reality in the mortality risk of patients. It is concluded that additional BNP testing is not needed after applying the Hestia decision rule. Whether the same conclusion is valid for BNP testing performed after triaging according to the sPESI rule is currently being analysed and these results will be reported at the ESC congress.

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
Investigation of a new pathophysiological axis for risk stratification of normotensive pulmonary embolism: prognostic impact of copeptin


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 to confirm CTEPH. Baseline demographics and clinical characteristics were included in a multivariate logistic 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 "likely 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 score including these 6 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 covariates associated with CTEPH, assessed at a median of 1.5 years after PE diagnosis. If externally validated, the score may guide targeting CTEPH screening to high-risk patients.

Table 1: Predictors of CTEPH

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Frequency</th>
<th>Odds ratio (95% CI)</th>
<th>Points in score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>2.0% (1.7–2.3)</td>
<td>3.6</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18% (0.0–18)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Unprovoked PE</td>
<td>15% (0.0–15)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Symptom onset &gt; 2 weeks before PE diagnosis</td>
<td>5% (0.0–5)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Right ventricular dysfunction (echo or CT)</td>
<td>9% (0.0–9)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Thrombolysis or embolotherapy</td>
<td>5% (0.0–5)</td>
<td>0.0</td>
<td>-3</td>
</tr>
</tbody>
</table>

4179 | BEDSIDE

Derivation of a new score to predict chronic thromboembolic pulmonary hypertension after acute pulmonary embolism


Background: Pulmonary angiography has been suggested as PE-related death or complications) and 14 patients (3.6%) died. The 2008 and the 2014 ESC guideline algorithms classified a larger 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 [0.64–0.79]) 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 [5.3–42.7; 95% CI]) and in the FAST score (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 two scores. The modified FAST score appears to be more suitable for risk stratification of normotensive PE patients compared to the Bova score.

Table 1. Predictors of CTEPH

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Frequency</th>
<th>Odds ratio (95% CI)</th>
<th>Points in score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>2.0% (1.7–2.3)</td>
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</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18% (0.0–18)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Unprovoked PE</td>
<td>15% (0.0–15)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Symptom onset &gt; 2 weeks before PE diagnosis</td>
<td>5% (0.0–5)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Right ventricular dysfunction (echo or CT)</td>
<td>9% (0.0–9)</td>
<td>0.0</td>
<td>-3</td>
</tr>
<tr>
<td>Thrombolysis or embolotherapy</td>
<td>5% (0.0–5)</td>
<td>0.0</td>
<td>-3</td>
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Conclusion: CTEPH ruled out CTEPH confirmed (% of patients)

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</table>

4180 | BEDSIDE

RV dysynchrony predicts clinical outcomes after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension

T. Tsugu, M. Murata, T. Kawakami, R. Yasuda, H. Tokuda, Y. Minakata, M. Kataoka, H. Tsurai, H. Kanazawa, K. Fukushima, Keio University School of Medicine, Tokyo, Japan.

Background: Pulmonary angiography (BPA) may improve hemodynamics and exercise tolerance in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Recently, we reported a significant correlation between three-dimensional echocardiographic right ventricle (RV) parameters 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 two-dimensional speckle-tracking echocardiography (2DSTE) and three-dimensional transharmonic 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 (6MWTD) 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-month follow-up. RVF, RVEDV, and RVEF were significantly reduced after BPA. TAPSE, RVFAC, RVFED, and RV mid free wall longitudinal strain (MFWSL) were significantly improved after BPA, implicating that RV systolic function was ameliorated. RV dysfunction was also improved after BPA. Receiver operating characteristic analysis revealed that SDTTP was a good predictor for improvement of 6MWTD (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 dyssynchrony 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 N-terminal prohormone of brain natriuretic peptide (NT-proBNP), a biomarker of right ventricular dysfunction, are associated with poorer outcomes in patients with pulmonary arterial hypertension (PAH). Riociguat significantly reduced NT-proBNP levels compared with placebo in pts with PAH during the 12-wk PATENT-1 study.

Purpose: We present the 2-yr NT-proBNP data from PATENT-2.

Methods: Pts with PAH who were treatment-naïve or pretreated with ERA or prostanoids 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 pretreated with concomitant ERA were excluded. NT-proBNP was measured at baseline, 12 wks and 2 yrs.

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±1595 pg/ml (n=196) for the underlying LD may explain the worst prognosis of patients with PH-LD in comparison with PH-LHD. 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.

Conclusions: Patients with I/HPAH are younger, with a 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 medications 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
T. Dawes1, A. De Marva2, W. Shi3, D. Rueckert4, G. Watson5, L. Howard2, S. Gibbs6, S. Cook7, M. Wilkins8, D. O’Regan9, Imperial College London, Department of Medicine, London, United Kingdom; Imperial College London, Medical Research Council Clinical Sciences Centre, Faculty of Medicine, London, United Kingdom; Imperial College London, Department of Computing, London, United Kingdom; Imperial College London, Division of Experimental Medicine, London, United Kingdom; Imperial College Healthcare NHS Trust, Department of National Pulmonary Hypertension Service, London, United Kingdom; National Heart Centre Singapore, Singapore, Singapore

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 remodeled 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 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 (6MWTD) 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 6MWTD (all p<0.001) and predicted 5-year mortality significantly better than RVEF (receiver operating characteristics area under curve: 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 baseline 3D systolic function.
RVEF (longitudinal 39%, circumferential 33%, radial 28%, difference: p<0.001). RV basal freewall and septal function provided the most informative functional changes.

Conclusions: The failing RV in PAH is manifest by independently prognostic adaptations in septal/freewall mechanics and long axis dysfunction. Analysis of RV contraction in the pressure overloaded heart is facilitated by machine learning techniques and provides greater prognostic power than global measures of loss of function irrespective of hemodynamic parameters. We propose this as a new technique for predicting outcome from functional cardiovascular phenotypes.

Acknowledgment: Welcome Trust PhD Studentship; MRC; UK; NHRI Biomedical Research Centre, BHF project grant.

ADVANCES IN CARDIAC REGENERATION

4189 | BENCH
Leukemia inhibitory factor enhances cardiomyocyte regeneration after myocardial infarction from endogenous stem cells 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 CreLa2Z 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 CreLa2Z 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 (3.04±0.38%/mm², MI; 0.47±0.16%/mm², 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±1.53 X-gal-negative cardiomyocytes/mm², whereas control mice had 12.34±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±2.2% 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 transplantation CreLa2Z mice indicated that LIF did not stimulate cardiogenic differentiation via circulating bone marrow-derived cells during the 4 weeks following MI.

Conclusions: LIF stimulates, in part, stem cell-derived cardiomyocyte regeneration by activating cardiac stem or precursor cells, but not circulating bone marrow-derived cells.

Acknowledgement/Funding: Grant-in-Aid for Scientific Research, Developmental Scientific Research, Scientific Research on Priority Areas from the Ministry of Education

4190 | BENCH
Epigenetic modulation of cardiac progenitor cells through miR-29a/Dnmt3a axis promotes their cardiac differentiation

A. De Pauw1, B. Sekkas2, A. Loriot3, C. De Smet4, D. Catalucci4, D. Hilfiker-Kleiner5, J.-L. Balligand1. 1. Institute of Experimental and Clinical Research (IREC), Brussels, Belgium; 2. Belgian Federal Agency for Medicines and Health Products, Brussels, Belgium; 3. Louvain Drug Research Institute (LDRI), Brussels, Belgium; 4. National Research Council, Milan, Italy; 5. Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

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'-Azacytidine 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 CPC (Axin2: 362±64%, Snai2: 461±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 Dick-1 (310±57%; p<0.05). Like several Wnt/β-catenin repressor genes, Dick-1 expression is DNA methylation sensitive and susceptible to be regulated by the de novo DNA methyltransferases Dnmt3. Indeed, Dnmnt3a was downregulated in CPC treated with DIFF; while siRNA targeting Dnmnt3a decreased Wnt-1 promoter methylation (34.24±21.99%; p<0.05) and increased Wnt-1 gene expression in non-differentiated cells (425±524%; p<0.05). Dnmnt3a silencing promoted CPC cardiac differentiation in co-culture assay (assessed 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 Dnmnt3a, in DIFF-treated CPC. Indeed, modulation of miR-29a using mimic or anti-miR affected Dnmnt3a protein level, promoter methylation of Wnt-1 and Wnt-1 expression (mimic: 839±257%; LNA: 515±9%; p<0.05). Importantly, LNA treatment also significantly decreased CPC differentiation in co-culture assay (63±4% vs. ct; p<0.001). Altogether, this suggests that miR-29a controls CPC differentiation through Dnmnt3a-dependent regulation of Wnt-1, important for cardiac regeneration.

We conclude that CPC differentiation involves the epigenetic regulation of canonical Wnt/β-catenin activity through miR-29a/Dnmt3a axis, possibly amenable to therapeutic modulation for cardiac repair.

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 arrhythmogenicity of this cell type are missing, and there have been conflicting results on pro- or antiarrhythmic effects of stem cell-derived cardiomyocytes (CM) after transplantation. Thus, we investigated electrical integration and arrhythmogenic 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 purified by antibiotic selection. After LAD ligation, iPSCM (500,000 cells/10 μl) or PBS (10μl) were injected into adult mouse hearts. 6 weeks later, electrophysiologist 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 and electrical integration of iPSCM in the perifracnt 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±6.1 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±9.4 V/s). Action potential duration to 50% repolarization (APD50) was longer (18.2±3.3 ms vs. 10.7±2.9 ms, APD90 was shorter (65.1±20.2 ms vs. 101.9±15.4 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±3.3 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<0.05).

Conclusions: Transplanted iPSCM were able to integrate into the perifract 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

4191 | SPOTLIGHT
How cold is too cold: the effect of seasonal temperature variation on risk of STEMI

S. Liu, R.A. Ducas, B. Hiebert, L. Olien, R. Philip, J.W. Tam. St Boniface General Hospital, Cardiology, Winnipeg, Canada

Background: Several studies have demonstrated a correlation between cold weather and incidence of myocardial infarction; however there is no clear con-
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. Poison 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 STEMI. 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 associ-
ated 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 1 to 2 days prior to STEMI. Increased public aware-
ness and or reallocation of health care resources should be considered to re-
source to the seasonal increased incidence of STEMI.

4196 | BEDSIDE
Pericardial matter and NO2 air pollution trigger ST-elevation myo-
cardial infarction: a case cross over study of the Belgian STEMI
registry
J.-F. Argacha1, P. Collart2, P. Kayaert3, T. De Vos4, A. Wauters5, C. Bauloye3, P. Evrard3, P. Sinnema6, M.J. Clays5 on behalf of Belgian
Interdisciplinary Working Group on Acute Cardiology (BIWAC). 1University Hospital (UZ) Brussels, cardiology, Brussels, Belgium; 2Epidemiology and
Biostatistics department, Public Health UlB, ULB, Brussels, Belgium; 3Brussels Institute for Management of the Environment, Brussels, Belgium; 4ULB Erasme
University Hospital, Department of Cardiology, Brussels, Belgium; 5Cliniques St-Luc UCL, Brussels, Belgium; 6CHU Mont Godinne, Mont Godinne,
Belgium; 7Gasthuisberg University Hospital, Leuven, Belgium; 8ZNA Middelheim Hospital, Antwerp, Belgium

Background: Previous studies have shown that air pollution particulate matter
(PM) is associated with increased risk of myocardial infarction. Effects of air pol-
ution on the particular subset of transmural myocardial infarction (STEMI), the
role of gaseous air pollutants such as NO2 and ozone and the susceptibility of
speciﬁc 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: Over the 6 year study period, there were 1817 STEMI. 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
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Conclusion: There is a clear association between daily temperature and STEMI
risk with predictability seen 1 to 2 days prior to STEMI. Increased public aware-
ness and or reallocation of health care resources should be considered to re-
source to the seasonal increased incidence of STEMI.

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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Pisana, Pisa, Italy; 2Institute of Clinical Physiology of CNR, Pisa, Italy;
3Department of Prevention, ASL Roma G, Colleferro, Italy; 4Lazio Regional
Health Service, Epidemiology, Rome, Italy

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 cardiovascular 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
responsible for soil and water contamination.

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/mq) were recruited in a cross sectional
health surveillance study. Blood samples were collected for analysis of β-HCH and
lipid profile.

Results: β-HCH was 77 (33–177) nanograms/liter in the overall population. As expected, lipid-corrected β-HCH concentrations were associated with age
(p<0.001) and BMI (p<0.001).

Conclusion: Higher β-HCH concentrations were independently associated with
elevated 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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Uppsala University, UCR-Uppsala Clinical Research Center, Uppsala, Sweden; 4Duke
University Medical Center, Durham, United States of America; 5The University
of Auckland, Green Lane Cardiovascular Service, Auckland City Hospital,
Auckland, New Zealand

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-
TOTE trial the ABC-stroke score outperformed the traditional CHADS2-VASc
score (C index 0.67 vs. 0.62, p=0.001).

Purpose: To externally validate the ABC-stroke risk score 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 quali-
ﬁed for external validation of a stroke risk score in AF. Blood was collected at ran-
domisation, 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-pits.

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.

**4204 | BEDSIDE**

**Exercise capacity can significantly improve SCORE risk prediction model in low risk asymptomatic adults**

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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 in predicting 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 the study follow up of 9.2±4.0 years. Kaplan-Mayer survival analysis showed that both high SCORE and low exercise capacity are 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.

**4205 | BEDSIDE**

**Overestimation of incident ASCVD events by the ACC/AHA risk score in the German population: The KORA and the Heinz Nixdorf Recall Studies**

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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 in 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, and 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?**

**4237 | BEDSIDE**

**Two-dimensional diastolic speckle tracking echocardiography in the triage of patients with acute chest pain department**

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**Background:** Two-dimensional speckle tracking echocardiography (2D-STE) has become important to be useful for the diagnosis of myocardial ischemia by detecting delay in regional myocardial expansion after an episode of angina. The hypothesis is that 2D-STE is useful in the triage of patients with possible acute coronary syndrome (ACS) who visit emergency department (ED) complaining of chest pain.

**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 (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 values 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 are 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.
4238 | 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 (SLSL), systolic longitudinal strain rate (SLSLR) and early diastolic longitudinal strain rate (DLSLR) 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 SLSLR was observed between days 1 and 2 (from −8.06±3.03 to −15.48±4.29, p<0.0001 and from −6.70±2.2 to −1.24±0.33, 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 DLSLR was evenly distributed between days 1, 2, 3, 7, 1.07±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.

Differences between SR t, SR 1 and SR e
Conclusion: The most 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: Of 28,217 patients with ACS enrolled in the 5 registries, 1209 (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 dysfunc- tion, 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 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.

4255 | BEDSIDE
Modified 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 modified shock index (MSI) - a ratio of heart rate (HR) to mean blood pressure (MBP) 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 not selected those who presented with STEMI (n=1402). They 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 23.5%; 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 (95±18 vs 71±14; p<0.001) and higher HR values (76±17 vs 108±19; p<0.001); Killip ≥4 (18.0% vs 56.3%; p<0.001), Killip ≥4 (2.9% vs 28%; p<0.001), anaemia (20.9% vs 48.4%; p<0.001) and renal insufficiency (eGFR ≤60 ml/min (21.8% vs 46.4%; p<0.001).
They also presented more severe coronary artery disease – left main coronary artery or 3 vessels disease (18.3% 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 (2.6% 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 mor-
tality [OR 7.18; 95% CI (3.39–14.68); 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.

4256 | BEDSIDE
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 are 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.
Results: Among the study patients (N=220), ECMO was initiated during cardiac-pulmonary 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-
comes. The weaning and survival rates were dependent on the aetiologies of shock or cardiac arrest.

UNDERSTANDING POST INFARCTION RISK FOR A BETTER LONG TERM SURVIVAL

4260 | BEDSIDE
Chronology of events after hospital discharge following acute myocardial infarction is not uniform. Five-year follow-up of the FAST-MI 2005 registry

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Background: Contemporary data on chronology of events after acute myocardial infarction (AMI) are scarce.

Aim and methods: We analysed the chronology of 5-year mortality post hospital discharge in the nationwide French FAST-MI 2005 registry of STEMI and NSTEMI patients admitted in 223 institutions over one month in 2005; 5-year mortality follow-up was 97%. We determined splines in event curves and sought optimal curve fitting according to time elapsed since the acute event.

Results: In 2894 patients discharged alive, 5-year mortality was 34% in NSTEMI (n=1377) and 16% in STEMI (n=1517). Figure 1. In NSTEMI patients, the best spline points were found at 5 months and 18 months, with declining event rates and near-perfect linear correlations for each time interval. Slope coefficients were: 29.0 (r²=0.999, P<0.0001) from discharge to 5 months; 10.3 (r²=0.999, P<0.0001) from 5 to 18 months; and 7.5 (r²=0.999, P<0.0001) from 18 months to 5 years. In STEMI patients, the optimal spline points were found at 6 weeks and 5 months. Slope coefficients were: 29.0 (r²=0.999, P<0.0001) from discharge to 6 weeks; 10.9 (r²=0.992, P<0.0001) from 6 weeks to 5 months; and 4.1 (r²=0.998, P<0.0001) from 5 months to 5 years.

Conclusion: Mortality following discharge after AMI is not uniform with time. Event curves can be modelled with 3 slopes of declining steepness; a first period with a high event rate up to 5 months (NSTEMI) or 6 weeks (STEMI), a second period from 5 months to 18 months (NSTEMI) and 6 weeks to 5 months (STEMI) with an intermediate event rate and a third period corresponding to fully stabilized disease (from 18 months onward in NSTEMI and 5 months onward for STEMI). The chronology of events suggests that different therapeutic strategies might be considered for each of the three periods.

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4261 | BEDSIDE
Long term relative survival and excess mortality after acute myocardial infarction, 2003-2010: a national cohort study

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Background: Survival after AMI is high, however, there are no whole-country studies of survival after STEMI and NSTEMI which account for background mortality.

Methods: Nationwide population-based cohort (247 hospitals, 583,466 patients, England and Wales, 2003–10), using data from the Myocardial Ischaemia National Audit Project (MINAP). Age, sex, and calendar year-specific population mortality rates for England and Wales were matched to calculate expected survival, and 5-year cumulative relative survival using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR).

Results: Excess mortality increased significantly with age. For STEMI, EMRRs were 1.91 (95% CI; 1.80 to 2.03), 4.22 (CI; 4.00 to 4.46), 9.34 (95% CI; 8.90 to 9.86) and 17.67 (CI; 16.70 to 18.71) for 56–65yrs, 66 to 75 yrs, 76–85 yrs and >85 yrs respectively. Compared with STEMI, NSTEMI had significantly better survival (EMRR=0.82, 95% CI; 0.80 to 0.84 and 0.54, 95% CI; 0.48 to 0.61). No significant sex-dependent effect was evident for NSTEMI (Fig. 1).

Conclusion: Long-term survival and excess mortality after AMI is high, however, there are no whole-country studies of survival after STEMI and NSTEMI which account for background mortality.
logistic EuroSCORE was 28.4±13.3%. NYHA class III/IV was reported in 92.5%. At 5 years, the mean effective orifice area (EOA) was 1.6±0.6 cm² (n=34), mean gradient was 11.7±5.4 mmHg (n=39), and peak gradient was 21.2±9.8 mmHg (n=40). In paired patient data, the difference between discharge and 5-year EOA was 0.1±5.7 cm² (p=0.056) and mean gradient was 2.2±5.7 mmHg (p=0.090).

Left ventricular ejection fraction (LVEF) at 5 years was 55.7±16.1% (n=26). At discharge and 5 years, respectively, aortic regurgitation (AR) was evaluated as none/trace in 65.9% (n=172/261) and 57.5% (n=234/408), mild in 28.4% (n=74/261) and 37.5% (n=15/40), and moderate in 5.7% (n=15/261) and 5.0% (n=20). No severe AR was reported at follow-up. Valve thrombosis, when observed in 2 patients, was observed within 30 days. No valve-related explants after 30 days and no case of structural valve deterioration have been reported.

Conclusions: Long-term echocardiographic outcomes in high-risk patients with severe AR suggest that haemodynamic function of first-generation balloon-expandable THVs at 5 years, with no worsening of AR severity over time. Data gained from these early feasibility studies may help evaluate treatment options for intermediate-risk patients.

Acknowledgement/Funding: Edwards Lifesciences

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 were 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 morbidity.

Results: Median Logistic EuroSCORE was similar for SC, DA, and TA, but significantly lower in the TF cohort (22.1% 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<0.02) cohorts. Estimated one-year survival was similar for TF (84.6±4.0%) and SC (80.5±3.3%, p=0.27), but significantly worse for TA (74.7±6.1%, p<0.001) and DA (75.2±3.3%, p<0.001). A Cox proportional haz-

Conclusion: Transapical TAVI using local anesthesia only is feasible and save 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 shown to act 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.

Methods: We directly compared sNEP and NTproBNP as risk stratifiers.

Results: 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.

Discussion: The head-to-head sNEP vs. NTproBNP comparison showed good calibration and similar discrimination (figure) and reclassification for both endpoints in all models.

Conclusion: Soluble Neprilysin compared to NTproBNP for heart failure risk stratification in ambulatory patients

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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 multivariable 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 malignancies 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.

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.

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 endpoint of all-cause mortality in HF patients at hospital discharge and HF outpatients respectively with data from a nationwide HF registry.

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

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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 versus no diuretic medication. An age difference of 5 years and a PS difference of less than 0.01 were accepted. This resulted in a 1:1 matched population of 3,252 patients at hospital discharge and 13,950 as outpatients.

Results: sNEP was significantly associated, in age-adjusted Cox regression analyses, with the composite endpoint at 2 months (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.04–1.70, p=0.02) and long-term follow-up (HR 1.23, 95% CI 1.01–1.40, p=0.01). At discharge, sNEP levels decreased from 0.70 to 0.52 ng/ml (p=0.06).

Conclusion: 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.

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Conclusions: A report from the Swedish Heart Failure registry based on a cohort of 27,374 patients. Hazard ratio (HR) for all-cause one-year mortality was estimated.

Results: See Table 1.

Table 1

<table>
<thead>
<tr>
<th>Hospital discharge</th>
<th>No diuretics</th>
<th>19.5</th>
<th>377/1926</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>18.1</td>
<td>294/1626</td>
<td>0.898 (0.766–1.053)</td>
<td>0.19</td>
</tr>
<tr>
<td>Outpatients</td>
<td>No diuretics</td>
<td>4.7</td>
<td>128/2745</td>
<td>1</td>
</tr>
<tr>
<td>Diuretics</td>
<td>6.6</td>
<td>161/2745</td>
<td>1.432 (1.142–1.795)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion(s): In this observational report we found that in clinically stable outpatients with HF diuretics are associated with increased risk of one-year all-cause mortality. In contrast, diuretics in HF patients at hospital discharge are not associated with increased one-year mortality. The clinical implications of these findings are that diuretics should be discontinued when symptomatically feasible in outpatients.

Acknowledgement/Funding: The Swedish Heart-Lung Foundation, Region Västra Götaland
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.

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.

Use of digoxin is safe in patients with atrial fibrillation and heart failure: a nationwide propensity matched study.

Methods: From Danish nationwide registries, digoxin-naïve HF patients with co-existing AF from 1996–2012 were identified and included if they were in continuous or persistent atrial fibrin. Patients were excluded if they were treated with amiodarone. Digoxin users and non-users were compared in propensity score matched cox regression models with respect to primary outcomes of all-cause mortality and readmission due to HF and/or AF.

Results: The study population comprised 4,868 digoxin users, and 4,868 non-users with a median age of 75 years. Over a median follow-up of 38 months, 3,693 (37.9%) patients died and 5,838 (60.0%) patients were readmitted due to HF and/or AF. Use of digoxin was associated with a reduced risk of death (hazard ratio [HR]: 0.92, 95%-CI: 0.86–0.98), but a slightly increased risk of readmission (HR: 1.07, 95%-CI: 1.01–1.12). However, considering death as a competing risk, the cumulative incidences of readmission were close to similar (64.9% for digoxin users and 64.4% for non-users).

Conclusion: In digoxin-naïve HF patients with AF use of digoxin was safe and associated with a slightly reduced risk of death, whereas no difference was observed regarding HF AF readmission.

How to make a diagnosis of microvascular angiopathy; the diagnostic potency of rest-stress myocardial perfusion magnetic resonance imaging.

Background: Microvascular Angina (MVA) causes chest pain without significant stenosis and spasm in epicardial coronary artery. Its diagnosis is difficult because few efficient diagnostic modalities have been reported in the past studies.

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 ergonimine maleate turned out to be negative. Subsequently contrast-enhanced myocardial perfusion MRI was performed under the rest conditions and the stress conditions with adenosine triphosphate (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.

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 problem of diagnostic difficulty of MVA.

Use of pre-procedural antiplatelet and anticoagulant therapy on myocardial no-reflow following percutaneous coronary intervention.

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.

Results: No-reflow occurring during percutaneous coronary intervention (PCI) has been associated with poor in-hospital outcomes.

Conclusion: The objectives of this study were to evaluate the incidence of no-reflow events and independent predictor of adverse events and to assess whether baseline pre-procedural treatment options may affect clinical outcomes.

Effect of pre-procedural antiplatelet and anticoagulant therapy on myocardial no-reflow following percutaneous coronary intervention.

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 analyzing their treatments and clinical outcomes.

Results: 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.

Conclusion: No-reflow occurred in 128 of 5997 patients who have undergone PCI.
The association between coronary artery calcium & coronary flow reserve assessed by integrated rubidium positron emission tomography/CT in women with angina and no obstructive coronary artery disease


Purpose: The aim was to evaluate the association between CAC and CFR in patients with angina pectoris and NO-CAD suspected for CMD.

Methods: Patients were randomly selected from a cohort of women with angina 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 (QFR) CFR was 2.67 (2.29– 3.10). No significant correlation between CFR and CAC was found (R2=0.0012; p=0.911 for all patients, and R2=0.015; p=0.379 for patients with CAC above 0. CAC and CFR were correlated to the presence of hypertension and CFR was correlated to diabetes. Furthermore, increasing age and atheromatisis on CAG were associated with a higher CAC (Table 1).

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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.

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 > 75 mm; n=31, G-AN group), AN without stenosis (diameter of AN < 75 mm; n=26, AN group), >75% coronary stenosis (n=12, S group), <75% coronary stenosis (n=23, n-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 26 patients (20.47%) had DM. The groups were similar in age (66.39±10.65 vs 66.38±10.29, p=ns). There was no significant difference in DM between diabetic and non-diabetic patients [A (0.81±0.18 cm² vs 0.85±0.13 cm²) and Vmax (4.25±0.56 vs 4.21±0.48/min); 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 was 1.15±0.55 m/s in diabetic patients, while not significantly different (0.34±0.98 vs 0.30±0.05; p=0.063). DM was the best independent predictor of CFR [β=-0.461, CI 95% (-0.0781 to -0.0142), p<0.005].

Conclusion: Diabetes mellitus additionally impairs coronary microvascular function in patients with severe aortic stenosis and nonobstructed coronary arteries. The markedly reduced coronary flow reserve in asymptomatic diabetic AS patients suggests these patients should receive special attention as they might significantly impact the occurrence of the no-reflow.
(TRA) for percutaneous coronary intervention (PCI) reduces local vascular complications and bleeding compared with femoral access in patients presenting with acute coronary syndrome (ACS).

**Purpose:** We sought to determine if TRA is associated with better in-hospital outcomes in a large, real world population of patients with ACS.

**Methods:** Data were derived from the International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-TC; NCT01218776) registry, a prospective survey of patients presenting with ACS over a 5-year period (January 2010 to January 2015). Outcomes measured were in-hospital mortality and the combined endpoint of periprocedural major complications, which included myocardial infarction type 4, abrupt closure (type 4b), loss of side branches, distal embolization, and no-reflow phenomenon.

**Results:** Of 6006 ACS patients undergoing PCI, 3856 (60.9%) underwent TRA, with TRA being employed among male sex and patients with lower risk characteristics; patients were younger with a lower burden of risk factors. Patients undergoing TRA had significantly lower periprocedural complications (3.4% versus 10.3%, p < 0.001). After adjustment for demographic and clinical characteristics, the risk of periprocedural complications was reduced by 40% (OR: 0.60; 95% CI: 0.45–0.81). The in-hospital death rate was 3.1% in the TRA group compared with 4.0% in the femoral group (Unadjusted OR: 0.76; 95% CI: 0.57–1.00). This borderline difference was no longer observed after multivariate adjustment (OR: 1.06; 95% CI: 0.75–1.48).

**Conclusions:** Different incidents in-hospital mortality were seen between TRA and femoral approach. However, the lower rate of periprocedural complications may be a reason to use TRA.

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**The effects of nicorandil on microvascular function in patients with STEMI undergoing primary PCI**


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**Background:** Nicorandil, as specific coronary vasodilator with dual mechanism of action and cardioprotective effects, was suggested to reduce the degree of microvascular dysfunction and obstruction responsible for slow or no reflow after primary percutaneous coronary intervention (PCI).

**Purpose:** The aim of the study was to evaluate the effects of nicorandil on microvascular function evaluated by index of microvascular resistance (IMR) in patients with acute myocardial infarction with ST segment elevation (STEMI) undergoing PCI.

**Methods:** Sixty-four patients with STEMI undergoing primary PCI were randomly divided into two groups: Nicorandil group (32 pts; mean age 56±9, mean 26) and Control group (32 pts, mean age 60±8, mean 22). In Nicorandil group, 12 mg of nicorandil was administered intraoperatively after successful stent implantation. IMR was measured in both groups immediately after PCI. ST segment resolution was monitored before intervention and 60 minutes after terminating the procedure. Transthoracic measurement of coronary flow reserve (CFR) in infarct related artery was performed during hospitalization.

**Results:** IMR was significantly lower in Nicorandil in comparison to Control group (10.0±3.7 vs. 23.9±20.9mmHg/0.1 s, p < 0.001). There was no significant difference in ST segment resolution between Nicorandil and Control group (5.3±2.2mm vs. 4.4±2.3mm, p=0.205). Transthoracic Doppler CFR measurement (2.69±0.38 vs. 2.88±0.44, p=0.25) was significantly higher in Nicorandil group. (p < 0.05).

**Conclusion:** According to the results of the study intracoronary nicorandil in patients with STEMI undergoing PCI by improving microvasculature circulation, seems to significantly decreases IMR, and improves coronary flow reserve.

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**The resistive reserve ratio is associated with acute infarct characteristics in patients with acute STEMI**


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**Introduction:** This study aimed to assess the relationship between the resistive reserve ratio (RRR) with myocardial infarction and microvascular obstruction assessed by 1.5T contrast enhanced CMR in a population of patients with ST-segment elevation myocardial infarction undergoing primary PCI. Cardiac MRI was performed approximately 3 months after their referral on a Siemens MAGNETOM Avanto (Erlangen, Germany) 1.5-Tesla scanner with a 12-element phased array cardiac surface coil.

The imaging protocol included cine MRI with steady state free precession, T2-weighted edema imaging and early and late gadolinium enhancement imaging. The initial area-at-risk (AAR) was delineated with T2-weighted CMR. Microvascular obstruction was defined as a central dark zone on early contrast enhancement imaging post-contrast injection and present within an area of late gadolinium enhancement. Myocardial infarction was imaged using a segmented phase-sensitive inversion recovery turbo fast low-angle shot radiofrequency pulse sequence 15 minutes after intravenous injection of 0.15 mmol/kg of gadoterate meglumine (Gd2+-DOTA, Dotarem, Guebert S.A.). In addition, patients had a repeat CMR at 6 months.

**Methods:** Mean±SD: 226 near-consecutive patients (mean age 59.3±11.4, 73% male) with STEMI were enrolled 2 days post-MI, mean LV ejection fraction was 54.9±9.6%, mean infarct size (%LVMass) 17.9±13.4%. Mean RRR 2.07±1.07 and CFR 1.74±0.84. There was a strong correlation between CFR and RRR (r=0.53, p<0.001). There was a modest correlation between the T2 AAR and RRR (r=-0.21, p<0.002 and also CFR (r=-0.17, p=0.004). There was a weak correlation between RRR and the LV ejection fraction at 6 months (r=0.13, p=0.05) but not with CFR.

**Conclusion:** The RRR predicts acute infarct characteristics and was more closely associated with myocardial injury in acute STEMI than CFR.

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**The index of microvascular resistance is a novel biomarker for myocardial haemorrhage and risk stratification in acute reperfused STEMI**


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**Background:** The index of microvascular resistance (IMR) is an invasive measure of microvascular function but its relationships with myocardial pathologies, including intra-myocardial haemorrhage (IMH) and microvascular obstruction (MVO) in survivors of ST-elevation myocardial infarction (STEMI), is incompletely understood. IMH has primary and secondary components, and so may be modifiable with targeted therapies in at-risk patients.

**Purpose:** To assess whether IMR measured at the end of primary percutaneous coronary intervention (PCI) might discriminate STEMI patients at risk of subsequent IMH.

**Methods:** We performed a single centre cohort study in 245 reperfused STEMI patients. IMR was measured at the end of PCI 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). IMR 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 [Q3] was 25 [15–48], 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 [19–47]) than in patients without IMH (17 [12–33]), 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:** IMR measured at the end of PCI in patients with Non-diabetic and Insulin-Mimetic Nicorandil was associated with IMH than MVO, and is independently associated with LVEF at 6-months. Since IMH is a secondary phenomenon post-MI, IMR measured at the end of PCI has potential to stratify patients at risk of myocardial haemorrhage for more intensive therapy.

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**Prognostic values of coronary microvascular function in patients with angina symptoms and impact of impaired glucose homeostasis**

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1. University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden; 2. Sahlgrenska Academy, Department of Clinical Physiology, Gothenburg, Sweden

**Background:** Myocardial ischemia as a consequence of microvascular dysfunction is of clinical importance, but still challenging to diagnose. The purpose of the study was to examine the association between impaired glucose homeostasis and coronary microvascular dysfunction assessed by coronary flow reserve (CFR) in non-diabetic patients with angina symptoms without myocardial ischemia. Secondly we sought to examine whether this risk is similar in both genders.

**Methods:** 201 patients (127 men and 74 women) referred to myocardial perfusion scintigraphy (MPS) due to angina symptoms without MPS-verified ischemia were examined and followed up regarding cardiovascular events. All patients underwent blood sampling for laboratory analysis and adenosine-assisted CFR examinations. Changes in CFR were associated with left anterior descending coronary artery by transthoracic echocardiography.

**Results:** During a follow-up time of 5.1 years 25 cardiovascular events occurred, 18 in women and 7 in men. Mean CFR was 2.8±0.9 and 14% displayed impaired
CFR = 2.0. In a survival analysis adjusting for cardiovascular risk factors CFR 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 CFR (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 = 0.665). Also, women with CFR below 2.0 displayed increased HOMA-IR as compared to women with CFR equal or above 2.0 (p<0.05).

Conclusions: An initial clinical trial with angiina symptoms but no MPS-verified ischemia, abnormal CFR is of prognostic value. Insulin resistance determined by HOMA-IR is associated with impaired CFR, 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 clinical 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 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 intervals to detect (VFNID) and supraventricular arrhythmias and changes in out-of-box settings. Similar findings were also found for initial VFNID programming.

Results: Mean age 66±12 years. 73% male. The figure shows an example of tricular tachycardia discrimination limit (SVTLimit). Included ventricular fibrillation number of intervals to detect (VFNID) and supraventricular arrhythmias and changes in out-of-box settings. Programming variables of interest in-deidentified CareLink Data Warehouse were queried from 2008–2014. Initial programming was based on the earliest transmission post-implant. Initial programming time was investigated in reference to programming evidence publications and changes in out-of-box settings. Similar findings were also found for initial VFNID programming.

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.

P4298 | 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 86.4% (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 adjustment for known 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.

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**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 assess angina frequency (AF) and the Patient Health Questionnaire-9 (PHQ-9) to screen for depression. A lower AF score is indicative of more frequent chest pain.

**Results:** Mean PHQ-9 scores categorized patients as not depressed (score of 1 to 4), mildly depressed (score of 5 to 9), moderately depressed (score of 10–14), moderate depression (score of 15 to 19), and severely depressed (score of 20 to 27). The PHQ-9 scores categorized patients as not depressed (score of 1 to 4), mildly depressed (score of 5 to 9), moderately depressed (score of 10–14), moderate depression (score of 15 to 19), and severely depressed (score of 20 to 27). The PHQ-9 scores were independent predictors of AF even in the subset of patients without significant CAD.

**Conclusions:** Depression is a major and independent contributor to AP in patients with and without CAD. Whether treatment of underlying depression improves AP needs to be further studied.

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**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 represents 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 0–1), intermediate (3–4) and high (5–6) risk. Clinical and procedural data, 30-day, 12-month 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 higher 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.

**Conclusions:** 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.

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**P4303 | BEDSIDE**

**Non-ST-elevation acute coronary syndromes with renal impairment - which formula serves better?**

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**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 67.1±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 CG, 48.8% with MDRD and 45.8% with CKD-EPI. All formulas had a good discriminatory 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).

**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.
**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 who survived >1 year (N=63,434 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:** To lose 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 reinfarction) 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**

**P4306 | 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 subjects underwent conventional echocardiography with strain analysis of left ventricular function in accordance with American Society of Echocardiography guidelines. Strain was measured using a 16-segment model, and the left ventricular GLS was calculated using a custom strain software (Vingmed Norway). LVEF was calculated using the American Society of Echocardiography guidelines. A Cox regression was used to assess the relationship between persistent use of established secondary prevention drugs and survival. Hazard ratios and 95% confidence intervals (CIs) were calculated. The log-rank test was used to compare survival curves. The chi-squared test was used to compare categorical variables. The Student's t-test was used to compare continuous variables. A two-tailed p-value <0.05 was considered significant.

**Results:** Among the 273 stages 3–5 CKD subjects, 274 LS (69% of all eligible) participated, of whom 245 were asymptomatic. The feasibility of LV GLS was 85%. Median observation time was 36 months (range 24–48 months). The correlation between eGFR and GLS was 0.25 (p=0.001). Further, the relationship between eGFR and GLS was significant (p=0.001). The association between eGFR and GLS was significant (p=0.001). The association between eGFR and GLS was significant (p=0.001). The association between eGFR and GLS was significant (p=0.001). The association between eGFR and GLS was significant (p=0.001).

**Conclusion:** Patients with moderate renal impairment have subclinical left ventricular systolic dysfunction, which may be associated with the severity of CKD. This study demonstrates the feasibility of using strain imaging to identify subclinical cardiac functional abnormalities in CKD.
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 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 exclusion of these findings, its routine use could be a reliable tool to diagnose AAR and to alleviate the burden of repeated EMB.

P4309 | 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-LAs were reduced in the impaired group (p<0.001). Moreover, LA stiffness was increased in the impaired group (p<0.001). 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 hands, 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: In patients with preserved longitudinal LV systolic function, LA structure and function are preserved. However, LA 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 dysfunction, 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 inhibit from insults induced by angiotensin-II (Ang-II); (2) whether the mechanism is associated with ROCK1 inhibition; (3) whether different enantiomers of amlodipine (in terms of levotrector, dextroratory and racemic) have the same effects on endothelium and ROCK1 activity.

**Methods:** Human umbilical vein endothelial cells (HUVECs) were used and were divided into five groups: blank control; Ang-II (10–6 mol/L); levotrector (5·10–6 mol/L) + Ang-II (10–6 mol/L); dextro-rotatory (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. Nitric oxide (NO) concentration within HUVECs was quantitatively assessed by 4-amo-5-methylamin-2,7-difluorescein (DAF-FM) diacetate which was stained 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 and concentration of NO were profoundly reduced in Ang-II group. Nonetheless, 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 reverse Ang-II-induced apoptosis as indicated by Bel-2 up-regulation, Bax down-regulation, and apoptotic index reduction. Overall, the efficacies appeared to be more prominent with dextro-rotatory and racemic amlodipine than with levotrector amlodipine.

**Conclusion:** We show that endothelial p53 is critically involved in the pathologies of vascular dysfunction. Phosphorylation of eNOS by up-regulating PTEN expression. We also found that p53 expression was markedly increased in vessels of ischemic tissues and that inhibition of eNOS and phosphorylated-eNOS happened. Endothelial dysfunction as well as profound blood flow recovery in ischemic tissues. These results indicate that endothelial p53 is critically involved in regulating vascular function under hyperglycemic and hypoxic conditions. Inhibition of endothelial p53 would become a novel therapeutic target in patients with systemic metabolic dysfunction.
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, 35–69 yrs, 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 edema.

3 patients with aortic prosthesis expired within 6–12 hours 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 TEE. An obstruction of valve gradients as assessed on 2DECHO. 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 left sided prosthetic valve thrombosis. Thrombolytic therapy is more 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 transesophageal 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-hours) 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 active 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=0.63), 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, diabetes was associated with more than a 2-fold increased 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 (6.6: 4.2–8.3). Diabetes was also associated with mortality from other (non-ischaemic) heart diseases, stroke, cirrhosis, renal disease, and the 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 association with BP was about 3 times stronger among those without diabetes (p for interaction <0.001). 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.

**Conclusions:** Overall, diabetes was associated with more than a 2-fold increased risk of IHD mortality, but with more extreme relative risks in women and in early middle age, leading to reduced median survival of up to 10 years. 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-n3) 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. Possible 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. The incidence of MI was included as both a continuous and a categorical variable.

**Results:** During a median of 17 years of follow-up, 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

<table>
<thead>
<tr>
<th>Quotients of intake</th>
<th>ALA intake (g/d)</th>
<th>Men Incident Hazard ratio (95% CI)</th>
<th>ALA intake (g/d)</th>
<th>Women Incident Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 &lt; 0.57</td>
<td>390</td>
<td>Q1 &lt; 1.24</td>
<td>Q2 1.67–1.94</td>
<td>409</td>
</tr>
<tr>
<td>Q3 1.34–2.19</td>
<td>248</td>
<td>1.00 (0.86–1.17)</td>
<td>Q3 1.43–1.62</td>
<td>168</td>
</tr>
<tr>
<td>Q4 2.19–2.54</td>
<td>247</td>
<td>0.97 (0.84–1.11)</td>
<td>Q4 1.62–1.88</td>
<td>163</td>
</tr>
<tr>
<td>Q5 ≥2.54</td>
<td>440</td>
<td>0.89 (0.74–1.06)</td>
<td>Q5 ≥2.54</td>
<td>188</td>
</tr>
</tbody>
</table>

p-value: 0.57 | p-value: 0.21

ALA, alpha-linolenic acid; MI, myocardial infarction; Q, quintile.

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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-n3 acid or linoleic acid.

**Conclusion:** Dietary intake of ALA was not significantly associated with incident MI neither among men nor women.

P4323 | BEDSIDE
Association between persistent psychological distress and 12 year cardiovascular and total mortality in patients with stable coronary artery disease

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**Background:** Psychological distress has been associated with higher mortality, but the importance of persistence of symptoms over time is not known.

**Aim:** 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 Pravasril-1b (LIPID) trial completed ≥4 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 ≥ 1) 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, Health 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.

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 2.19 (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 3 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

P4326 | 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-treated diabetes (DM) compared to men with DM. Women 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).

**Conclusions:** DM is associated with a higher prevalence of HPR in both sexes, particularly in women. The unadjusted risk for ST associated with DM is attenuated after adjusting for HPR across sexes, suggesting that modulation of platelet function may affect long-term ST risk in DM patients.

**BEST POSTERS IN RISK FACTORS AND OUTCOMES AFTER PCI**

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P4327 | BEDSIDE
Mortality trends after unprotected left main stem 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% CI 0.9, 0.5 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.

P4328 | BEDSIDE
Impact of platelet reactivity in anemic and non-anemic patients with coronary artery disease undergoing percutaneous coronary intervention: insights from the adapt-ds 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 (cardiac death, MI, or def/prob stent thrombosis) and bleeding at 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: 0.93–1.84) and non-anemic patients (adjHR: 1.37; 95% CI: 1.08–1.72; p for interaction >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.

P4329 | BEDSIDE
Randomized comparison of 9-month strut stents coverage of biolimus and everolimus drug-eluting stents assessed by OCT in patients with STEMI
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Aim: The aim of this trial was to compare healing (assessed by optical coherence tomography-OCT) of biolimus A9 and everolimus drug-eluting stents at 9-month follow-up in patients with ST-segment elevation myocardial infarction (STEMI) treated by primary PCI (pPCI). 9-month clinical and angiographic data were also compared in both groups.

Methods: 201 patients with STEMI treated by primary PCI were randomly enrolled in the trial. 101 patients were randomized to the biolimus A9 stent group and 100 patients to the everolimus group. All patients were pre-treated with a short-course triple therapy (unfractionated heparin, aspirin and clopidogrel). The use of inhibitors of GPIIb/IIIa and thrombus-aspiration were left at the discretion of physicians, however both were strongly recommended. Stent implantation was carried out according to the standard clinical practice employing low pressure stent deployment with high-pressure postdilatation using shorter, non-compliant balloon. All patients were scheduled for 9-month clinical, angiographic and OCT follow-up. Primary end-point of this study were the number of uncovered struts.

Results: All procedures were carried out without complications in both groups. Baseline demographic and procedural characteristic were well balanced in both groups. The rate of MACE did not differ significantly at 30 days between both groups. There was one acute stent thrombosis requiring immediate re-PCI in the everolimus stent group and one asymptomatic stent thrombosis in the biolimus group (revealed during stage PCI of non-culprit lesion). Furthermore, there was one non-cardiac death in the biolimus group. 9-month angiographic and OCT follow-up underwent 87% patients in everolimus and 90% patients in biolimus group respectively. At 9-month follow, the rate of MACE and angiographic restenosis were comparable and very low in both groups (2 vs. 1% and 1 vs 1% respectively; P=NS). All in-segment and in-stent angiographic data (reference diameter, minimal diameter, mean diameter, % stenosis) were comparable at 9-month in both groups. OCT data presents Table. The rate of uncovered struts were significantly higher in biolimus group (19.67±16.52 vs. 9.99±10.38; p<0.0001). On the other hand, there was a trend to higher mean and minimal lumen diameter (3.35mm±0.56 vs. 3.2mm±0.43; p=0.06 and 2.88mm±0.55 vs. 2.74mm±0.49; p=0.09).

Conclusions: At 9-month follow-up, second generation everolimus drug-eluting stent shows better healing when compared to biolimus second generation drug-eluting stent. However, the stents strut coverage is considerably high in both groups.
BEST POSTERS IN VENTRICULAR FUNCTION / HAEMODYNAMICS

P4331 | 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
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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 SphygmCor 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 ratio by 8% (p<0.05), MLHFG score by 66% (p<0.001); and the linear regression analysis showed increased arterial stiffness in sBP by 29%; VT1 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: Intermittent 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.

P4332 | 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 dyspnoea as main clinical symptom. Impairment of lung function may cause symptoms of heart failure, although no overt cardiovascular or structural heart disease is present. The association between pulmonary hypertension 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, range 46–65 years, 50.8% men) in the Gutenberg Health Study we performed spirometry with the microMedical siro USB and multimodal echocardiography with an iE33 echocardiography system with an S5–1 sector array transducer, a phased array with 80 elements and a 5- to 1-MHz operating frequency. The primary objective is to assess one year safety and efficacy of the parachute device in subjects with ischemic heart failure: one year meta-analysis and bad naehmpeach experience
H. Moellmann on behalf of PARACHUTE investigators. Kerkhoff Heart and Thorax Center, Bad Nauheim, Germany

Background: Left ventricle (LV) remodeling after anterior wall myocardial infarction (AWMI) leads to increased LV volumes, myocardial stress, and ultimately heart failure (HF). Treatment options are limited for these high-risk HF patients.

Aims: The primary objective is to assess one year safety and efficacy of the CardioKinetic Parachute Implant System in the partitioning of the left ventricle in subjects with heart failure due to ischemic heart disease across trials completed to date (PARACHUTE Cohort A, PARACHUTE US Feasibility, and PARACHUTE III) and compare these results to the observations from recent cases performed in Germany.

Methods: One hundred thirty-four subjects with NYHA class II-IV HF secondary to AWMI, with akinetic or dyskinetic wall motion abnormality, and LV ejection fraction <40%, were enrolled in Europe and the United States. The major endpoints evaluated at one year will be stroke, all-cause death, and the combination of all-cause death and repeat hospitalization for worsening HF. Hemodynamic assessments will be evaluated with echo, and functional capacity assessed by NYHA and 6MWT.

Results: Of the 134 subjects enrolled, 128 were successfully treated (96%). The rates of stroke, all-cause death, and the combination of all-cause death and repeat hospitalization for worsening HF were 2.4%, 8.8%, and 23.8%, respectively. Improvement of systolic cardiac function (p<0.05) was noted in LV volume indices, EF%, stroke work, and contractility index, along with a trend in fractional shortening, at 1-year follow-up relative to baseline values. This was accompanied by significant reductions in left atrial volume and significantly improved diastolic function. The 1-year mean NYHA Class of subjects (1.9±0.7) was significantly reduced (p<0.0001) from baseline NYHA Class (2.5±0.5) reflecting functional improvement. Performance on 6-minute walk test with also improved from P4333 | BEDSIDE
A single-centre experience in the hemodynamic improvement and prognosis of heart transplantation candidates with group 2 reactive pulmonary hypertension treated with sildenafil
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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 50 mg tid, for at least 15 months.

Results: Mean age was 55±11 years, 73% were male. Half of the patients were in NYHA class IV, with median BNP 665 (IQR 665) pg/dL and peak VO2 12.6 (IQR 2.5) mL/kg/min. Hemodynamic baseline parameters: mean pulmonary arterial pressure (mPAP) 45 (IQR 14) mmHg, pulmonary capillary wedged pressure (PCWP) 27 (IQR 13) mmHg, CI 1.8 (IQR 0.7) mL/min/m², PVR 5.5 (IQR 3.2) Wood units, TPG 17 (IQR 8) mmHg. For 56 patients, data from a follow-up routine catheterization was available. After a median follow-up of 168 days (IQR 207) days of treatment the NYHA class improved, with lowering of BNP, mPAP and PCWR, and increase of VO2 max and CI (p<0.05). PCWR was reduced (p<0.03) and mean systemic arterial pressure did not change (p=0.07). Half of the group had at least one hospitalization, 24% underwent HTx, 34% underwent HTx and were died (median 1658 days to follow-up). There was a positive hemodynamic response in 36%; this group had a numerically higher HTx rate (50%) than those without hemodynamic response (22%). We found no significant difference in death (20 vs. 14%) nor in first hospitalization (60 vs. 80%) when comparing patients with and without positive hemodynamic response.

Conclusion: There was improvement in clinical and hemodynamic parameters in reactive group 2 PH patients referred for HTx after sildenafil treatment. There was no significant difference in the outcomes of patients with positive hemodynamic response compared to those without. With a trend to higher HTx performance, eventually achieving eligibility of achieving of eligibility.

P4334 | BEDSIDE
Percutaneous ventricular restoration (PVR) therapy using the parachute device in subjects with ischemic heart failure: one year meta-analysis and bad naehmpeach experience
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Background: Pulmonary arterial vasodilator treatment with phosphodiesterase 5 inhibitors is sometimes used in order to meet eligibility criteria for heart transplantation (HTx).

Aims: 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).
Results: All the patients were characterized by low RR variance both at rest and during tilt (731±746 and 490±467 μs²) 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±34 μs²). At follow-up, patients died, 7 of Group 1 (31±14 mo from disease onset) and 1 of Group 2 (56 mo from disease onset).

Conclusions: 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 progressing ALS.

Accordingly, differences 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 suggest 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.

P4336 | BEDSIDE
Cardiac pacemaker stimulates the brain as well as the heart in humans - a PET functional study
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Purpose: Cardiac pacemaker implantation is a standard therapy for patients with clinically significant bradyarrhythmia. After cardiac pacemaker implantation, some patients complain of palpitation, implying possible activation of cortical receptive fields ofafferent nerves such as anterior cingulate cortex (ACC). ACC also modulates autonomic nervous system in collaboration with hypothalamus and brainstem. We thus examined brain activity and plasma catecholamine levels in response to cardiac electrical stimulation in humans.

Methods: We studied 10 patients (74.7±1.9 yrs, 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 to VVI 80–90 bpm with 1.5V intensity. Blood samples were obtained from the cubital vein before and after CBF measurements for stimulation using SPM8, a common analysis tool for neuroimages. Blood samples obtained from the cubital vein before and after CBF measurements for stimulation using SPM8, a common analysis tool for neuroimages.

Results: Intense stimulation significantly increased CBF in ACC as compared with sham stimulation using SPM8, a common analysis tool for neuroimages. Blood samples were obtained from the cubital vein before and after CBF measurements for stimulation using SPM8, a common analysis tool for neuroimages.
Best Posters in autonomic nervous system in hypertension / Ablation of atrial fibrillation I

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 of the 1st generation PVAC.

Methods: We consecutively enrolled 40 patients (60±11 years) with highly symptomatic, drug refractory AF for PVI using phased RF ablation technique. Patients 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 with 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 PVI (43.7±7.0 vs. 27.0±6.5, fluoroscopy time (29.5±5.5 vs. 23.4±7.0) and procedure time (93.8±1.9 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 (1344J to 1474J) 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 biophen effort 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 PVF and freedom from AF.

P4341 | BEDSIDE
First in man evaluation of a new ablation catheter Thermocool smarttouch sf in atrial fibrillation ablation
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Background: A sufficient tissue contact and an effective cooling of ablation catheters seems to be important for the success rate of complex ablation procedures.

Hypothesis: “First in man” evaluation of the new ablation catheter Thermocool SmartTouch SF, which combines a newly highly effective open irrigated cooling system with a real time monitoring of tissue contact force. Three important properties of the catheter were evaluated: 1. the reproducibility of electroanatomical substrate maps (EAM), 2. The proportion of effective tissue contact during ablation, 3. Thrombogenicity during ablation.

Methods: For the evaluation of the mapping accuracy three independent operators generated a substrate map of the left atrium (low voltage areas were defined as voltage <0.5mV) in the same patient. Subsequently the reproducibility of the low voltage areas was analyzed. For the evaluation of the tissue contact the mean tissue contact force and the percentage of ablation time within a predefined contact force (4–50g) were quantified. For the evaluation of the thrombogenicity high intensive ultrasound signals (HITs) in transcranial doppler flow sonography were counted during ablation.

Results: In total 12 patients suffering from atrial fibrillation were treated with the new ablation catheter (9 male, age 61±13 years, LA diameter 46±9mm). The low voltage areas had a matching of 92% in all 3 physicians. The mean tissue contact force for PVI with ablation >4 g was 2.4±0.9g (previously 85.3±0.5g). Ablation time was registered within the predefined tissue contact force range. Under ablation within this contact force range almost no HIT could be counted. No catheter associated complication occurred.

Conclusions: The new ablation catheter Thermocool smart touch SF has very good mapping properties. Additionally, a high degree of predefined tissue contact force was reached during ablation. This fact together with the highly effective cooling tip of the catheter lead to an optimal prevention of thromboembolic events during ablation.

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 CPVI 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 (CF−) in a 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 48 (4.2%) vs. 7 of 24 (29.2%) in the CF+ and CF− group respectively, p=0.005). The procedure time was significantly lower in the CF+ group (117.9±23.3 min vs. 131.4±25.3 min, p=0.033), RF and fluoroscopy time did not differ between groups (31.5±7.0 min vs. 11.5±8.8 min in the CF+ and the CF− group, respectively).

Conclusions: 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 ablation approach 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 PVI with PVAC Gold were studied. All procedures were performed with use of a non-sterable transseptal sheath. The primary endpoint was defined...
as documented recurrent AF or atrial tachycardia >30 seconds considering a blanking period of 3 months after the procedure. 52 patients had completed more than 3 months follow-up. 

Results: Mean procedure and fluoroscopy times were 68±20 minutes (35–139) and 13.8±2.1 (7.4–27.3) minutes, respectively. The mean number of applications was 22 ± 9. The mean energy delivery time was 1084±235 (600–1902) seconds. Complete acute PVI was achieved in 89/91 patients (98%). 36/52 patients (69%) were in stable sinus rhythm after one procedure during a follow up of 7.5±1.8 months. 5 patients with recurrence of AF underwent a redo-procedure. One patient developed TIA with complete neurological remission within 24 hours of the procedure. 

Conclusion: In patients with PAF, stable sinus rhythm could be achieved in 69% of patients after PVI using the novel PVAC Gold. The PVAC Gold procedure is associated with very short procedure and fluoroscopy times. 

P4344 | BEDSIDE 

Do patients 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. 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 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. Antithrombin recurrences 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 I increased (20–42–28–44 at baseline, 6, 12 and 24 months) and decreased in EHRA II (23–10–15–7), III (13–4–2–2) and IV (1–0–0–0). EHRA classes most often improved by one class (II to I, n=20), (III to II, n=1), less often two or three classes (III to I, n=10), (IV to I, n=1). Complete or long-lasting symptom relief as perceived by both the patient and the physician. Patient-perceived symptoms (AF6) significantly improved already at 6 months, continued to improve at 12 months and then remained unchanged at 24 months. In contrast, the EHRA class continued to improve from 12 to 24 months, implying that the physicians were more prone to perceive symptom improvement than the patient.

P4345 | 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 atrial pulmonary vein isolation (PVI) with radiofrequency energy is associated with an 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 catheter ablation.

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 ablation circles around the septal and lateral PVs were divided into 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 reconnection and reconnection points were 12.4±6.4 and 10.1±4.6 mg (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>Predominant angle</th>
<th>Angle &lt; 45°</th>
<th>Angle &gt; 45°</th>
</tr>
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<tbody>
<tr>
<td>Reconnected PV segments</td>
<td>Absent 136 (96%)</td>
<td>Present 6 (4%)</td>
</tr>
<tr>
<td></td>
<td>(3% (111))</td>
<td>(23 (89%))</td>
</tr>
</tbody>
</table>

Conclusions: Not only total contact force, but also the angle between CF-sensing catheter and tissue seems to play a crucial role in durable PVI. Long-term efficacy have to be evaluated in further studies.
Ablation of atrial fibrillation I / Ablation of atrial fibrillation II

P4348 | SPOTLIGHT
Risk factors of recurrence of paroxysmal atrial fibrillation after radiofrequency catheter ablation

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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 triple-plane echocardiography (RT-3PE) and quantitative tissue velocity imaging (QTVI) were used to evaluate the LA structure and function preservatively (off-line EchoPac workstaion). 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-R group with 81 patients and the AF-F group with 33 patients.

Results: Univariate analysis showed that LAdiap, mitral peak A, E/A ratio, LAVmax, LAVpl, LAVmixi, LAAEF, LATEF, LAexpi, Va were related to the recurrence of AF. In a multivariate logistic regression model, LAVmixi, LAAEF, Va showed predictive value of 84.7% (area under ROC curve, 0.886; 95% CI, 0.555–0.755) for AF recurrence. The cutoff value of 25% for LAAEF was associated with a sensitivity of 75.3% (area under ROC curve, 0.674; 95% CI, 0.573–0.769) for AF recurrence.

Conclusion: The LAA EF and the left atrial appendage were the risk factors of recurrence of PAF after RFCA.

P4349 | BEDSIDE
Low flow velocities in the left atrial appendage can predict atrial fibrillation recurrence in patients undergoing ablation


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 versus 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 these technologies 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 g and high catheter stability) with manual navigation (higher pressure, lower stability).

Methods and results: Two groups 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 (52.3% vs 51.6%), three veins in 26 procedures (23.4%) vs 11 (8.9%), two in 30 procedures (24.2%) vs 37 (29.6%) 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 left superior vein (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 60.8% (p<NS).

Conclusion: The majority of patients submitted to atrial fibrillation re-ablation had 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 episodes and in relation to the equation with many variables and new algorithms should also include catheter stability.

ABLATION OF ATRIAL FIBRILLATION II

P4351 | BEDSIDE
Effect of type of monitoring on verification of atrial fibrillation recurrence after catheter ablation: Comparison of the 7 day Holter monitoring and implantable monitor with remote control

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Introduction: The intensity of monitoring of patients after catheter ablation (CA) does not have currently clear recommendations. It depends on the setting (clinical follow-up, hospital of scientific study) and on clinical characteristics of patients.

Methods: 187 patients without structural myocardial disease with documented symptomatic paroxysmal atrial fibrillation (AF) indicated to CA were randomized into two monitoring techniques. For the first group (90 patients) was used a standard 7-day Holter monitoring (3 and 12 M), a second group of patients (92) underwent 7±3 days before ablation implantation of a SQ monitor in combination with remote control. As a recurrence of atrial fibrillation was defined each episode with a duration >30 seconds. All antiarrhythmic drugs except betablockers were stopped before ablation. CA was performed in a centre with a long experience with AF ablation using 3D technology. Wide Antral pulmonary veins isolation, point by point ablation, intracardiac echocardiography, steerable sheaths were used.

Results: Results of monitoring after AF ablation FS are presented in Table 1.

<table>
<thead>
<tr>
<th>AF burden 12 M (%)</th>
<th>AF burden 3 M (%)</th>
<th>AF burden 12 M (%)</th>
<th>AF burden 3 M (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2 (3M)</td>
<td>5.1 (12M)</td>
<td>19.8 (3M)</td>
<td>19.8 (12M)</td>
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</table>

Conclusion: Reliable detection of AF recurrence after ablation depends on the intensity of monitoring and recurrence characteristics (burden, temporal pattern, symptoms). Intensive monitoring using SQ monitor and remote control leads to more accurate detection of AF recurrence compared to standard 7-day Holter monitoring. It detects multiple events and prolongs the follow-up period. The decrease in the number of thromboembolism may significantly affect the long-term management of anticoagulant therapy in patients after ablation of AF. Using of SQ monitoring against 7-day Holter is still characterized by a higher percentage invalid episodes (23.1% vs 11.2%) due to the detection myopotentials.
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) isolated 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 51%, 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 (CAROTO-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 6±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±34.6cm² vs 185.7±30.0cm² p=0.001), higher LASA not isolated (150.5±28.2cm² vs 127.9±21.0cm², p=0.002) and lower proportions of LASA isolated (25.5±6.3% vs 30.7±8.3%, p=0.008), compared to 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 was an independent predictor of AF recurrence in persistent AF patients (HR 2.66 95% CI (1.47, 4.80), p<0.01).

Conclusion: LASA not isolated is an important predictor of AF recurrence after ablation of persistent but not paroxysmal AF. Importantly, LASA not isolated is LASA not isolated is an important predictor of AF recurrence after initial PVI.

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: At 376±221 days after the first procedure, 47 patients (38%) had recurrence of AF. AHI and left atrial volume index (LAVI) were significantly greater in patients with than without AF recurrence (AHI: 21±12 vs 14±10, p=0.011; LAVI: 45±7 vs 32±10, p<0.0001). LAVI was an independent predictor of AF recurrence after initial PVI in patients with both PAF and PEF (PAF: HR 1.04, 95% CI 1.01–1.07, p=0.008; PEF: HR 1.04, 95% CI 1.01–1.07, p=0.002). However, AHI was not 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 PAF, the sensitivity and specificity of an AHI ≥14.1 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)

Conclusion: AHI measured by type-3 PM is a useful predictor of outcome following initial PVI in patients with PAF.

P4355 | 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 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 with recurrence 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=0.001) were associated with non-responder and the duration of continuous AF (p=0.062) and mean amplitude of f-waves (p=0.013) 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 <0.065mV 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.

P4356 | 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 sinus to the AV node (AVN), have been contested.

Purpose: With the development of 3 dimensional (3D) endocardial electroanatomical mapping techniques, we compared the atrial conduction pattern from the earliest atrial activation site (EAS) via the FIPs to the AVN between paroxysmal and persistent atrial fibrillation (AF).

Methods: The 3D mapping data including the EAS and the conduction pattern via the FIP were evaluated in 95 AF patients (80 men, 59 paroxysmal AF, mean age 58±10 years) at baseline and during isoproterenol infusion. In patients with paroxysmal AF, the sensitivity and specificity of an AHI ≥14.1 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)

Conclusion: AHI measured by type-3 PM is a useful predictor of outcome following initial PVI in patients with PAF.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/509/434476/1598434716/10-January-2019
Impact of circumferential pulmonary vein ablation (CPVA) on heart function.

**Purpose:** 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).

**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 rotor mapping) 64 poles basket catheter during biatrial 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 rotor 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 rotors sources.

**Results:** Rotor activities were documented in both atria (right atrial rotors 2±1.1 [range 1–3], left atrial rotors 2±0.8 [range 0–3]). The primary endpoint was achieved in 9 patients. AF organization to AF 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 biatrial mapping. AF duration recovered in 29.48% patients despite acute conduction block during the index procedure. MI and the roof block were achieved in 89.7% patients during the last procedure. The mean follow-up was 20.6±11.8 months after the last procedure. A recurrence of persistent 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=8.8, 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 no significant trend for recurrence (44.4% vs. 22.4%, P=0.15).

**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.

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**Methods:** CPVA was performed in 9 patients with paroxysmal atrial fibrillation. Beat-to-beat HR and systemic 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 (RMMSD, 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), 24h, 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 (24h 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.

**Conclusions:** CPVA may be performed 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.
P4360 | SPOTLIGHT
An increased sympathetic tone after ablation predicts recurrence of atrial fibrillation: Investigation using cardiac iodine-123-metaiodobenzylguanidine (123I-MIBG) scintigraphy.

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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. However, multivariate analysis demonstrated that an increased sympathetic tone 3 months after ablation was significantly larger in AF after catheter ablation of AF in HF pts. The data raise the question of AF being the cause or the consequence of HF in patients with and without fibrosis.

Conclusion: In addition to the actual ablation success absence of LA fibrosis predicts a significantly larger improvement in LVEF after catheter ablation of AF in HF pts. The data raise the question of AF being the cause or the consequence of HF in patients with and without fibrosis.

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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Introduction: 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 fluoro 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 reduction.

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 unexcitability 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).

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±0.09 min to 0.09±0.01 min (p<0.0006) and median fluoroscopy dose from 883 cGy cm² to 476 cGy cm² (p<0.0001) was achieved (Table I).

Table 1. Results

<table>
<thead>
<tr>
<th>Procedure</th>
<th>CARTO® 3</th>
<th>CartoUnivu™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (min)</td>
<td>143±36</td>
<td>143±40</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>09:00±4:30</td>
<td>12:09±4:05</td>
</tr>
<tr>
<td>Area dose product (cGy² cm³)</td>
<td>476±280</td>
<td>883±550</td>
</tr>
</tbody>
</table>

Conclusion: CartoUnivu™ Module easily integrates into the workflow of pulmonary vein isolation with the endpoint of unexcitability of the ablation line without prolonging the procedure time. It is associated with a more than 50% reduction in fluoroscopic 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 (AED) has been used to identify dormant pulmonary rhythm monitoring in 32, and with 4-day-holer in 14 pts. LVEF was re-evaluated during FU.

Results: Overall 35 (76%) pts. were in stable SR after a median of 1 ablation procedure and a median FU of 6 months (IQR 2, 11). LVZs outside PVs were detected and treated in 18/46 (39%) patients. Success rate tended to be higher in patients without LVZs (82% vs.57%; p=ns). Overall enero uptake improved post-ablation significantly from 30% (IQR 25, 35) to 43% (IQR 35, 50), p<0.001.

Abstract P4360 – Clinical parameters associated with the recurrence of atrial fibrillation after ablation

<table>
<thead>
<tr>
<th>Age, years old</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
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<tr>
<td>With</td>
<td>Without</td>
<td>With</td>
<td>Without</td>
<td></td>
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</tr>
<tr>
<td>Age, years old</td>
<td>65±7</td>
<td>61±11</td>
<td>1.05</td>
<td>0.97–1.17</td>
<td>0.26</td>
<td>1.06</td>
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<tr>
<td>Male, n (%)</td>
<td>7 (88)</td>
<td>22 (69)</td>
<td>2.21</td>
<td>1.59–3.05</td>
<td>0.10</td>
<td>3.55</td>
</tr>
<tr>
<td>Persistent atrial fibrillation, n (%)</td>
<td>4 (50)</td>
<td>14 (44)</td>
<td>1.21</td>
<td>0.29–5.12</td>
<td>0.79</td>
<td>1.03</td>
</tr>
<tr>
<td>Left atrial volume index, cm³/m²</td>
<td>46±29</td>
<td>66±10</td>
<td>1.05</td>
<td>1.00–1.10</td>
<td>0.04</td>
<td>1.03</td>
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<tr>
<td>H/M15min at baseline</td>
<td>1.18±1.10</td>
<td>2.02±0.23</td>
<td>0.58</td>
<td>0.02±1.14</td>
<td>0.74</td>
<td>0.53</td>
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<tr>
<td>H/M240min at baseline</td>
<td>1.98±1.21</td>
<td>2.08±0.30</td>
<td>0.29</td>
<td>0.02±3.25</td>
<td>0.31</td>
<td>1.04</td>
</tr>
<tr>
<td>WR at baseline</td>
<td>36.3±4.8</td>
<td>33.9±9.2</td>
<td>1.10</td>
<td>0.86–1.13</td>
<td>0.35</td>
<td>1.12</td>
</tr>
<tr>
<td>WR at 3 months after ablation</td>
<td>2.08±1.13</td>
<td>2.00±0.24</td>
<td>5.14</td>
<td>0.03–4.75</td>
<td>0.32</td>
<td>0.11</td>
</tr>
<tr>
<td>WR at 3 months after ablation</td>
<td>41±10.8</td>
<td>30.9±10.1</td>
<td>1.13</td>
<td>0.14–1.24</td>
<td>0.003</td>
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</tr>
</tbody>
</table>
Ablation of atrial fibrillation III

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 non-paroxysmal AF as in vagally mediated AF, in which acetylcholine like signal transduction cascade via specific G protein-coupled receptor mediated. This study presented 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 and 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 PV conduction after intravenous ADE challenge was observed 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 terminalis (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 en-rolled. 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 moths further using ECG and Holter monitorings. Additional catheter ablation was offered to patients with recurrence of arrhythmia.

Results: Between 2006 and 2010, 38 patients underwent the procedure (age 60.5±8.7 years, body mass index 29.7±4.2 kg/m2, sex: 26 male). Nineteen patients (50%, 9 24% persistent and 13 34% long-standing persistent AF). The patients diagnosed as paroxysmal AF were 78.7% and the others as non-paroxysmal AF were 21.3%. The dormant PV conduction after intravenous ADE challenge was observed 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 terminalis (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). 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

P4365 | BENCH
A phantom study to assess the accuracy of a new electromagnetic catheter guidance technology (MediGuide)

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Introduction: This 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-Program, then a CT scan was performed on the phantom containing holes at 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 reproducibil-

Acknowledgement/Funding: None

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 exposition 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 skin level was directly and individually measured by radio-photoluminescence dosimeter chips at RAO, PA and LAO position as well as at patient’s forehead. In addition the indirect x-ray exposition of physician was measured by ring dosimeter at the left hand, at left forehead of physician and further at physician left chest above the x-ray lead protection by direct electronic dosimetry.

Results: The procedure and fluoroscopy time of CB was significantly shorter than
Ablation of atrial fibrillation III

Results: The majority of AF/AT recurrences after initial PVI with second-generation CB didn’t increase rate of LA tachycardias.

Conclusions: The data suggest that PAR ablation is a simple, safe, and effective strategy for the treatment of paroxysmal atrial fibrillation (AF) with better long-term outcome than PVIs. 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

P4366 | BEDSIDE

Left atrial size as the strongest predictor of mid-term outcome after ablation of atrial fibrillation using second-generation cryoballoon

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Background: Factors predicting outcome after pulmonary vein isolation (PVI) with second-generation cryoballoon (CBA) have not been sufficiently investigated. The aim of this study was to evaluate the impact of several clinical and procedural parameters on outcome after PVI with CBA.

Methods: Consecutive patients (pts) treated in our institution with CBA since May 2012 were enrolled in the study. After a single transseptal access and PV angiography PVI was performed using a 28-mm CBA. Mapping of PV signals before, during, and after each cryo application was performed with a 3F lasso catheter. The procedural endpoint after PVI was defined as complete elimination of all fragmented signals at the PV antrum with verification of entrance and exit block. The primary endpoint of this study was the first documented recurrence of AF of AF/AT mechanisms.

Results: The study group consisted of 341 pts (209 male) with the following characteristics: paroxysmal AF (PAF) 253 pts (74.2%), median age 60 (IQR's 52.5/75.4–83/66) years, LVEF 62 (59/62)%, history of AF 3.5 (1.9/8.2) years, CHA2DS2-VASC 1.6 (0.1)%. The mean procedure time was 2±0.03 h with a fluoroscopy time of 21±0.5 min. Roof line effectiveness of pulmonary antrum radial-linear (PAR) ablation in comparison with PVI was assessed using esophageal recordings and additional cryo applications between LSPV and RSPV were performed, creating roof line. Conduction block across the LA roof was assessed using established 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 a blanking period. Primary endpoint was defined as occurrence of any atrial arrhythmia >30 sec with antithrombotic drugs. Pts. with symptomatic recurrences of atrial arrhythmias after blanking period underwent repeated ablation or were treated with AADs according to their preference.

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.

Conclusion: The data show that PARI ablation is a simple, safe, and effective strategy for the treatment of paroxysmal AF with better long-term outcome than PVI. PARI ablation may work with multiple effective mechanisms against multiple AF mechanisms.

Acknowledgement/Funding: National natural science foundation of China/Registration Number:CHCTR-TRC-11001191

P4389 | 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 (PARI) 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 133 patients with documented paroxysmal AF were enrolled from 5 centers and randomized to PARI group or PVI 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 15±23 min in PARI group and 178±43 min in PVI group (P<0.001). The fluoroscopy time was 2±7 min in PARI group and 27±11 min in PVI group (P<0.002). AF triggering foci were eliminated in 59 patients (89.4%) in PARI group compared to 4 patients (6.0%) in PVI group (P<0.001). Vagal reflex occurred during ablation in 48 patients (72.7%) in PARI 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 PARI 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 PARI 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 PARI 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 show that PARI ablation is a simple, safe, and effective strategy for the treatment of paroxysmal AF with better long-term outcome than PVI. PARI ablation may work with multiple effective mechanisms against multiple AF mechanisms.

Acknowledgement/Funding: National natural science foundation of China/Registration Number:CHCTR-TRC-11001191

P4570 | BENCH

Impact of left atrial epicardial adiposity on recurrence of atrial fibrillation after catheter ablation

S.L. Zhang, Y. Sun, L.J. Gao, Y.L. Xia, Y.X. Dong, X.M. Yin, D. Chang, T. Cong, Y.Z. Yang, D.D. Mao. First Affiliated Hospital of Dalian Medical University, Department of Cardiology, Dalian, China, People’s Republic of

Background: Left atrial epicardial adiposity is associated with the mechanism of atrial fibrillation (AF).

Conclusion: The data show that PARI ablation is a simple, safe, and effective strategy for the treatment of paroxysmal AF with better long-term outcome than PVI. PARI ablation may work with multiple effective mechanisms against multiple AF mechanisms.

Acknowledgement/Funding: National natural science foundation of China/Registration Number:CHCTR-TRC-11001191

P4537 | BENCH

Impact of left atrial epicardial adiposity on recurrence of atrial fibrillation after catheter ablation

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Background: Left atrial epicardial adiposity is associated with the mechanism of atrial fibrillation (AF).
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, and thoracic aorta (LA-PA), and descending thoracic aorta (LA-THA) in a short-axis view at the mid LA, pericardial 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), Pericardial LA-ESO epicardial fat thickness was assessed by ordinal logistic regression. Univariate, LA-ESO, LA-PA, and LAD were significant predictor of AF burden. After adjusting for age, BMI, LA-TALA-PA 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.
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 fibrillation (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 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=0.50).

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

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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 increase in 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.

Conclusions: Delays in ablation from AF diagnosis negatively influence 5-year rates of AF/Aflutter recurrence. Older patients experienced greater delays and had more comorbidities. Patients >60 years of age receive 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 atrial fibrillation catheter ablation


Background: Plasma von Willebrand factor (vWF) level is associated with ischemic stroke events in patients with atrial fibrillation (AF). High plasma 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 76 patients who underwent catheter ablation for AF. Plasma vWF activity was 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 longstanding persistent AF was 26%, and the mean left atrial diameter was 41 (±9) 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. 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).
Introduction: Localized electrical rotors and focal impulse sources are prevalent sustaining mechanisms for human atrial fibrillation (AF), and can be treated by focal ablation. The cardiac autonomic nervous system also plays an important role in AF but the relation of rotors to ganglionated plexi (GP) has not been studied. The cardiac autonomic nervous system also plays an important role in AF but the relation of rotors to ganglionated plexi (GP) has not been studied.

Methods: We studied 76 patients with AF (61±19.1 years, 74% persistent) 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: 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.

Ablation of fibrillatory rotors and autonomic denervation in atrial fibrillation

Purpose: Patients with refractory paroxysmal AF who were scheduled for cryoballoon-based ablation for AF were included. Monocyte TLR-4 expression was evaluated by flow cytometric analysis in peripheral venous blood samples prior to ablation.

Results: 84 patients (52.4% male; 52±10.4 years) who underwent cryoballoon-based AF ablation with second-generation cryoballoon were included. At a follow-up of 12 months, 11 patients (13.1%) developed AF recurrence. Pre-procedural monocyte TLR-4 expression was significantly higher in patients with AF recurrence [24 (12–59) vs. 19 (9–45%), p=0.007]. In multivariate Cox regression analysis, monocyte TLR-4 expression (HR: 1.062, 95% CI: 1.021–1.105, p=0.003) and left atrial diameter (HR: 5.856, 95% CI: 1.641–20.984, p=0.006) were found to be independent predictors of AF recurrence.

Conclusion: Our findings suggest that along with several established pro-inflammatory markers, such as C-reactive protein or interleukins, pre-procedural monocyte TLR-4 expression may serve as a predictor in AF recurrence.

Adenosine in atrial fibrillation ablation: does it improve the outcome?
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Background: Pulmonary vein isolation is an essential part of the standard ablative treatment for atrial fibrillation. Vein reconnection has been referred as one of the main causes of recurrence after ablation. Adenosine testing at the end of the procedure allows to check for dormant conduction and to further deliver radiofrequency energy at the sites of reconnection aiming to achieve better efficacy and long-lasting pulmonary vein isolation. The impact of this strategy during follow-up after ablation is not well established.

Methods: We evaluated 305 consecutive patients submitted to pulmonary vein isolation since 1st January 2013, 60±11 years old, 47.5% hypertensive, 80.3% paroxysmal atrial fibrillation. The average left atrium volume was 101±28ml. At the end of the procedure, adenosine iv bolus was used in 162 pts (64.5%). Reconnection in at least one vein was observed in 43 pts (26.5%) and further radiofrequency energy was applied. During 173±128 days of follow-up recurrence free was present in 90.5% of patients in adenosine group vs 95.3% in the control group (p=0.76, multivariate, adjusted for difference between groups). Having reconnection and further radiofrequency energy applied in the adenosine group didn’t correlate with better prognosis, 93% free of recurrence in reconnection subgroup vs 89.6% in non reconnection subgroup (p=0.5).

Conclusion: In our registry of patients submitted to pulmonary vein isolation, further radiofrequency delivery in areas of adenosine induced reconnection didn’t improve success rates during follow up. These results do not support the routine use of adenosine during atrial fibrillation ablation.

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).

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±6.8 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 208 [54–402] mg/L, p=0.031), ProBNP (2.4 [1.3–3.7] vs 1.4 [0.6–3.3] mg/L, p=0.05), Idiotypic energy (145 [117–263] vs 100 [71–130] mgJ, p=0.004) and greater left atrium diameter (62.3±6.5 vs 57.2±5.9 mm, p=0.013) and BMI (32.6 [29.9–35.6] vs 27.7 [25.3–30.9] 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 leptin/BMI (RR=3.89, 95% CI: 1.29–10.129, 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.
Conclusions: High and comparable success rate in curing atrial fibrillation by Tar. Crossover from Navistar to nMARQ was never necessary. No complications (82% vs. 83%, p=0.64). In paroxysmal AF the success rate was 85% with Navistar.

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, Biosensor 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 type of AF (paroxysmal, persistent, atrial flutter or fibrillation) has not been compared.

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EP team since the beginning of our LAAC experience (2013). The team consists in 2 experienced electrophysiologists [AF ablation >200 per year], 1 dedicated echograher, 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. Proce-

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±4.7%. The HASBLED average score was 3.6±1; 4±37%.

All indications and contra-indications for OAC due to haemorrhagic events: neurological 71%, gastrointestinal 14%, urological 6%, episcleritis 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 anesthesia (technical procedure time 51±11 min, time after transapental puncture 35±8 min, time for device deployment 10±4 mn). Average scopy time was 6±3mn (2044±1125 μGy m²). The implanted device sizes were: 21 mm/4 pt (9%), 24 mm/19 pts (44%), 27 mm/16pts (37%), 30 mm/2 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-procedure complications, especially no pericardial effusion, no systemic embolization, no stroke and no major bleedings for the first 43 pts. Only one pt 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 outcome 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 corner-

stone 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 experi-

enced 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 first generation VGLA. From January 2009 and 17th May 2013. Follow-up of all pts was consistent with our standard clinical practice with a 7 day Holter being performed at the first clinic visit between 4 and 6 months and, for most patients, again at 12 months post-procedure. 12 lead ECGs were performed at all clinic vis-

its. 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. Acute procedural results show that 692 veins were acutely isolated with a mean

fluoroscopy time of 226 minutes and 20.4 minutes respectively. 170 (158 PAF and 12 persistent AF) patients reached 1 year of follow-up, 130 (82.3%) patients remained free of AF in the PAF group and 9 (75%) in the persever-

ent group. 87 PAF patients have now reached 24 months follow-up and 66 (75.9%) remain free of AF. 54 PAF patients have reached 36 months follow-up with 41 (75.9%) remaining free of AF. 32 PAF patients have reached 48 months follow-up and 24 (75%) remain free of AF. There were no periprocedure complications, especially no pericardial effusion, no systemic embolization, no stroke and no major bleedings for the first 43 pts. Only one pt 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 outcome success rate.

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Comparison of mid-term success rate between single-shot technologies for paroxysmal atrial fibrillation ablation


Introduction: In the last years, experts have focused on developing ablation tech-

iques, so-called single-shot ablation, with the possibility of a shortened learning curve, a single transapental 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 suc-

cess between three different single-shot technologies available in our Centre for pulmonary vein isolation (PVI): cryoenergy using the Arctic Front Advance™, ra-

diofrequency using the mRadio™ catheter and laser energy using the HeartLight™ system. Methods: We compared 50 patients with paroxysmal atrial fibrillation (AF) who un-

derwent AF ablation with the second-generation cryoballoon (CB) to 50 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-

ing 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 proce-

dure times in the LB group (148.2±45.0, 152.7±45.5, 190.3±47.3 min, respec-

tively, 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%, whilst in the ICMC was 84% with no statistically significant differ-

ence (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. Fluo-

roscopy times were similar in all groups, whilst procedural times using the LB were significantly longer than the other groups.

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Optimal ablation strategies in long standing persistent atrial fibrillation using CARTO calculated


Introduction: Catheter ablation (CA) is widely used as a treatment option for some form of atrial fibrillation (AF). CARTO System for paroxysmal AF where single procedure results are high. In non-paroxysmal AF, the best ablation strategy is yet to be determined as results are still suboptimal with patients often requir-

ing multiple procedures. We report preliminary results from a prospective study

Ablation of atrial fibrillation V 741

Correlation between LAPA and TTE

Conclusion: Assessment of LA remodeling by TTE with STE correlates well with the extent of LA fibrosis measured by EAM. Thus, STE may be useful in non-

invasive assessment of LA fibrosis and proper selection of candidates for CA. These preliminary findings warrant further examinations.
comparing thoracoscopic left atrial (LA) surgical ablation (SA) with conventional percutaneous catheter ablation in patients with de-novo long standing persistent atrial fibrillation (LS-PAF).

**Methods:** In the SA group, thoracoscopic bipolar radio frequency ablation was performed in 26 consecutive patients with pulmonary vein isolation (PVI) using a bilateral mini-thoracotomy. All LA walls were created using linear ablation connecting the two superior and inferior veins. The LA appendage was excluded in 14 patients. In the CA group, 25 consecutive patients underwent a stepwise lesion set: 1) PV; 2) linear ablation (LA roof and mitral isthmus); and 3) ablation of complete atrial flutter. The LSPAF. of LSPAF was associated with progressive longitudinal dissociation in conduction and a higher incidence of focal fibrillation waves. The goal of this study is to provide direct evidence that the substrate of LSPAF consists of an electrical double-layer of focal fibrillation waves that are out of phase, may conduct transmurally and create breakthrough waves in the opposite layer.

**Results:** In the study, 24 pt undergoing their first ablation for persist AF (6/24 (25%) in 12 of 21 pt (57%). Median number of sources obtained was 10 ± 7 (range 1-37) in 12 of 21 pt (57%). Median number of sources in patient per RA was 1 [1-3], and 3 [1-4] in LA. Rate of RA sources 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. All (17%) were detected within a typical circumferential PVI 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 10/24 (42%) of patients. Of the two patients (9%) AF converted to a regular atrial fibrillation (AF), 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 re-viewed for patient characteristics and outcomes.

**Conclusions:** 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=0.006) and in-hospital mortality (POAF 17% vs control 4%, p=0.006). While the index admission length of stay was similar, POAF was associated with significantly increased hospital costs (POAF $26724±7308 vs $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.

**Purpose:** In patients with paroxysmal atrial fibrillation (PAF), the second genera- tion cryoballo- tion (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 paroxysmal nerve (PN) palsy (PNP). Considering the increased efficacy and risk of complications, the necessity and safety of the recommended two times 4-minute cryother- apy 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 cryoballoon.

**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 <400 cm³. Patients are randomised to two times 1.2 or 3 minutes of cryoballoon 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 adenosine. During applications of the right PVs the PN is constantly stimulated and excursion of the diaphragm is monitored manually. If no PVI can be achieved with the assigned cryotherapy duration 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 were randomised to the 1 minute group, 9 in the 2- and 3 minutes group. In all patients the 28 mm cryoballoon was used. In the 1 minute group 25/32 PVI were primary successful, in the 2 minutes group 27/36 and in the 3 minutes group 25/36. 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 PNP after isolation of the right superior PV. In 9/36 right sided PVS in the 2- and 3 minutes group, applications had to be terminated prematurely due to loss of PN capture whereas no application had to be terminated in the one minute group. All PNP’s were (eventually) transient.

**Conclusion:** Using the second generation cryoballoon two times 113±13 seconds of cryotherapy achieves 78% PVI without PNP. These preliminary results indicate that shorter initial cryoapplications might be considered.

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**Having sinus rhythm definitely pays off. PRAgue-12 randomized study sub-analysis**

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**Background:** Concomitant surgical ablation (SA) of atrial fibrillation (AF) is routinely performed in cardiac surgery patients. Recent meta-analyses and reviews have shown its good efficacy in restoring and maintaining sinus rhythm but also an unclear clinical benefit for patients.

**Methods:** PRAgue-12 is a prospective, randomized study, assessing the effect of adding SA of AF to other cardiac surgery (SA patients vs. Non-SA patients). In present sub-analysis, patients from the study were examined and grouped according to their complete AF-free survival during the first postoperative year (patients who had sinus rhythm in all postoperative check-ups were considered AF-free, patient with AF recurrence were Non AF-Free). Occurrence of death, stroke, heart failure and bleeding was compared between both groups (AF-Free vs. Non AF-Free).

**Results:** One hundred ninety-two patients were analyzed (104 SA patients and 88 Non-SA patients), out of which 61 (32%) were AF-free and 131 (68%) were Non AF-Free. The primary combined endpoint (death, stroke, heart failure) was present in 6 AF-free patients vs 45 Non AF-free patients (HR 0.25, 95% CI 0.11–0.59, p=0.001; Figure 1). Separately, only heart failure was significantly different between both groups (5 patients AF-Free vs. 39 patients Non AF-Free, HR 0.25, 95% CI 0.09–0.66, p=0.003), other endpoints were nonsignificant. Adjusted Cox-regression analysis has shown that the AF-Free survival (p=0.001), but not the surgical ablation (p=0.844) was the predictor of occurrence of clinical complications after the surgery.

**Conclusions:** In AF patients who undergo a cardiac surgery, restoring and maintaining of stable sinus rhythm is related with significantly lower occurrence of clinical complications during one year after the surgery.

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**High incidence of low esophageal temperatures during second generation cryoballoon therapy for atrial fibrillation**

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Introduction The second generation cryoballoon (CB) (Arctic Front Advance, Medtronic) achieves significantly faster pulmonary vein (PV) isolation times and lower late atrial fibrillation 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, oesophageal lesions, atro-oesophageal 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±4.9kg/m². In 9/17 patients with low ET BMI was <25kg/m². In the 13 patients having a BMI >31 kg/m², ET were all <24°C.

**Conclusions:** In our study population second generation CB PV isolation leads to ET <20°C in 22%, 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: MAIC 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 ROCET 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.

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 effect of rivaroxaban compared with warfarin for prevention of stroke or TIA. (p=0.04).

Acknowledgement/Funding: This study was funded by Pfizer and BMS

P4399 | BEDSIDE
Predictive value of CHA2DS2-VASc score for thromboembolic events in non selected outpatients without atrial fibrillation
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Background: Nowadays CHA2DS2VASc 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 a 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 22 vs 42% (p < 0.001), heart failure 6 vs 17% (p < 0.001), previous stroke/TIA 4.6 vs 11.8% (p < 0.001), GFR < 60 mL/min/m² 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 single 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 37 aspirin. Coagulation profile, clot strength and fibrin clot lysis indices are analysed by Thromboelastography (TEG), fibrinolysis and turbidimetric assay.

Results: Using TEG, the ability of warfarin and rivaroxaban to delay fibrin clot formation was confirmed, with delay times increased as opposed to aspirin (7.3 min vs 8.4 min vs 5.0 min, p < 0.0001). More gentle u-angle (63.2° vs 63.6° vs 69.1°, p < 0.004) was seen in warfarin and rivaroxaban compared as antplatelet user. No significant differences were seen in Maximum Amplitude (MA) of clot achieved between 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 180 s vs 204 s, p = 0.026) when compared to aspirin. When compared directly with warfarin, rivaroxaban resulted 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 u-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 resulting in formation of clots which are more responsive to lysis.
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/or supratherapeutic INR range).

Results: The study population comprised 29,717 incident AF patients and 19,113 incident VTE patients who initiated warfarin. For both cohorts, patient characteristics that contributed to sub- and supratherapeutic INR were identified. 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 sub and/or supratherapeutic INRs was more common in AF patients who were current smokers (AF: OR 1:21; 95% CI 1.06-1.38; 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). Constantly, poor anticoagulation control on warfarin, as measured by TTR.

Conclusions: In a real world clinical practice setting there is a high amount of unpredictable inter-individual TTR variability and in some patients good anticoagulation control is more challenging to achieve and maintain than in others. These findings draw attention to the difficulty of achieving high-quality anticoagulation control with warfarin clinical practice and may help to identify patients who will require closer monitoring or innovative management strategies to optimise the outcomes of oral anticoagulant therapy.

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. To decide the current guidelines recommend 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 thrombi 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 B3 AF patients (mean age, 66±9.8 years; 62% men) who underwent transesophageal echocardiography (TEE) to exclude LA thrombus before electrical cardioversion or radiofrequency pulmonary vein isolation for AF were retrospectively evaluated. The patients were divided into 2 groups according to anticoagulation therapy: Warfarin (n=31) and NOAC (n=52; dabigatran: n=25, rivaroxaban: n=22, apixaban: n=5). In all patients, each anticoagulants were continued for more than 4 weeks before TEE.

Results: In the warfarin-group, LA thrombi were detected in 3 patients (9.7%). On the other hand, 7 patients in the NOAC-group had LA thrombi (13.2%). The prevalence of LA thrombi was equivalent between 2 groups. Baseline characteristics and TEE findings and prevalence of persistent AF were compared between 2 groups.

In the NOAC-group, the patients with LA thrombus had more risk factors than those without LA thrombus (mean CHA2DS2 score: 2±1.5 vs. 1±1.09, p<0.05). Furthermore, in the patients with LA thrombus, the prevalence of LA spontaneous echo contrast was greater than in those without thrombus significantly (85.7% vs. 33.3%, p<0.05). Although LA appendage emptying velocity was lower in the patients with LA thrombus than in those without LA thrombus, it was not statistically significant (24.3±13.8 vs. 37.1±19.8, p>0.05).

Conclusions: The prevalence of LA thrombi was not rare in the patients with AF under NOAC therapy. Even though the patients take any anticoagulant, especially in the high risk, TEE is necessary to detect LA thrombi before cardioversion or radiofrequency pulmonary vein isolation for the prevention of systemic embolization.

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-valual 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.

Conclusions: The need of dosage adjustment of NOAC along follow-up is frequent in patients with AF after ADHF, especially among the elderly or those with renal impairment. Further studies are needed to clarify the clinical importance of these needs of drug dosing adjustment and the ideal renal function monitoring regime in heart failure and other subgroups of patients with AF.

P4404 | BEDSIDE Evolving antithrombotic treatment patterns in patients with 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 75±9 years; C2 (2011–13), n=11,652, mean CHA2DS2-VASc 3.3; C3 (2013–14), n=9938, mean CHA2DS2-VASc 3.2. Baseline characteristics and antithrombotic therapy initiated at diagnosis were analysed by cohort.

Conclusions: The proportion of patients on anticoagulant (AC) therapy increased (C1 57.5%; C2 62.3%; C3 67.5%). Use of vitamin K antagonist (VKA) ±antiplatelet (AP) therapy decreased (C1 53.3%; C2 48.5%; C3 41.1%), while use of non-VKA oral ACs increased (C1 30.8±25.6 vs. 47.3±18.8, p=0.07). In the NOAC-group, the patients with LA thrombus had more risk factors than patients without LA thrombus (target international normalized ratio [INR] = 2.0–3.0) for 3–4 weeks before electrical or pharmacological cardioversion without exclusion of LA thrombi by transesophageal echocardiography (TEE). However, there is little information on the safety of cardioversion without TEE on NOAC therapy.

Hypothetical dosing adjustments

Conclusions: The need of dosage adjustment of NOAC along follow-up is frequent in patients with AF after ADHF, especially among the elderly or those with renal impairment. Further studies are needed to clarify the clinical importance of these needs of drug dosing adjustment and the ideal renal function monitoring regime in heart failure and other subgroups of patients with AF.
of AC was mainly in patients with CHA2DS2-VASc ≥ 2, with a smaller increase in patients with a score of 1. Use of AC in patients with a score of 0 (but with an investigator-defined stroke risk factor) varied from 35.3–45.0%.

Conclusion: Since the introduction of NOACs, newly diagnosed at-risk AF patients are more often receiving guidelinerecommended therapy driven by increased use of NOACs and less treatment with VKAs 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: a 2-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 thromboembolic and bleeding outcomes, remains unproved.

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 events and bleeding events were 4.1/100 person years and 9.6/100 person years respectively. All three scores (CHA2DS2, CHA2DS2-VASc and HAS-BLED) could detect all embolic events (c=0.808–0.838) and ischaemic stroke (0.825-0.880), but not bleeding events (c=0.459–0.498). Warfarin use was independently associated with increased rates of intracranial bleed (hazard ratio (HR)=11.1, P<0.038) and other non-intracranial or gastrointestinal bleeds (HR=3.26, P=0.028), but not associated with reduced risk of ischaemic stroke (HR=0.629, P=0.558), or mortality during follow-up (HR=0.892, P=0.634).

Conclusions: Anticoagulation with warfarin did not reduce embolic risk in dialysis patients, but also increased the risk of intracranial or other bleeds. Convention risk scores remain good discriminators of embolic but not bleeding events in dialysis patients.

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 among the provincial, prefecture level and county level hospitals for acute myocardial infarction (AMI) in China.

Methods: From Jan. 2013 to Sep. 2014, 16,113 ST-segment elevation myocardial infarction (STEMI) patients and 6,463 non-STMI (NSTEMI) patients from 89 China hospitals were registered in the China Acute myocardial infarction (CAMI) Registry. 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 or angiotensin receptor blockers). Use of primary percutaneous intervention for AMI, 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 all 10 performance measures, the rate of patients undergoing reperfusion therapy (thrombolytic therapy or PCI) in STEMI patients within symptom onset less than 12 hours is 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 that for NSTEMI were 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, further work is required to assess STMI patients in an area with a high occurrence of acute myocardial infarction to determine the effectiveness of strategies for improving quality of care. Further studies are required to determine the effectiveness of strategies for improving quality of care and standard for STEMI 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 circumflex artery (LCX) lesions is of paramount importance for management and outcome. Using lead aVR, we assessed the ST 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 lead aVR and absence of typical ECG leads in the development of death, myocardial infarction and new onset atrial fibrillation.

Conclusions: Lead aVR was used as primary angioplasty or within 24 hrs of hospital admission was taken for study. 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 variables, 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 HASS-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, 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

P4406 | BEDSIDE
L-theanine, a new armamentarium for culprit artery localization in acute inferior wall myocardial infarction; will it be the first point for artery localization?

Background: Early discrimination of culprit artery in acute inferior ST elevation myocardial infarction (STEMI) caused by right coronary artery (RCA) and left circumflex artery (LCX) lesions is of paramount importance for management and outcome. Existing criteria have poor sensitivity for LCX and poor specificity for RCA. If reliable smaller ECG patterns can be recognized, it will be possible to determine the culprit coronary artery earlier and facilitate the management. OBJECTIVE: To study if use of LCX and RCA as primary angioplasty or within 24 hrs of hospital admission was taken for study. 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 variables, 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 HASS-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, 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.
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–minutes intervals, 576 points during 48 hours. Endothelial function was assessed before discharge by measuring nitric oxide (NO) release from umbilical vein endothelial cells cultured at 10 mmol/l L-Arginine. Intra-individual NO release was correlated with glucose variability (day 1–3 days and day 8–10 days).

Results: Glycemic variability, as indicated by the mean amplitude of glycemic excursions (MAGE), was measured and divided into 3 groups. The MAGE values by MAGE tertiles (≥5.15 mmol/L, 3.36–5.15 mmol/L, 3.36<mmol/L) had significant difference among 3 groups (figure). Blood glucose fluctuation was correlated with MAGE, 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 involved in the setting of myocardial injury.

Purpose: 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 baseline and 4 months after STEMI using late gadolinium contrast-enhanced CMR. Corin concentrations were determined from blood samples drawn at a median of 3.3 days after STEMI (1–33 days). All patients were recruited within 4 months of STEMI. Logistic regression models were used to assess the relationship between corin concentrations and IS.

Results: This study cohort included 50 patients (median age: 59 years (IQR 51–66 years); females: 7 (14%)). Corin concentrations (median = 1084 pg/ml, IQR 709–1743 pg/ml) were significantly associated with 4-month IS (r=0.36, 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

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Background: Early reports showed that any delay in reperfusion with primary PCI may have a prognostic relevance as an index of the setting of myocardial injury.

Purpose: We sought to assess the prognostic impact of FMCCT 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 profile.

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.

<table>
<thead>
<tr>
<th>No transfer (n=1330)</th>
<th>Transfer (n=350)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>67.0±11.6</td>
<td>66.7±13.2</td>
</tr>
<tr>
<td>Females</td>
<td>26.7%</td>
<td>26.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24.3%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>41.3%</td>
<td>36.1%</td>
</tr>
<tr>
<td>TIMI Risk Index</td>
<td>30.9±16.3</td>
<td>31.5±19.1</td>
</tr>
<tr>
<td>FMCCT time</td>
<td>77 [63–97]</td>
<td>104 [89–132]</td>
</tr>
<tr>
<td>Luminex time</td>
<td>180 [123–260]</td>
<td>231 [118–398]</td>
</tr>
<tr>
<td>Open vessel before PCI</td>
<td>33.2%</td>
<td>37.1%</td>
</tr>
<tr>
<td>Open vessel after PCI</td>
<td>95.7%</td>
<td>97.9%</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>7.1%</td>
<td>6.6%</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.

P4415 | 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) STE 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.

P4416 | BEDSIDE
High-sensitivity troponin T for prediction of left ventricular function and infarct size one year following STEMI

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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), repurposed by PCI for first-time STEMI, were enrolled in this single-centre, observational study. Serial hs-cTnT, creatinine 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; p < 0.001), and infarct size (IS; p = 0.021) 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 characteristics analysis, the area 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, 0.91) 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.

Conclusion: 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 I

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 aid of 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 mass, 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±3.9 vs. 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 pejorative course (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=1.129 [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 independently associated with LVR.

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, infiltrating 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 reduced risk of CVD, with specific characteristics, anomalous glyemic 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 MedDietscore (range 0–55). Higher values indicate greater adherence to the Mediterranean diet. The sample was classified in two categories: low MedDietscore (<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 myocardial 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 0.615–1.032, 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

P4419 | BEDSIDE

Introduction: Current practice guidelines for management of patients with NSTEMI strongly recommend using GRACE risk score for thrombotic risk stratification at hospital discharge.

Purpose: The aim of this study is to analyse the capability of the GRACE score when it comes to predicting the risk of post-discharge death in patients with NSTEMI.

Methods: 1,885 consecutive patients with primary diagnosis of NSTEMI at discharge have been investigated. GRACE score was calculated as a continuous variable and categorised (High-intermediate-low risk). Patients were classified as NONCA or OCAD depending on their stenotic lesions (NONCA or ≥50% in LMCA).

Results: 20.6% had NONCA. GRACE score was 126±27 in the NONCA group (118±18 vs. OCAD, p<0.001). The GRACE score classified more high-risk patients in NONCA (59.9% vs than in OCAD 50% and p=0.005). There were 454 (24.3%) deaths; 72 in the NONCA group (18.8%). As a continuous variable GRACE score was significantly associated with death (HR=1.034; 95% CI 1.03 to 1.04), this remained in both, NONCA and OCAD, subgroups.

The GRACE classification showed a significant association with mortality for high-risk stratum both in NONCA and OCAD groups. However, in NONCA intermediate risk patients there was no significant association with death (HR=1.017, 95% CI 0.22 to 4.90).

By Youden’s test the optimal cutoff GRACE score was estimated to identify patients at risk of death within the group of NONCA. A score >132 yielded a sensitivity (SN) of 84% and specificity (SP) of 65% (vs. SN and SP of 90% and 45%, respectively, exhibited by the original cutoff >120 to define high risk death). It also achieve an index of net reclassification improvement of 9.2% (95% CI 2.3%-16.1%; p=0.009).

Conclusions: Data suggests that the GRACE score for predicting risk of post-discharged death classified erroneously patients with NSTEMI and NONCA, overestimating the risk of death; since these patients are penalised 14 points by not performing ICP at hospital. Results highlight the need to redefine GRACE cutoffs for patients with NONCA in the context of an NSTEMI.

P4420 | BEDSIDE
Infarction acute phase STEMI / Post infraction period I


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Background: Multivessel disease (MVD) in patients presenting with ST Elevation Myocardial Infarction (STEMI) is common. Currently the ESC and the ACC/AHA guidelines recommend revascularization of the culprit artery only but 2 recent
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% (68%–93% as FFR 100%). A sensitivity 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 guide to complete revascularisation led to an 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, routine to complete revascularisation leading to an average saving of €302/patient (CMR) and €395/patient (echo) either direct or FFR guided is associated with a three-year unfavorable prognosis.

**P4421 | BENCH**

**The personalized assessment of severity of st-segment elevation myocardial infarction:** clinical, angiographic and genetic polymorphisms, associated with lipid disorders and hypertension

V. Kasthtalap on behalf of Inozemtseva A.A., Gordeeva L.A., Barabash O.L.

**Aim:** To investigate the clinical significance of single-nucleotide polymorphisms (SNPs) APOA1 (rs670, APOA5 (rs662799), ACE (rs4646994) in patients with ST-segment elevation myocardial infarction (STEMI).

**Materials:** 179 patients (114 males (63.7%), 65 females (36.3%), the mean age 61.8±11.1 years) admitted with a diagnosis of STEMI were included in the study. Blood samples were collected on days 2–14 for genotyping. DNA was isolated from peripheral blood lymphocytes by phenol-chloroform extraction followed by ethanol precipitation. Amplification of SNPs APOA1 G-75A (rs670), APOA5 T -1131C (rs662799), ACE (rs4646994) was detected using the real-time polymerase chain reaction (PCR). Clinical and demographic data, anthropometric measures, laboratory data and instrumental findings were assessed; end-points were measured at 1 and 3 years. The endpoints were death, recurrent myocardial infarction, acute cerebrovascular accident (ACVA), progressive angina. Data analysis was performed using the STATISTICA program (version 8.0; StatSoft, Tulsa, Oklahoma) and the genetic calculators (GeneXpert) with the creation of multiplicative, common, additive, dominant inheritance models.

**Results:** The apolipoprotein A1 (APOA1) C allele reported a statistically significant association with the presence of multivessel coronary artery disease (OR=1.59; 95% CI: 1.09–2.33; p=0.02). The apoA1-GG genotype demonstrated a significant association with the presence of multivesel coronary artery disease (OR=1.59; 95% CI: 1.09–2.33; p=0.02). The apoA1-GG genotype demonstrated a significant association with the presence of obesity (OR=2.64; 95% CI: 1.37–8.55; p=0.02). The GG-genotype is also associated with less frequency of primary PCI, usually because of severe multivessel coronary artery disease (OR=1.59; 95% CI: 1.09–2.33; p=0.02). The APOA1-GG genotype demonstrated a significant association with the presence of obesity (OR=0.61; 95% CI: 0.38–0.96; p=0.03).

**Conclusions:** Our study demonstrated that in patients undergoing PPCI, routine to complete revascularisation leading to an average saving of €302/patient (CMR) and €395/patient (echo) either direct or FFR guided is associated with a three-year unfavorable prognosis.
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%). Predefined 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 with 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 op group (p=0.0001). Control group of pts had more hypertensives (p=0.0212), smokers (p=0.0001) and with more pts with previous angina (p=0.0318) and previous AMI (p=0.0001). 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.

**Conclusions:** 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, diuretics 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 (anti-AMI) and underwent percutaneous coronary intervention (PCI).

**Methods:** 36 anti-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 anti-AMI. Although 15.8% of LV SEC patients were NSTEMI, LVT developed only in STEMI. 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 STEMI 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 reversely related to LVT formation. STEMI patients with SEC and future LVT formation who had underwent 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.

**Predictors of LVT in patients with LVSEC**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>STEMI patients with LV SEC</th>
<th>STEMI patients with LV SEC treated with primary PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7 (77.8%)</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>5 (55.6%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Pulmonary edema on admission</td>
<td>4 (44.4%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>3 (33.3%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>≥ 46.0%</td>
<td>≥ 46.0%</td>
</tr>
<tr>
<td>WMSI</td>
<td>2.15±0.224</td>
<td>1.97±0.193</td>
</tr>
<tr>
<td>Lowest Hb during hospital stay (g/dL)</td>
<td>11.59±1.76</td>
<td>13.42±1.54</td>
</tr>
<tr>
<td>CHF hospitalization during follow-up</td>
<td>3 (33.3%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Conclusions:** Among anti-AMI patients with LV SEC, LVT developed in 23.7%, only in STEMI patients. SEC formation was not associated with embolic events but with post-MI CHF hospitalization.

**P4427 | BEDSIDE**
Predictive value of plasma galectin-3 levels for in-hospital and long-term complications of patients with right ventricular myocardial infarction

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**Background:** There is uncertainty regarding the risk of major complications in patients with the right ventricle (RV) myocardial infarction (MI) on the background of the posterior Q-MI of the left ventricle (LV). Galectin-3 takes part in many mechanisms of atherothrombosis, such as inflammation, proliferation and fibrosis, and
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±7.87 years. Galectin-3 levels were determined with enzyme immunoassay on day 2 of MI. Follow-up was 2.6±1.4 years. Study endpoints were: unstable angina (UA), recurrent myocardial infarction (Re-MI), stroke, or 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 complicated 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<0.001). 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 follow-up.

**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.

**P4420 | 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 has better clinical outcomes regarding of cholesterol level. 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 of hs-CRP reduction during one-year (≥80% 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 (HR 0.69, 95% CI 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**

Long term prognostic value of worsening renal function and uric acid in-hospital changes in patients with acute myocardial infarction

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**Purpose:** We investigated the incidence and prognostic value of worsening renal function (WRF) and uric acid (UA) in-hospital changes regarding 1 year mortality in 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 UA elevation only (38.2 vs 11.7%, log-rank p=0.0011) 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 mg/dl have a synergistic adverse effect on 1-year outcome in AMI patients. Among them WRF appear as a stronger predictor of adverse outcome.

**P4430 | BEDSIDE**

The role of unprocessed meat consumption on the 10-year (2004-2014) acute coronary syndrome (ACS) prognosis

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**Background:** Results of recent studies are equivocal regarding the effect of unprocessed red meat consumption on the increased risk of Cardiovascular Disease (CVD), in the general population; while processed meat has been linked to a significantly higher risk for developing heart disease. However, similar studies on the secondary coronary heart disease prevention are scarce.

**Purpose:** The present study aimed to investigate the association between the long-term risk of 10-year ACS prognosis.

**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). Multiple logistic regression models were applied to estimate the impact of unprocessed red meat consumption (as assessed by using a validated semi-quantitative food frequency questionnaire) in the ACS prognosis. **Results:** No significant association was observed between red meat intake and CVD incidence after taking into account various potential confounders; red meat intake 1–2 times/week (OR=0.870, 95% CI 0.536–1.412, p=0.572), 3–5 times/week (OR=0.851, 95% CI 0.518–1.399, p=0.524) and >5 times/week (OR=0.760, 95% CI 0.429–1.346, p=0.347).

**Conclusion:** The guidelines or recommendations, about the total red meat intake, either in primary or secondary heart disease prevention should probably be re-evaluated. Further research on the consumption of processed vs. unprocessed meat on the long-term ACS prognosis is needed to evaluate the different effects on heart health.

**Acknowledgement/Funding:** None to declare
P4431 | BEDSIDE

The long-term prognosis of patients diagnosed as type 2 myocardial infarction does not differ from that of patients with myocardial infarction.

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Introduction: The differentiation between patients (pts) with type 2 myocardial infarction (T2MI) and those with myocardial injury.

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 cTnI 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 cTnI 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 co-factors and additive regarding the use of novel biomarkers.

Conclusion: 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.

P4433 | 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 STE-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 coronarography for planned primary PCI.

Methods: From January 2009 to December 2010, in a single high-volume center, 1949 consecutive patients underwent urgent coronarography 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<0.01), had less ad-hoc PCI (70% vs 91%; p<0.01), 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).

Conclusion: 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 2.45; 95% CI 2.01–4.13; p<0.001) (figure 1 and 2).

P4432 | BEDSIDE

Spot urine albumin to creatinine ratio outperforms novel acute kidney injury biomarkers in patients with acute myocardial infarction

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Background: Acute kidney injury (AKI) is a frequent complication in patients hospitalized for acute myocardial infarction (AMI), and is associated with in-hospital and long-term morbidity and mortality.

Purpose: We prospectively assessed the diagnostic performance of spot urine albumin to creatinine ratio (uACR) in an adequately sized multicenter cohort of patients admitted to hospital with AMI. We further compared uACR to novel renal injury biomarkers in patients with acute myocardial infarction.

Methods: From January 2009 to December 2010, in a single high-volume center, 1949 consecutive patients underwent urgent coronary angiography 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<0.01), had less ad-hoc PCI (70% vs 91%; p<0.01), 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).

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.

P4434 | 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: Left ventricular (LV) function is a key determinant of outcome after ST-segment elevation myocardial infarction (STEMI). LV global longitudinal strain (LV-GLS) has shown to be a sensitive measure of myocardium deformation and may act as a major prognostic marker. Our aim is to assess the predictive value of LV-GLS on all-cause mortality and heart failure (HF) hospitalization and compare it to other echocardiographic parameters, to GRACE and TIMI risk scores and to BNP on admission.

Methods: We retrospectively analysed consecutive patients (P) with STEMI and no prior cardiovascular event who were admitted to our centre during 18 months. Clinical profile and laboratory data were collected on admission and transthoracic echocardiogram was performed 72 to 96h after STEMI. Semiautomatic LV-GLS was calculated offline as the mean value of longitudinal strain from apical (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.
P4435 | BEDSIDE
Improved survival after out-of-hospital cardiac arrest most substantial in younger patients - results from a statewide quality improvement initiative in North Carolina (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%), 1938 (31.1%), 1983 (31.8%) and 1348 (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=0.01; 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=0.03). 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=0.06; 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.

P4436 | BEDSIDE
CPR quality in out-of-hospital cardiac arrest patients treated with basic- versus advanced life support with and without mechanical chest compressions

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Background: Focus on providing high-quality cardiopulmonary resuscitation (CPR) has increased during recent years; major changes have been implemented in the resuscitation guidelines and the use of mechanical chest compression systems have gained popularity. However, only few studies have addressed the impact of these measures on CPR quality in out-of-hospital cardiac arrest patients.

Methods: Data on adult non-traumatic out-of-hospital cardiac arrest patients treated by the emergency medical service in the central Denmark region between 1 April 2013 and 31 January 2014 were prospectively collected before (Pre-intervention) and after (Post-intervention) implementation of the LUCAS mechanical chest compression device. Patients were subdivided according to treatment by the paramedic-manned ambulances (BLS group), the physician-manned Pre-hospital Critical Care Teams and Helicopter EMS (ALS group). Patient medical records and electrocardiograms with transthoracic impedance signals, registered from the LIFEPAK defibrillator, were reviewed. Quality of CPR was assessed in terms of no-flow time (NFT), no-flow fraction (NFF) and chest compression rate.

Results: Attempt of resuscitation was reported on 856 patients of which 111 comprised the Pre-intervention group (BLS=31 and ALS=80) and 482 comprised the Post-intervention group (BLS=66, ALS=259 and ALS + LUCAS=157). A total of 263 patients were excluded due to missing data. The post-intervention group receiving LUCAS CPR was more likely to have a witnessed, bystander cardiac arrest with VF/VT, lower commodity and received better CPR quality with a NFF of 25% vs. 36% (p<0.001) and shorter pre- and post-shock pauses, NFT of 18 seconds vs. 24 seconds (p<0.001), compared with the Post-intervention group receiving manual CPR only. The majority of patients (84%) were resuscitated with the involvement of physicians (ALS group), and these patients had significantly lower NFF compared with the BLS group, 31% vs. 38% (p<0.001). The quality of BLS and ALS provided CPR seen in this study was remarkable improved compared to the previous evaluation of CPR quality in 2005.

Conclusion: Implementation of mechanical chest compressions during CPR was associated with lower no-flow fraction. The physician provided ALS was superior to the paramedic provided BLS, however, both BLS and ALS have improved remarkable during the past 10 years.


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.

Methods: We assessed the hypothesis that higher glucose levels are associated with worse outcomes in patients after cardiac arrest in the current therapeutic hypothermia era.

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 admission, 6 h, and 24 h after the procedure, and the Q1, Q2, Q3, and Q4 groups, respectively. Survival in patients after cardiac arrest was 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 in patients after cardiac arrest.

Conclusions: In patients after cardiac arrest, the outcomes, severity of illness, and time intervals 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.
P4438 | BEDSIDE
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 in-hospital mortality, and less than 10% of patients will survive without neurological damage. Accordingly, early coronary angiography (CA) has been proposed in OHCA patients in order to improve survival.

Aim: To identify the impact of coronary angiography 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 left ventricular 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 logistic analysis, APACHE II score (p = 0.002), level of lactates at admission (p < 0.0006), 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 (GOS 5).

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 limited 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.

P4439 | BEDSIDE
Using of LUCAS device for CPR by regional non-urban Medical Emergency Service
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Background: LUCAS II was developed for automatic chest compressions during cardiopulmonary resuscitation (CPR). Current evidence on the use of this device in out-of-hospital cardiac arrest (OHCA) is still insufficient.

Purpose: The main purpose of this study was to compare the effect of CPR for OHCA with and without LUCAS by Regional non-urban Medical Emergency Service (EMS) in physician-present pre-hospital medical system (randes-vouz system).

Methods: We analyzed a prospective registry of all consecutive OHCA patients in four EMS stations, two of them used LUCAS device in all CPR, the EMS crews in other two stations used manual CPR. Individuals with contraindication to LUCAS or with EMS-witnessed arrest were excluded.

Results: From May 2010 to June 2014 337 patients were included in the OHCA registry. Fifty-nine patients were excluded from the analysis because of contra-indications to LUCAS or EMS-witnessed arrest. Data from 278 patients were included in the analysis, 144 with LUCAS and 134 with manual CPR. Baseline characteristics are shown in Table 1.

We observed more witnessed arrests in LUCAS group (64,18% vs. 79,17%; p = 0,0074) and more asystoly as initial rhythm in LUCAS group (48,51% vs. 69,44%; p = 0,0004). We did not find significant differences in return of spontaneous circulation (ROSC) between the groups (30,6% in non-LUCAS vs. 25% in LUCAS). In analysing in-hospital cardiac arrest (31,25% vs. 25% in non-LUCAS vs. 24,18% in LUCAS, p = 0,31) and in ROSC initial rhythm was ventricular fibrillation (51,43% in non-LUCAS vs. 46,43% in LUCAS, p = 0,80). In LUCAS group we observed significant more conversions from non-shockable to shockable rhythm (10,10% vs. 20,7%, p = 0,0396). 180 days follow up was provided by in-patients neurological prognosis with ROSC in both groups. We observed significant more survivors in non-LUCAS group (p = 0,0198). Figure 1. We did not find any survival difference in arrests of presumed cardiac etiology (p = 0,3175), Figure 2.

Conclusions: The use of automated chest compressions with LUCAS system in our study did not improve survival rate in OHCA. We observed significantly higher 180 days mortality in LUCAS treated patients by regional non-urban EMS.

P4440 | BEDSIDE
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 membrane oxygenation (ECMO) or inotropic support. The vitamin D level was measured as plasma 25(OH)D concentrations 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 55.4±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%). 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 (LVEF < 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 1.66–14.08, 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.
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. Before the procedure, the stem cells were isolated from the patient's bone marrow by density gradient centrifugation. 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 pathological methods and imistic 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 = 0.00, 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 1.2 (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-diastolic volume and ejection fraction estimated both by biplane Simpson method 2D and 3D ultrasound. These data were supported by speckle tracking analysis at 12 months 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 local IRB. Every patient voluntarily signed an informed consent before being included in the study. Transatlantic cardiac echo was done on 100 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. 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 (14.0;19.0) mm Hg versus 14.0 (10.7;16.7) mm Hg in patients with normal 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 study. 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; 1493 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% vs 4%, p <0.001) and rates of stroke (3% vs 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% vs 9.1%), 60 months (55.1% vs 17.3%) and 84 months (60.9% vs 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 strategy 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 patients treated by PCI with PCI within 12h managed by MICUs 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</th>
<th>1 &lt;120 min</th>
<th>2 &gt;120 min</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>6,645</td>
<td>1,111</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>122 (1.8%)</td>
<td>46 (4.1%)</td>
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</tbody>
</table>
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. A system delay <120 min remains a major goal to achieve for prehospital teams.

Methods: Between October 2012 and August 2013, all patients admitted for STEMI was evaluated by cardiac magnetic resonance (CMR) imaging using total ischemic left ventricular dysfunction (IS) was evaluated by cardiac magnetic resonance (CMR) imaging using total ischemic left ventricular dysfunction (IS) to identify patients who potentially could be suitable for early discharge. Risk of IS was evaluated by cardiac magnetic resonance (CMR) imaging using total ischemic left ventricular dysfunction (IS).

Results: There were 28.9% cardiac events. The incremental value of LVEF, strain parameters and global myocardial scar to relevant clinical variables was determined by echocardiography. Endocardial CS is a powerful predictor of cardiac events and apoptosis. The role of myeloperoxidase and monocyte chemoattractant protein-1 in the improvement of left ventricular function after ST-segment elevation myocardial infarction K. Kupczynska¹, B.W. Michalski¹, M. Krzeminska-Pakula¹, E. Szymczyk¹, L. Peczek², P. Lipiec¹, J.D. Kasprzak³, ¹Medical University of Lodz, Chair and Department of Cardiology, Lodz, Poland; ²Center of Molecular & Macromolecular Studies, Polish Academy of Sciences, Lodz, Poland

Aim: 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 (MetS). Studies, Polish Academy of Sciences, Lodz, Poland

Methods: The study population comprised 69 patients (mean age 52±10 years, 83% men) with first STEMI and single pPCI. We selected 33 patients with MetS according to the criteria of the International Diabetes Federation. Patients underwent transthoracic echocardiographic examination. Blood samples were analysed for myeloperoxidase (MPO) and monocyte chemoattractant protein-1 (MCP-1). Complete clinical evaluation was performed within 72 hours after STEMI and repeated after 12 months. LV function improvement was defined as increase of EF of more than 5%.

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 MetS. Among patients without MetS 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 MetS increased level of MPO had a very good predictive value for the occurrence of EF improvement. However in patients without MetS only increased concentration of MCP-1 had a good predictive value for better LV systolic function.
P4450 | BEDSIDE
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 gained 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, MedDi-eT score 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 (Wilk’s Λ=0.997, p=0.079) and current smoking (Wilk’s Λ=0.997, p=0.083); while history of CVD, hypercholesterolemia, BMI, MedDi-eT score and physical activity were in the second highest rank. Respectively, in females, physical inactivity (Wilk’s Λ=0.902, p=0.011), low adherence to the Mediterranean diet (<27) (Wilk’s Λ=0.993, p=0.086) and current smoking (Wilk’s Λ=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

P4451 | BEDSIDE
Impact of proportion of rapid eye movement sleep on all-cause mortality and stroke in patients with acute myocardial infarction

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Aims: We hypothesized that proportion of rapid eye movement (REM) sleep may have significant clinical outcomes.

Methods: This study included 392 patients undergoing primary percutaneous coronary intervention. All patients underwent polysomnography on first admission and were divided into two groups based on the third tertile of the proportion of REM sleep (19.0% – 35.6%). Main outcomes measured were all-cause mortality, recurrent acute coronary syndrome (ACS), and stroke.

Results: The median follow-up duration was 4.0 years. Patients with a higher proportion of REM sleep (n=132) showed lower all-cause mortality (6.8% vs 10.4%) and a significantly lower incidence of stroke (1.2% vs 6.2%, p=0.028) as compared with patients with a median and lower proportion of REM sleep (n=260). ACS equally occurred between the two groups (10.8% vs 10.4%). Kaplan-Meier curve demonstrated that stroke-free survival estimates in patients with a higher proportion of REM sleep was significantly better than those of a median and lower proportion of REM sleep. A stepwise forward Cox regression analysis adjusted for REM sleep, apnea-hypopnea index >15 events/h, higher age >75 years, hypertension, diabetes, dyslipidemia, current smoking, anterior infarct, and peak creatinine kinase levels indicated that the proportion of REM sleep was negatively correlated with all-cause mortality and stroke (hazard ratios: 0.945, 95% confidence interval (CI) 0.894–0.999, p=0.045, hazard ratio: 0.920, 95% CI 0.853–0.992, p=0.042, respectively).

Conclusion: The risk of all-cause mortality and stroke decreased as the proportion of REM sleep increased.

P4452 | BEDSIDE
Influence of music therapy in patients with early post-infarction angina

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Most studies have shown that early post-infarction angina (EPA) implies an unfavorable long-term prognosis among patients with acute myocardial infarction (AMI). Unrelied anxiety can produce an increase in sympathetic nervous system activity leading to an increase in cardiac workload. The purpose of this study was to evaluate the effectiveness of music therapy for reduction of anxiety and pain in patients with EPA.

Material and methods: The effectiveness of music in reducing anxiety and pain during EPA attacks was tested using a two-group pretest–posttest experimental design with 210 patients with EPA. Patients were randomly assigned to receive 30 min of meditative music (N=105) or treatment as usual (N=105). Anxiety, pain sensations, and pain distress were measured with visual analogue scales at start of chest pain episodes and 30 min later.

Results: Repeated measures MANOVA indicated significant group differences in anxiety, pain sensation, and pain distress from pretest to posttest (p<0.0001). Post hoc dependent t-tests and univariate repeated measures ANOVA (p=0.006) indicated that in the meditative music group anxiety, pain sensation, and pain distress all decreased significantly (p<0.0012), while in the treatment as usual group, no significant differences occurred. Independent t-tests indicated significantly less posttest anxiety, pain sensation, and pain distress in the meditative music group than in treatment as usual groups (p=0.0146).

Conclusion: Meditative music was more effective than treatment as usual in decreasing anxiety and pain in patients with EPA. Patients should have beneficial of using meditative music as an adjuvant to medication during EPA episodes.

P4453 | BEDSIDE
Effects of chronic beta-blocker treatment on admission haemodynamics in STEMI patients treated with Primary Angioplasty

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Background: Deteriorated haemodynamics are associated with increased mortality in patients with ST Elevation Myocardial Infarction (STEMI). Beta-blockers may worse 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 the risk of either cardiacogenic shock (CS) or pre-shock was 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.

ACUTE CARDiac CARE in the EMERGENCY DEPARTMENT

P4454 | BEDSIDE
Direct comparison of the safety and efficacy of two rule-out strategies for acute myocardial infarction–2h-algorithm versus combination of 1h-algorithm and undetectable levels at presentation

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Purpose: Addressing the increasingly recognized, yet unmet clinical need for
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). Beyond 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 in- hospital death, shock, congestive heart failure and reinfarction. 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 significant differences. 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 between 3 to 6 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 treatment, 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 1.05–3.52, p=0.03). The combination of positive troponin and ACS-like ECG abnormalities resulted in a significantly increased risk of in-hospital death/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.
patients (96.2%) had BBL, and 37 (69.8%) PF, compared with 7 (15.2%) and 2 (4.3%) in the non-AHF group (p < 0.001 for both).

In the non-AHF group, the thoracic FAST protocol was indicative of an alternative diagnosis in 21/46 (56.7%) and normal in 18 (39.1%) of the patients. The clinicians used Thorax X-ray, BNP, and other standard measures to establish their clinical diagnosis as usual, and they would also have access to the Echo and LUS exams if they wished to.

Purpose: A focused ultrasound protocol combining LUS and Echo might be a fast and helpful tool in diagnosing AHF, also providing aid with differential diagnosis and high life threatening cardio pulmonary conditions among dyspneic patients in the ED.

Methods: All patients with acute chest pain and normal hs-cTnT levels (≤ 0.01 ng/mL) were prospectively included during one year. Number of MACE (cardiac death, MI, revascularization and heart failure) was assessed during 1-year follow-up. A risk stratification algorithm was developed based on clinical characteristics predicting MACE. Additionally, downstream tests were evaluated.

Results: 924 patients were included. No patient suffered from MI during index presentation and 31% experienced cardiac death or MI during follow-up. MACE mainly comprised of revascularizations (86%) and occurred in 6% of patients. Presentation with typical angina, more risk factors and higher hs-cTnT levels on admission were independent predictors of MACE with odds ratios of 30.61 (95% CI: 11.4–82.1), 1.30 (1.0–1.7) and 1.08 (1.0–1.2), respectively. A diagnostic algorithm (Figure) based on the initial hs-cTnT level and patient history classifies 88% of patients as very low risk for cardiac death and MI or MACE (0.5% and 2.3%). However a high rate of additional testing (84% of all tests) was observed in this very low risk group.

Conclusions: Patients with acute chest pain and normal hs-cTnT levels have a very low risk of MI and mortality. The majority (88%) of these patients can be identified as very low risk based on clinical characteristics. Downstream testing in very low risk patients does not seem meaningful.

Acknowledgement/Funding: Funding for the research was provided by the Netherlands Heart Foundation grant 2014051 (MWS).

P4459 | BEDSIDE

Differential diagnosis at admission between Tako-tsubo cardiomyopathy and acute apical-anterior myocardial infarction in postmenopausal women

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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 at-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 mid/distal left anterior descending coronary artery. The patients with TTC significantly more often showed PR-segment depression (82% versus 3%, p<0.001), J-waves (26% versus 3%, p=0.03), maximum ST-segment elevation >2mm (84% versus 37%, p<0.001) and QT elongation in lead II (42% versus 10%, p<0.01) than those with AMI. At multifactorial analysis, PR-segment depression (OR=37.2, 95% CI: 3.4–424, p=0.002) and maximum ST-segment elevation >2mm (OR=11.1, 95% CI: 1.7–79.4, p=0.01) remained the only independent predictors of TTC and the co-existence of both parameters excluded AMI with 100% specificity. The two groups did not differ with regard to age, first troponin-I value, echocardiographic LV ejection fraction and distribution of hyperakinetik LV segments.

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.

P4460 | BEDSIDE

High-sensitivity cardiac troponin on presentation to rule out acute myocardial infarction

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Background: Whilst guidelines recommend that troponin concentrations above the 99th percentile be used for the diagnosis of myocardial infarction, the optimal threshold to rule out myocardial infarction is unknown.

Methods: In a prospective multi-centre trial we identified 4,886 consecutive patients (6416 years, 57% 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 on 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.

Results: Myocardial infarction was diagnosed on the index presentation in 656 patients (14.3%) and a further 123 patients (3.7%) who presented with suspected acute myocardial infarction or cardiac death respectively at 30 days. Troponin concentration on presentation less than 5 ng/L gave a NPV of 99.6% (95% confidence interval [CI] 99.4 to 99.9%) for the primary outcome across all patients (Figure).
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.

P4463 | BEDSIDE
Myocardial deformation by strain echocardiography identify patients with acute coronary syndrome and non-diagnostic ecg presenting in a chest pain unit
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Objective: Clinical assessment often cannot risk stratify patients hospitalized with chest pain and non-diagnostic ECG or myocardial enzymes. An inappropriate admission of patients with non-cardiac chest pain is an enormous cost factor.

Methods: 2315 patients who presented in the chest pain unit (CPU) with symptoms suggestive of acute coronary syndrome (ACS) were screened. All patients with relevant changes in electrocardiography (ECG) or myocardial enzymes were excluded. 264 consecutive patients (mean 58±7 years, 88 men) were prospectively included and underwent myocardial deformation imaging by echocardiography and a coronary angiography (CA) within 2±1 days after admission.

Results: Anatomically obstructive coronary artery disease (CAD) (<70% diameter stenosis) was present in 110 patients (42%). Longitudinal, circumferential and radial strain and strain rate data were evaluated and differed between patients with and without CAD. Global systolic circumferential (GCS) and longitudinal strain (GLS) showed greatest area under the curves (AUC) with 0.835 (95% CI 0.753 to 0.918) and 0.823 (95% CI 0.739 to 0.906). Optimal cut-off values were calculated as –22.7% for GCS (sensitivity 87%, specificity 76%, accuracy 81%) and as –18.8% for GLS (sensitivity 86%, specificity 73%, accuracy 79%) to differentiate between these patients.

Conclusions: In patients with suspected ACS but without ECG changes or myocardial enzymes abnormalities myocardial deformation imaging can identify patients with and without CAD.

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 joins 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 intra-operative or in-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.

P4465 | BEDSIDE
The impact of risk factors on predicting significant stenosis in the presence and absence of coronary calcification: results from the Euro-CCAD study
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Background: Despite the well established risk factors of hypertension, dyslipidemia, diabetes, smoking, and family history of coronary artery disease (CAD), their individual impact in contributing to the development of significant luminal stenosis (≥50%) according to the presence or absence of coronary artery calcification (CAC) remains unclear. Euro-CCAD is a multi-centre international study that investigates the pathophysiology of symptomatic calcific coronary artery disease (CCAD).

Objective: The aim of this study was to assess the individual impact of the conventional CAD risk factors on the occurrence of significant luminal stenosis in patients with and without CAD.

Methods: We analysed data collected from 5520 (age 60±12 years, 61% males) symptomatic patients at intermediate risk for CAD, who received electron beam or multi-detector computed tomographic CAC scoring as well as coronary an-
P4467 | 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/eGFR ratio (CV/GFR); Low (<2.21: n=892), Mid (2.22–3.30: n=830), and High (3.31–<: n=830). And we also divide into 3 subgroups on the basis of CHA2DS2-VASc score (Low: 0–1, mid: 2–3, high: 4–6 point). Clinical outcomes were defined as major adverse cardiovascular event (MACE) which included all cause death, myocardial infarction, stroke, or hospitalization for worsening heart failure.

Results: Mean follow up period was 455 days. There was a stepwise increase in MACE with increasing CHA2DS2-VASc score and CV/GFR (figure). CHA2DS2-VASc score and CV/GFR were the independent predictor of MACE after adjustment of multiple cofounders (CHA2DS2-VASc:p<0.001; CV/GFR: per increase, OR: 1.02, 95% CI: 1.00–1.04, p=0.036). The c statistic of the MACE prediction model changed from 0.583 to 0.654 (p<0.001), and the net reclassification improvement increased significantly after the addition of CHA2DS2-VASc as a continuous variable (35%, CI: 21.9–48.1%, p<0.001).

Conclusions: This study demonstrated that CHA2DS2 score could provide prognostic information in CHD without known AF.

P4468 | BEDSIDE
Predictors of longterm outcomes in spontaneous coronary artery dissection

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Introduction: Spontaneous coronary artery dissection (SCAD) is an unusual cause of acute coronary syndrome. Although the prognosis is good the management is not well established.

Purpose: Describe the clinical presentation, management and long term outcomes of a retrospective cohort with SCAD.

Methods: A total of 37 patients registered in our institution from 2000 to 2014 were retrospectively studied. The definition of 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.

Results: 27 patients diagnosed SCAD (male/female 15/22, age 54±12 [SD] years) were included in the analysis. The clinical presentation was myocardial infarction in 86.5% of patients. SCAD developed after physical or emotional stress in 4 patients (10%) and 7 patients (20%) had hypothyroidism. The left anterior descending artery was involved in 22 patients (60%) and left main was involved in 1 patient. 5 patients had multi-vessel SCAD (13.5%). Recurrences of SCAD were shown in 2 patients (5%). According to the classification proposed by Saw 21 patients (57%) had type 1 dissection (evident arterial wall stain), 11 patients (30%) had type 2 (diffuse stenosis of varying severity) and 5 of them (13%) had type 3 (mimic atherosclerosis) dissection. Coronary artery tortuosity was present in 17 patients (46%) and it is significantly related with MACE (p<0.001) and complications during PCI (p<0.001). The management of SCAD was revascularization of the culprit lesion in 67.5% of patients (23 - PCI, 1 - ACTP, 1 - CABG) with in-hospital death of 8% (3 patients: 2 cases which the dissection progressed retrogradely during PCI and involved the left main and complicated by cardiogenic shock and 1 case involving also the aortic root). 21.6% of cases were initially treated with fibrinolysis which was also significantly related with MACE (p<0.001). PCI failed CHADS2 score in 95.9% of cases. 2 or more stents were needed in 50% of cases and the medium stent length was 46.7±3.2 cm [SD]. During a median follow-up of 1023 days angiography and 85% of them didn’t have any images of dissection.

Conclusions: The registry showed that after spontaneous dissection the prognosis in the longterm follow up is acceptable and most of the MACE occur during the acute phase. PCI of these types of lesions are generally successful but usually involve a long stent length. Tortuosity in coronary arteries, previous thrombolysis and the retrograde progression of dissection during PCI involving the left main are related to bad prognosis.
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 HIV vascularity, in a conventional 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 comprehensive data from coronary angiography 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=0.012) in mean Gensini score, between the HIV positive group (25.72) in patients with HIV and the median time of onset is between 2 and 3 years.

Conclusions: Previous studies have shown a higher burden of coronary artery disease in people with HIV living in our country. The single centre study has perhaps surprisingly 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. These findings may represent more aggressive risk factor management in our cohort, including statin use, lowering the burden of coronary vascular disease.

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 have deposit of mucoid substance in multiple locations including the myocardium. 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 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 physical or emotional stress and 20% had hypothyroidism. The left anterior descending artery was involved in 22 patients (60%) and left main was involved in 2 patients. 13% had multi-vessel SCAD and 8% recurrences, mostly women (66%). There was significant relationship between having hypothyroidism and present a SCAD (p<0.03), experience a recurrence (p=0.035) or having multiple dissection (p=0.002). The average time between relapses is 1023 days.

According to the classification proposed by Saw the majority of them was type 1 (50%). Coronary artery tortuosity was present in 17 patients (45%) and the SCAD was associated with MACE (p=0.001) and complications during PCI (p=0.001). The management of SCAD was revascularization of the culprit lesion in 68.4% of patients (24 PCI, 1 ACPT, 1 CABG) with in-hospital death of 8%. Fibrinolysis was initially performed in 21.6% of cases which was also significantly related with MAC (p=0.001). Coronary artery tortuosity was present in 17 patients (45%) and it is significantly related with MACE (p=0.001) and complications during PCI (p=0.001). PCI was successful in 96% of cases. 2 or more stents were needed in 50% of cases and the medium stent length was 45.5±32.3 mm. During a median follow-up duration of 3.8 years there were 14 deaths, 11 MACE, and 10 non-MACE, but without 14 deaths, patients were reviewed by angiography and 85% of them didn’t have any images of dissection.

Conclusion: Hypothyroidism may be a novel association and potentially carry a higher risk factor for SCAD. Patients with hyperthyroidism have more risk of recurrence and multiple dissection. SCAD recurrences are not uncommon, mostly in women and the median time of onset is between 2 and 3 years.

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 patients.

Purpose: This study aims to investigate the clinical features, angiographic findings, 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 registered 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 9,799 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; 89.6% 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 (17.4±7.6 min vs. 24.2±7.7 min, P<0.002), but a longer door-to-balloon time (111.1±106.6 min vs. 101.8±85.7 min, P=0.004). 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).

However, there was no significant difference in the adjusted MACE rate at one year (HR 1.10, 95% CI 0.79–1.53, P=0.388), even after the propensity-matched analysis (HR 0.80, 95% CI 0.52–1.23, P=0.307).

Analyses of age difference with MACEs

<table>
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<tr>
<th></th>
<th>One-month MACEs</th>
<th>Twelve-month MACEs</th>
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<tbody>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>P value</td>
<td>Hazard ratio (95% CI)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.53 (0.33–0.84)</td>
<td>0.007</td>
</tr>
<tr>
<td>Adjusted for sex</td>
<td>0.63 (0.32–0.93)</td>
<td>0.006</td>
</tr>
<tr>
<td>Multivariable adjusted</td>
<td>1.10 (0.56–2.10)</td>
<td>0.813</td>
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CI, confidence interval; MACE, major adverse cardiac event.

Conclusions: 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.
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 per apolipoprotein B (LDL-C/apoB) ratio reflecting small LDL particles.

Purpose: The purpose of our study was to test the hypothesis that 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, and 297 (45.3%) had impaired fasting glucose (IFG) ≥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 significantly increased risk of T2DM (26.6% vs. 9.8%; adjusted OR 3.34 [2.17–5.6]; p < 0.001). A 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 < 0.001, 1.40 [1.33–1.47]; p < 0.001 and 0.54 [0.41–0.71]; p < 0.001, respectively) and also when we separately analyzed patients with IFG (OR 0.67 [0.46–0.97]; p = 0.032, 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 glyemia.

Impact of diabetes on 2-year clinical outcomes in patients with acute myocardial infarction: Korean registry of DIAMOND (diabetic acute myocardial infarction disease)

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Background: We established diabetic acute myocardial infarction (AMI) cohort in order to expand 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 DIAMOND (Diabetic Acute Myocardial Infarction Disease) study 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, 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 (63% 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.
visit than at hospital discharge: FU-GFR = 60 ml/min (20% vs. 7.8%; p = 0.05), FU-GFR = 30 ml/min (4.4% vs. 0.3%; p < 0.05), discharge-GFR < 60 ml/min (6.7% vs. 9.5%; p=ns), discharge-GFR < 30 ml/min (0% vs. 0.7%; p=ns). There were no statistically significant differences between newDM and controls with respect to the incidence of in-hospital contrast induced acute kidney injury (2.2% vs. 7.2%; p=ns), as well as the number of patients in whom PCI (22.2% vs. 19.9; p=ns) or CABC (4.4% vs. 7.1%; p=ns) procedures had been performed during FU. Patients within newDM group were more often treated with diuretics (44.4% vs. 24%; p < 0.05). Univariate logistic regression analysis revealed that newDM was associated with FU-GFR = 60 ml/min occurrence at 7-month FU (OR: 2.95 CI: 1.28-6.88).

Conclusions: New onset diabetes mellitus is associated with increased prevalence of decreased renal function at 7-month follow-up after AMI.

P4477 | 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 stents (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; 367, 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). In univariable Cox regression analysis, hazard ratio for the primary endpoint was not significantly different between DES-and POBA-era. A similar result was found between BMS-era and POBA-era. Multivariate Cox regression analysis revealed that lower BMI, statin use, higher LVEF and eGFR were associated with reduction of the long-term clinical outcomes.

Kaplan-Meier curves for 3-year All-cause mortality and ACS

Conclusions: Despite the higher risk profiles of the elderly patients in the current DES-era, long-term clinical outcomes following PCI were similar among POBA-, BMS- and DES-eras.

P4478 | BEDSIDE
Circulating monocytes are strongly associated with coronary artery calcification (CAC) density in a population of asymptomatic subjects
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Background: Coronary 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 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 and imaging symptom status, results of coronary CT angiography and clinical consequences of coronary CTA in patients with an Agatston Score of zero.

Methods: Nine centers participated in the German cardiac CT registry (at least a 64-slice system, adequate expertise in the reporting of coronary CT angiography). In the time period between 2004 to 2009, 7081 patients were enrolled in the registry. Data concerning patients baseline characteristics, procedural parameters, indication, coronary findings as well as clinical consequences were documented.

Results: A total of 2016 individuals with absence of coronary calcification (Agatston Score zero) were identified (47% female, mean age 54±11 years, mean BMI 26.4±4.5). CT was performed in 88% of the patients in an elective setting and 12% in an acute setting. In the vast majority of patients, CT was performed either 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 number 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 HDL-level 57 mg/dl, mean triglyceride level 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 an mean effective radiation dose of 3.2 mSv. In 80.2% of patients CTA was excluded, in 17.5% non-obstructive CAD (stenosis ≥50%) was detected and in 2.3% obstructive lesions were detected in a small percentage of patients without coronary calcifications.

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.

P4480 | BEDSIDE
Machine learning applied to clinical and coronary CT angiography variables for prediction of MACE
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Purpose: We investigated a machine learning (ML) approach for prediction of MACE from clinical and coronary CT angiography (CCTA) data available from the CONFIRM Registry.

Methods: Data from 10030 patients (58±13yrs; 5628 males) without known CAD, and with 5 yr outcomes from the CONFIRM registry were considered. All patients underwent CCTA for clinical purposes and were followed for MACE
(death/MI/ACS/late recanalisation). 44 CCTA parameters and 25 clinical parameters were available for ML, including segment stenosis score, segment involvement score, modified Duke CAD index, number of segments with non-calcified, mixed or calcified plaques, age, sex, gender and cardiovascular risk factors. After automated feature selection by information gain ranking, boosted ensemble ML models were developed and tested by ten-fold stratified repeated cross-validation. ROC analysis was used to compare 5yr MACE prediction using ML applied to clinical data (ML-clinical), CCTA data (ML-CCTA) and to both clinical and CCTA data combined (ML-combined). Additionally, the Framingham risk score (FRS) was used as a conventional comparator.

Results: During 5yr follow-up, 991 patients had MACE events. All 3 ML models (ML-clinical, ML-CCTA, ML-combined) had a higher area under-the-curve (AUC) compared to FRS for 5yr MACE prediction (0.79 [0.77–0.80], 0.78 [0.76–0.79], 0.83 [0.82–0.84] vs. 0.61 [0.59–0.63] respectively, all p values <0.001). There was no difference in the AUC between ML-clinical and ML-CCTA models (p=0.19), but ML-combined was superior to both ML-clinical and ML-CCTA (both p values <0.001).

Figure 1. ROC curves for 5yr MACE

Conclusion: ML predicts 5yr MACE from clinical or CCTA data, with superior performance compared to FRS. The most effective strategy for using ML is to integrate both clinical and CCTA data.

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P4481 | BEDSIDE
Long-term prognostic performance of low-dose 64-slice coronary CT angiography with prospective ecg triggering

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Background: Little is known about prognosis ≥2 years after coronary CT angiography (CCTA), only about older CCTA methods.

Purpose: We assessed the long-term prognostic performance of low-dose 64-slice CCTA with prospective ECG triggering in patients with known or suspected coronary artery disease.

Methods: We included 434 patients undergoing low-dose CCTA, stratified according to maximal coronary lesions in CCTA: normal, non-obstructive (narrowing <50%), obstructive (narrowing ≥50%) and previously revascularised. Coronary artery calcium score (CACS) was assessed. Follow-up was performed using hospital records and telephone interviews regarding major adverse cardiac events (MACE): cardiac death, non-fatal myocardial infarction or elective revascularization. Revascularizations within 6 weeks after CCTA were excluded to avoid a bias between diagnosis and prognosis of CCTA.

Results: Mean effective radiation dose was 1.7±0.6 mSv. At baseline, 153 (35%) patients had normal arteries, 87 (20%) non-obstructive lesions, 131 (30%) obstructive stenosis and 34 (8%) were revascularised. Twenty-nine (7%) patients 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
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%)

Kaplan-Meier analysis

Figure 1: Kaplan-Meier analysis of MACE event-free survival.
vessel 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.

P4484 | BEDSIDE
Carotid plaque predicts severity of coronary atherosclerosis in asymptomatic diabetics: a prospective study
A. Jeewarathinem1, S. Venuraju1, S. Ruano1, A. Durno1, M. Rosenthal2, D. Nair3, M. Cohen4, D. Darko4, R. Rahki1, A. Lahn1. 1Wellington Hospital, Clinical Imaging and Research Centre, London, United Kingdom; 2Royal Free Hospital, London, United Kingdom; 3Barnet General Hospital, London, United Kingdom; 4Central Middlesex Hospital, London, United Kingdom

Aims: We sought to prospectively evaluate the prevalence and significance of carotid plaque in asymptomatic diabetics with or without coronary atherosclerosis.

Methods: As part of an ongoing trial (PROCEED-Progression of coronary atherosclerosis in diabetics), Evaluation of CT coronary angiography and novel biomarkers to evaluate inflammation and endothelial function a cohort of 248 asymptomatic diabetic patients were prospectively studied. They underwent both carotid Doppler to evaluate CIMT and carotid plaque and CT coronary angiogram (CCTA).

Results: The average age was 61.4±8.5, BMI 29.5±9.7 and 145 (59%) were males. Patients with microvascular disease (MVD) were 117 (47%), carotid plaque prevalence 115 (46%), mean CIMT was 0.7±0.19 mm, duration of diabetes 13.76±7.8 years and waist hip ratio 0.95±0.09.

A total of 31 (12.5%) patients were found to have obstructive carotid 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 = 0.019), hypertension (Odds ratio 5.9, 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 h/o CAD (Odds ratio 2, CI 1–4, P = 0.07) are significantly associated.

On multiple logistic regression, after adjusting for traditional and other risk factors, carotid plaque still show significance (P = 0.03) with obstructive coronary plaque, odds ratio 0.38 (95% CI 0.15–0.93). A significant association between prevalence of carotid plaque and significant coronary atherosclerosis was noted in a Chi square analysis (P = 0.003). Odds ratio of 3.5 (95% CI of 1.4–7.4)

Conclusion: Presence of carotid plaque was a strong predictor of obstructive coronary plaque in asymptomatic diabetics. The early detection of carotid plaque will help us to further risk stratify patients from traditionally available risk scoring algorithms (FRE, QRisk etc) in predicting severity of coronary artery disease.

P4485 | BEDSIDE
Duration of diabetes is a major determinant of optimal time to initiate cardiovascular screening in asymptomatic type-2 diabetic subjects: results from the proceed study
S. Venuraju1, A. Jeewarathinem1, D. Darko2, M. Rosenthal2, M. Cohen4, D. Nair5, A. Lahn1 on behalf of PROCEED Study. 1Wellington Hospital, London, United Kingdom; 2Central Middlesex Hospital, London, United Kingdom; 3Royal Free Hospital, Diabetes and Endocrinology, London, United Kingdom; 4Barnet General Hospital, London, United Kingdom; 5Royal Free Hospital, London, United Kingdom

Introduction: Evidence from cardiac imaging with CT coronary angiography (CTCA) and coronary artery calcium (CAC) imaging suggest there is significant coronary artery disease (CAD) in asymptomatic type-2 diabetic patients. However, there is currently no consensus about the optimal time to screen for cardiovascular disease (CVD) in this higher risk population.

Aim: The aim of this study was (1) to determine what factors are predictive of significant CAD and (2) when is the optimal time to screen asymptomatic diabetic subjects.

Methods: 263 asymptomatic diabetic patients were investigated with CAC scoring and CTCA as part of the Progression of Coronary Atherosclerosis in Asymptomatic Diabetic Subjects: Evaluation of the Role of CT Coronary Angiography and Novel Biomarkers (PROCEED) study. Invasive Endothelial Function and Vascular Inflammation (PROCEED) study. Regression analysis was used to determine which of the demographic and clinical parameters best predicted significant CAD. Significant plaque defined as being one causing more than 50% luminal stenosis.

Results: The number of diabetes in the study population was 13 years. Mean age was 62.05±8.5 years with 58.6% males and mean BMI was 29.54±6.7 kg/m². Median CAC score for the entire study population was 105.91 (316.97) Agatston Units. 47.5% of patients were known to have documented microvascular disease. In a regression multi-variable analysis, duration of diabetes (p = 0.018), CAC score (p < 0.001), BMI (p = 0.018) and HDL (P = 0.002) were significant predictors of a >50% plaque. When CAC was excluded, systolic blood pressure (p = 0.032) also became significant. Using a ROC curve analysis, we determined that duration of diabetes, from diagnosis, of 12.5 years predicted the significant CAD with a sensitivity of 71.3% and a specificity of 57%. Combining all the multi-variate predictors, the area under the curve increased to 0.84 from 0.65 for duration of diabetes alone.

Conclusions: Patients with a diagnosis of diabetes for at least 12.5 years should be considered for screening for CVD.

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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 eicosapentaenoic 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: 19–61%) in all patients irrespective of a significant CAD with a previous history of LDL-cholesterolemia. Previous study showed that the annual progression of CCS was associated with future cardiovascular events. Therefore, it is of interest to find factors involving CCS progression. Among several cardiovascular risk factors, the number of circulating CD34 positive cell was reported to be associated with vascular function and cardiovascular risks.

Purpose: To examine the association the number of CD34 positive cell and annual progression of CCS in the PEACH trial.

Methods: The PEACH trial analyzed 156 patients with CCS of 1 to 999, hyper-cholesterolemia, 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 + eicosapentaenoic 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 CCS 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 HDL-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 (≤ 0.84μl) (Odds ratio: 2.70, 95% confidential interval: 1.26–5.81, p = 0.01) and ODDS ratio: 2.74, 95% confidential interval: 1.23–6.12, p = 0.01) were independent predictors of the CCS progression, even after adjustment of age > 60 years, hypertension, diabetes, and current smoking.

Conclusion: The study demonstrated the lower number of circulating CD34 positive cell is a novel predictor of CCS progression in patients with hypercholes- terolemia 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
F.K. Schneck1, M. Renker1, A. Rolf2, H.M. Neß1, O. Doerr1, T. Bauer1, H. Moellmann2, C. Liebetrau2, C.W. Hamm1, J. Rixe1. 1University Hospital of Giessen and Marburg, Medical Clinic I, Cardiology and Angiology, Giessen, Germany; 2Kerckhoff Heart and Thorax Center, Department of Cardiology, Bad Neuenahr, Germany

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 stenot patency with MDCT is usually impaired 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, 1:4x-65ml of contrast agent at 6ml/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 at a mean interval of 7 months after implantation. 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.

Clinical advances in computed tomography angiography
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), RX (n=4), diagonal branches (n=2) and marginal branches (n=2), respectively. Out of 32 coronary scaffolds, 30 (94%) were determined assessable. Scalability was impaired by motion artefacts in two scaffolds (one BVS in RCA and one in a diagonal branch), but no BVS was classified unevaluable due to beam-hardening artefacts, partial volume effects or other artefacts caused by scaffold components. Regarding unevaluable 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, MDCAT allows for the evaluation ofundeclared coronary scaffolds on routinely acquired coronary angiography. Only a small number of BVS is unevaluable in MDCAT, 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 computed tomography angiography (CCTA -table administration of intravenous esmolol is safe, effective and allows for combined primary SEP was only observed in 2 (1.5%) patients. A significant reduction in SBP (144±22 to 108±16 mmHg; p < 0.001) was observed during CCTA. A HR above 80 bpm was observed in 5 (4%) patients. Esmolol drove the HR reduction protocol using intravenous esmolol as bail out for failed oral metoprolol regimens in patients assigned for cardiac CT angiography (CCTA) with 64-MSCT. Commonly used pre-medication regimens with oral or intravenous metoprolol are frequently unsatisfactory.

Purpose: The aim of the present study is to evaluate the safety and efficacy of a HR reducing protocol using intravenous esmolol as bail out for failed oral metoprolol regimens in patients assigned for cardiac CT angiography (CCTA) with 64-MSCT.

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 > 90 bpm during contrast image acquisition. The primary safety endpoint (SEP) was primary EEP (86% to 95%; p < 0.001) for white patients, 0.52 (95% CI: 0.39–0.69, p = 0.82) for black patients, 0.98 (95% CI: 0.86–1.13, p = 0.82) for white patients, 0.52 (95% CI: 0.39–0.69, p < 0.001) for Afro-Caribbean, and 0.75 (95% CI: 0.41–1.35, p = 0.33) for Chinese patients. In the cohort with no chest pain or tightness, stenting, PTCA, or CABG, 50.3% had coronary calcification (CAC > 0).

Table 1

<table>
<thead>
<tr>
<th>Percentiles</th>
<th>10</th>
<th>25</th>
<th>50</th>
<th>75</th>
<th>95</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45.6</td>
<td>74.1</td>
</tr>
<tr>
<td>White</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45.4</td>
<td>75.1</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45.4</td>
<td>75.1</td>
</tr>
<tr>
<td>Chinese</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>45.6</td>
<td>75.4</td>
</tr>
</tbody>
</table>

Conclusions: 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.

P4489 | 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. Our aim 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).

Purpose: 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 (including fractional flow reserve assessment–FFR). We defined hsCAD by the presence of occlusive/subocclusive stenoses or FFR < 0.80. Unevaluable segments in CTA were considered positive in the CTA group; in the CTA-intention-to-diagnose (CTA-ID) group they were considered as false positives or false negatives ("worst case scenario"). An integrated protocol including CTA and CTP for interpretable segments was tested (CT-IP).

Results: 95 patients were included in the analysis (62±8.2 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 CTA and CTP showed the highest AUC (0.92, 95% CI 0.86–0.89). The model including CTA and CTP showed the highest AUC (0.81, 95% CI 0.73–0.89).

Conclusion: In our population, quantification of CAC allowed the optimization of the subsequent CT protocol; proceeding to a stress-rest perfusion protocol if CAC was greater than 100 maximised both sensitivity and specificity in the detection of hsCAD.

P4490 | BEDSIDE
Predictive value of coronary artery lumen area quantification for hemodynamically relevant coronary stenoses by computed tomography angiography
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Purpose: Coronary CTA is validated to rule out coronary artery disease (CAD), but it is known that false positive high-grade lesions result in lower sensitivity. Additional quantitative lesion measurements may increase accuracy and identify hemodynamic relevance of a stenosis.

Therefore the purpose was to evaluate the added value of minimal lumina area (MLA) quantification by CTA to predict hemodynamic significance of coronary lesions by invasive angiography (ICA) requiring coronary revascularization.

Materials and methods: One-hundred fifty-six patients (mean age 65.8, 28% female) who underwent multislice CTA presented with at least one high-grade stenosis (>50%) in a proximal coronary vessel (lumen diameter ≥5 mm²) and subsequently underwent invasive angiography (ICA). The stenoses were quantified in CT, including minimal lumina area (MLA) and diameter (MLD) and maximal area and diameters stenoses. Reference was ICA including percutaneous intervention (PCI) or coronary bypass grafting (CABG). ROC–Analysis with increm-

Results: Overall, 220 high-grade stenoses (26 RCA, 10 LM, 137 LAD, 47 CX) in proximal segments were evaluated. Eighty-eight (42%) were positive. Minimal lumina area of ≤1.8 mm² was identified as the most accurate cut-off

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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).

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% 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±13.8 mm, p<0.05, and 12.7±15.5 mm vs. 6.7±7.9 mm, p<0.01, respectively). The multivariable analysis revealed that the independent predictors of failed CTO-PCI were blunt stump (Odds ratio [OR] 7.04; p<0.001; CI 2.46–21.6), bending >45° (OR 4.43; p<0.001, 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.

P4493 | BEDSIDE
Lesion-specific myocardial mass: a new index for diagnosis and treatment of coronary artery disease
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A lesion-specific myocardial mass (LMM) can be calculated from coronary CT angiography by allometric scaling law. The aim of this study was to estimate the influence of the amount of LMM on the diagnostic performance of %DS or MLD to predict functional ischemia. 208 lesions in 132 patients were enrolled. The LMM was defined as each myocardial mass per each supply vessel.

Lesions with positive FFR had larger LMM (Table 1). At the same MLD, functionally significant ischemia was produced at lesions with larger LMM (Figure 1). Based on these slope of regression lines, lesions can be divided into 2 groups according to FFR value. Diagnostic performance of a new index with LMM divided by MLD to predict functionally significant ischemia was assessed. With the best cut-off value of 38.4, the AUC of the ROC was 0.82 with 62% of sensitivity and 96% of specificity, which is higher than that of DS≥50% (AUC=0.74). LMM showed weak correlation with RD and MLD, and weak negative correlation with DS%. A new index, LMM/MLD was predictive for ischemia as well as DS% (FFR <0.8). Our study suggests that 1mm of MLD CT can supply 34.8(g) of myocardium.

Table 1. Lesion characteristics

<table>
<thead>
<tr>
<th>FFR</th>
<th>% DS≥50%</th>
<th>MLD≥50%</th>
<th>LMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR</td>
<td>0.75±0.11</td>
<td>0.63±0.014</td>
<td>LMM 0.351±0.49</td>
</tr>
</tbody>
</table>

P4494 | BEDSIDE
Feasibility of coronary computed tomography angiography using multi-slice computed tomography (CT) scanners in low radiation dose turbo flash mode in third generation 192-slice dual-source
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Objectives: 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 current to improve patient radiation dose 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 2×192×0.6mm; 50ml contrast agent, Ultravist 370; flow 5ml/s). Automated attenuation-based selection of individualized tube parameters were used. Image quality (4-point rating score from 0 = nondiagnostic to 3 = excellent) and radiation dose were evaluated.

Results: 65 patients and 198 coronary arteries (mean age 59±11 years, 24 females) were analyzed by CTA. Mean heart rate was 61±8bpm after application of intravenous betablocker up to 20mg metoprolor prior CT scan. Mean radiation dose was 0.98±0.65mSv. Tube parameters were 498±73mA and 84±110 kV. Subjective image quality was 2±0.5. 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 vasonum. 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 with CT 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% men, mean 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 [-81 to –70] vs. –77 [-77 to –64] HU, p<0.01), expressed median (25th percentile to 75th percentile). Of all patients, EAT density was correlated with VAT volume (r=−0.27, p=0.01) and the number of metabolic syndrome’s components. (vs. −78 [−81 to −70] vs. −72 [−77 to −64] HU, p<0.05, CI 1.35–15.2), and 0.87 respectively.) The multivariable analysis revealed that in this study.

Technical developments in computed tomography angiography
nents (r=−0.27, p=0.01), but not age, body mass index. The EAT density in pa-
tients with metabolic syndrome was significantly lower than that in patients with-
out metabolic syndrome (−7.28 to −5.74 mmHg). The EAT density was signifi-
cantly associated with serum levels of triglyceride (r=−0.31, p<0.01), adiponectin (r=−0.33, p<0.01), and MCP-1 (r=−0.21, p=0.03). The EAT density was also associated with the number of stenotic vessels (r=−0.22, p=0.03) and Genisini score (r=−0.20, p=0.04). On the other hand, the EAT volume was sig-
nificantly associated with body mass index, HDL-cholesterol, adiponectin, and ox-
dized LDL-cholesterol. Finally, multiple logistic analysis revealed that lower EAT density was associated with the presence of CAD (odds ratio of lower EAT: 2.717, 95% CI 1.03 to 7.12, p=0.04) after adjustment of age, gender, hypertension, dia-
betes mellitus, dyslipidemia, and current smoking.

Conclusions: Lower EAT density is associated with cardio-metabolic risk factors. Our findings support that the quality of epicardial fat may affect the development of coronary artery disease.

P4498 | 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 tomography.

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-dimensional reconstruction. A paced QRS morphology was obtained by 12-lead ECG.

Results: Thirty leads were aimed to be positioned in the RV septum using fluoro-
scopy. However, only 10 leads (33%) 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 (<154 msec predicted leads located in the septum with sensitivity of 90%, specificity of 81% and predicative accuracy of 83%. QRS morphology of R pattern in aVL was more frequently observed in the apex group than in the septal (95% vs 40%, p=0.002) and free wall group (95% vs 50%, p=0.043). R pattern in aVL estimated the lead positioned at the apex with sensitivity of 95%, specificity of 56% and predicative accuracy of 78%.

Conclusion: Implantation of RV lead using fluoroscopy alone was often misleading. Paced QRS morphology and duration should be taken into account for the RV lead insertion.

P4499 | BEDSIDE

Assessment of the coronary sinus vein with multi-detector computed tomography angiography - implications for mitral valve reshaping 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 annulo-
plasty devices are percutaneously implanted into the coronary sinus vein (CS), reshap-
ing the mitral valve annulus. However, data on CS length, diameters and its location in relation to the left circumflex artery (RCX) 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±3y) with at least moderate FMR underwent contrast-enhanced, retrospectively ECG-gated dual-source CT (Siemens Somatom Definition, injection of 70 - 90mI of contrast) as part of a plan-
ing procedure prior to percutaneous mitral valve annuloplasty. Curved multipla-
nar reformats (cMPR) of the CS were rendered, and sinus vein length, proximal and distal sinus vein diameter, its proportion of the mitral annulus circum-
ference as well as relation to RCX were assessed by two readers in consensus. Left ventricular-endoaortic diameter (LV-EDD) and ejection fraction (LV-EF) were noted as assessed by echocardiography.

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COMPUTED TOMOGRAPHY USE IN STRUCTURAL HEART DISEASE

P4497 | 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 catheter ablation on atrial fibrillation

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Purpose: To evaluate the image quality characteristics of coronary CT angiog-
raphy (CTA) images reconstructed with standard filtered back projection recon-
struction (FBR), hybrid iterative reconstruction (HIR) and model-based iterative reconstruction (IMR) techniques.

Methods: Right and left PVs (39 male, age 64±7±9.3 years, BMI 28.2±5.6 kg/m²) who underwent 256-slice coronary CTA were reconstructed with FBR, HIR and IMR. Two readers evaluated the datasets qualitatively and quantita-
tively. 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=1 no image noise to 4=se-
vere noise, while image sharpness was evaluated on a five-point scale. Mean im-
age 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 im-
age sharpness as compared to FBR and HIR (p<0.0001 all). Image noise was significantly lower with HIR as compared to FBR 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±7.1 vs. 12.9±2.7; FBR vs. HIR vs. IMR, respectively; p<0.001 all), while mean attenuation did not differ among the three reconstruction methods (517±93.3 vs. 517.9±93.1 vs. 517.7±93.1 HU, p=1.0 all). Proximal CNR in FBR, HIR and IMR was 17.4±5.8 vs. 25.3±8.4 vs. 54.2±12.0 (p<0.001 all), while distal CNR was 16.2±5.0 vs. 23.5±7.4 vs. 55.2±12.4, respectively (p<0.001 all).

Conclusion: IMR significantly improves image quality accompanied by a sub-
stantial increase in CNR and decrease in image noise in coronary CTA.

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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 15.1±0.6mm (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 RAO. 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 (13.7±0.7mm vs. 13.5±0.9mm, 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-EF 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.

P4500 | BEDSIDE
Computed tomography angiography compared to transesophageal echocardiography for assessing mitral valve parameters prior to percutaneous edge-to-edge mitral valve repair
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Background: Transesophageal echocardiography (TEE) is the recommended modality for the assessment of patients with severe mitral valve regurgitation prior to percutaneous edge-to-edge mitral valve repair. However, eavaluability with TEE may be limited due to inadequate sonographic windows and relevant mitral leaflet abnormalities. Therefore, we compared computed tomography angiography (CTA) provides for an assessment of the mitral valve in any arbitrary plane with high spatial resolution and may be of additional value.

Purpose: We sought to evaluate the agreement between TEE and CTA for mitral valve parameters in patients referred for percutaneous edge-to-edge mitral valve repair.

Methods: Twenty-five patients (14 female, 78.0±6.4 years) underwent ECG-gated, dual-source CTA in addition to standard TEE as part of a planning procedure prior to mitral valve repair. Left ventricular end-diastolic diameter (LVEDD), mitral valve annulus diameters in long-axis and intercommissural views, and the lengths of the anterior (AML) and posterior mitral leaflet (PML) were assessed by an experienced observer in both TEE and CTA. Also, the distance between the fossa ovalis to the level of leaflet coaptation was measured, and mitral valve calcification was graded from 0 (no calcification) to 3 (severe). The correlation of both modalities was calculated using Spearman’s rank statistics.

Results: CTA and TEE showed excellent correlation for all parameters assessed: mean LVEDD was 62.5±11.4 mm in CTA vs. 59.0±11.2 mm in TEE (r=0.88, p<0.001). Mitral valve annulus diameters in long-axis and intercommissural views were graded 1 (interquartile ranges 0–1) by both modalities (r=0.59, p=0.002). Median AML length was 18±5.7 mm in CTA vs. 19.4±4.9 mm in TEE (r=0.67, p<0.001), whereas distal CS diameters did not (42±4.7 mm in CTA vs. 40±4.7 mm in TEE (r=0.56, p=0.004). Also, the lengths of both mitral valve leaflets showed good correlation between CTA and TEE: the former group (p=0.02).

Conclusion: Quantitative measurement of CT attenuation of RVM in the late phase may be able to detect presence of RVM fibrosis in PH subjects.

P4502 | BEDSIDE
Aortic valve orientation and root angles are associated with aortic dilatation pattern and acute aortic event risk
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Introduction: Asymmetric aortic root enlargement may lead to unequal thinning of the aortic wall, differential shear stresses and dissection. We sought the association of aortic root morphology with aortoventricular angle (AVAng), LVO-root angle (RootAng), root-aorta angle (AortAng) [Fig 1] and outcomes.

Purpose: Significant variability is noted in the Aortic angles in patients with aortic pathologies. This study aims to assess the correlation between the angles and aortic dilatation pattern as well as risk of acute aortic events, while comparing between BAV and TAV.

Methods: 102 [51 BAV & 51 TAV] patients with aortic disease [22 dissections] over last 6 years and 50 age and sex matched controls undergoing chest CT scans were studied. Two observers measured AVAng, RootAng, AortAng between the proximal aorta, aortic annulus and LV outflow tract [Fig 1] and orthogonal diameters along the thoracic aorta. The asymmetry index (AI) [AI] was calculated as the ratio of the maximal distance between root axis and right wall, and axis to left wall in coronal view.

Results: Among BAV population, AI was related to both Sinus of Valsalva [SOV] diameter [p=0.038] and Ascending Aorta [AA] [p=0.05] dimension. In TAV group, only the SOV was related to AortAng [p=0.002] and AI [p=0.000]. In the combined group, the SOV was related to RootAng [p=0.014] and AI [p=0.000]. The AA diameter was related to Rootang, fusion type and AVAng [p=0.05]. While comparing dissection vs no-dissection groups, AVAng and AortAng were greater in former group [p=0.02].

Conclusions: 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.
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):
2. To clarify the etiology of unobtrusive 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 diameter. 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 3D TEE also underestimated LAA diameter (−2 mm [−2.7; +6.7]). Angiographic 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. Monoplane LAA selective angiography seems not accurate for LAA sizing and may be avoided when non invasive imaging modalities are available.

P4505 | BEDSIDE
A novel mechanism to explain the discrepancy between anatomical aortic valve area and haemodynamic echocardiographic parameters, a pilot computational flow dynamics study

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Background: Previous studies have demonstrated that the severity of aortic valve (AV) stenosis as obtained from direct planimetry can be less when compared to haemodynamic measurements by continuous wave Doppler on echocardiography (Echoc). The cause for this discrepancy remains unknown.

Purpose: To evaluate the underlying mechanism of discrepancy between the anatomical AV area and haemodynamic Doppler measurements in patients with AV stenosis.

Methods: We performed computational flow dynamics (CFD) simulation on model derived from the ECG-gated cardiac computed tomography angiography (CTTA) data which included left ventricular outflow tract, aortic root and valve of 4 patients with severe AV stenosis on echo but CTTA direct planimetry area of >1cm². CFD simulation on the model was used to demonstrate distributions of pressure and velocity in the valve orifice and the aortic root. Anatomical AV area obtained by CTTA was compared with that derived from CFD simulation.

Results: CFD simulation revealed a skewed velocity profile across the valve orifice being maximum at the commissures and areas of calcification (Figure). Further analysis showed that this significant increasing in local velocity caused by the local narrowing has minor contribution to the overall trans-valvular flow rate. The anatomical valve areas derived with CFD were also >1 cm² as obtained from CT.

Conclusion: The preliminary data shows that the discrepancy between the anatomical AV area and haemodynamic Doppler measurements may be caused by the increased local velocity at narrow lumen regions induced by the irregular valve leaflet curvature or local calcification. The Doppler measurements may thus overestimate the severity of stenosis when compared to anatomical valve area.

COMPUTED TOMOGRAPHY ANGIOGRAPHY IN CLINICAL USE
teries in 22 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.

Conclusion: Contrast-enhanced 64-MDCT using stress test can evaluate myocardial ischemia and stenotic coronary artery.

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 transthoracic 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 ischemia) was performed in 22 patients. 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.

Conclusion: Contrast-enhanced 64-MDCT using stress test can evaluate myocardial ischemia and stenotic coronary artery.

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 tests 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 CTA 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 were analyzed. We classified patients as obstructive or non-obstructive according to the SCCT criteria.

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 tests 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 CTA were considered inappropriate, dismissing concerns that this test might be largely misused in clinical practice.
P4511 | BEDSIDE
Impact of coronary plaque characteristics assessed by 320-detector row computed tomography on myocardial injury associated with percutaneous coronary intervention for chronic total occlusion
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Background: Periprosthetic myocardial injury has been shown to be associated with coronary plaques in patients who underwent elective percutaneous coronary intervention (PCI). Specific plaque characteristics of culprit lesions detected on multidetector computed tomography (MDCT) were identified as predictors of PCI-related myocardial injury in patients with stable angina pectoris. We hypothesized that there will be a significant association between culprit lesion plaque characteristics assessed by pre-PCI MDCT and periprocedural myocardial injury associated with PCI for chronic total occlusion (CTO).

Methods: Forty-one de novo CTO lesions in stable angina patients who underwent pre-PCI 320-row MDCT and CTO revascularization at our institution from Dec 2001 to Jan 2016 (n=118, 61.0%) of post-PCI cardiac troponin I (cTnI) elevation was determined. The benefit to lower risk populations of CAC score-based screening was also assessed.

Methods and results: In total, 1,854 participants (aged 40–79 years) without history of CAD, stroke, or diabetes were enrolled. CAC scores of ≤100, and >100 were present in 33.8%, 8.2%, and 2.9% of the participants, respectively. The CAC scores rose significantly as the CAC score increased (P<0.001). The total CAC prevalence was 6.1%. The occult CAD prevalence in the CAC score of 5%–10%, 10%–20%, and >20% strata was 3.4%, 6.7%, 9.0%, and 11.6% (P=0.0001). EAT thickness ratio 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.

P4514 | BEDSIDE
Role of coronary artery calcium scoring in detection of coronary artery disease according to Framingham risk score in populations with low to intermediate risks
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Background: Coronary artery calcium (CAC) scoring by coronary computed tomography (CTC) has been proposed as an alternative to the Framingham risk score (FRS) for screening for coronary artery disease (CAD). However, current guidelines recommend that CAC screening should only be used for intermediate risk groups (FRS of 10–20%). The CAC distributions and CAD prevalence in various FRS strata were determined. The benefit to lower risk populations of CAC score-based screening was also assessed.

Method and results: We investigated 111 non-calcified or mild calcified lesions from 103 patients using 64-slice MDCT before percutaneous coronary intervention (PCI) and assessed by IVUS. EAT thickness ratio 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.

P4515 | BEDSIDE
Significance of epicardial adipose tissue thickness ratio as a predictor for coronary plaque vulnerability measured by multidetector computed tomography
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Background: Epicardial adipose tissue (EAT) measurement, using cardiac computed tomography (CT) has been shown to be linked with the development of coronary atherosclerosis. To date, no study has been undertaken that shows the relationship between EAT thickness across obstructive plaque and its plaque morphology. The aim of this study was to clarify the importance of EAT thickness across an obstructive plaque using intravascular ultrasound (IVUS) and multidetector computed tomography (MDCT).

Methods: We investigated 111 non-calcified 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 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 the total EAT thickness across the reference vessels and patients were assigned into two groups: I (<112%) or II (≥112%) EAT thickness ratio groups.

Results: 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 (39.6% vs. 17.2%, P=0.01) and lower plaque hounsfield 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 attenuated plaque 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.
Conclusions: (1.00±0.05 vs. 0.542±0.06, P<0.05) in response to TGF-β and decreased activity of RUNX3 expression level in TGF-βliferation and differentiation of CFs induced by TGF-β.

Background: Rosuvastatin has been reported to play a role in cardiac remodeling, which is related to the proliferation and differentiation of cardiac fibroblasts in China, People's Republic of; 2 Zhongshan Hospital, Fudan University, Radiology, Shanghai, People's Republic of China; People's Republic of China.

Purpose: 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 (FRF<0.75) were calculated.

Results: FFR was <0.75 in 12 lesions (20.7%). Lesions with FFR<0.75 showed smaller MLD (mm) (2.2±0.7 vs. 2.5±0.5, p<0.16), MLA (mm²) (5.7±3.0 vs. 6.9±2.8, p<0.25), larger plaque burden (%) (65.17±7.0 vs. 56.8±15.8, p<0.12), larger RI (1.19±0.33 vs. 0.98±0.28, p<0.06), and lower CT-Density (HU) (29 (9–49) vs. 45 (31–63), p<0.08) than those without. Cutoff values to predict FFR<0.75 were 1.9mm for MLD, 3.5mm² for MLA, 58.0% for plaque burden, 0.83 for RI, and 29HU for minimum CT-Density>29HU identified by CCT (odds ratio 13.4, 95% confidence intervals 3.12–49.8, p=0.005) and minimum CT-Density>29HU identified by CCT (odds ratio 13.4, 95% confidence intervals 1.36–132.29, p<0.03) were independent predictors for FFR<0.75. Diagnostic power of combination of smaller MLA, <3.5mm² and lower CT-Density<29 HU to predict FFR<0.75 showed 25.0% of sensitivity, 97.8% of specificity, 75.0% of positive predictive value, 83.3% of negative predictive value, and 82.8% of diagnostically accuracy.

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-β1, and the potential role of RUNX3.

Methods: CFs, isolated from Sprague-Dayley rats, were induced by TGF-β1 treatment for 24h. RUNX3 down- or up-regulation in CFs was performed by small interfering RNA (siRNA) or lentiviral transfection (LT), respectively. CFs, with or without regulation, were cultured with rosuvastatin or PBS followed by TGF-β1 stimulation. The proliferation of CFs was analysed by the BrdU, MTT assays and flow cytometry. The differentiation of CFs was analysed by expression of α-smooth muscle-actin (α-SMA).

Results: The down-regulation of RUNX3 induced by TGF-β1-cultured CFs proliferation of was observed by both BrdU assay and α-SMA expression level. The RUNX3 expression level in TGF-β1-G1 Group was significantly lower than that in Rosuvastatin+TGF-β1 group (0.539±0.07 vs. 0.959±0.06, P<0.05). CFs proliferation and differentiation both increased after RUNX3 was knocked down when cells was incubated with TGF-β1 following rosuvastatin pre-treatment, which was respectively induced in BrdU assay (0.576±0.04 vs. 0.743±0.06, P<0.05) and in α-SMA expression (0.450±0.05 vs. 0.837±0.03, P<0.05). More intriguingly, over-expression of RUNX3 in CFs’ obviously attenuated the proliferation and differentiation of CFs induced by TGF-β1 as well, which was respectively shown in BrdU examination (0.819±0.05 vs. 0.660±0.02, P<0.05) and α-SMA expression level (1.00±0.05 vs. 0.542±0.06, P<0.05). The statistical reduced Akt phosphorylation and decreased activity of β-catenin/cyclin D1 cascade were also found in the group with over-expression of RUNX3.

Conclusions: Rosuvastatin inhibits the proliferation and differentiation of CFs in response to TGF-β1 stimulation by activating the RUNX3 and repressing Akt expression, with the subsequent down-regulation of β-catenin/cyclin D1 cascade.

P4516 | BENCH
Mitochondria play an important role in the regulation of the nuclear Ca transient
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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 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 uniporter (mCU), dantrolene: mitochondrial RyR (mRyR1)) 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 stimulated the myocytes with angII ([3S]-CaCl2) and mitochondria in isolated aortas from diabetic mice were added to angII no increase in mitochondrial Ca concentration could be observed. In a next step the influence of this blocked mitochondrial Ca uptake on nuclear Ca concentration was examined by measuring nuclear and cytosolic Ca at the same time. Here, the 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 over proportional compared to the cytosolic Ca concentration, indicating that mitochondrial Ca uptake through the mRyR1 is somehow relevant for the regulation of cytosolic and mitochondrial Ca.

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

Background: Little evidence has emerged to demonstrate whether NOS dysfunction and BH4 reduction in the diabetic heart is a cause or consequence of diabetic cardiomyopathy. Besides, apart from 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 provide NOS activity, transgenic mice were generated with specific myocardial BH4 availability. 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.

Results: After 12 weeks of diabetes, WT mice exhibited diastolic dysfunction; membrane BH4 hydrogen isozyme (mBH4) was significantly increased. However, both the cardiomyocyte and global cardiac diastolic 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, preceded 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 transi
transition (Endo-MT) contributes to organ fibrosis and BMP7 administration helped to preserve the expression of endothelial cells markers. Myocardial fibrosis is a crucial pathogenic factor during viral myocarditis (VMI) pathogenesis. This study was designed to analyze the role of Endo-MT during cardiomyosis in viral cardiomopathy and to investigate whether BMP7 administration reduced myocardial fibrosis by inhibiting Endo-MT.

**Methods and results:** BALB/c mice were randomized into three groups: sham group, VMC group and VMC+BMP7 group. Impaired cardiac function and interstitial fibrosis were found in VMC model. Endo-MT was identified in CVB3-induced VMC model using confocal immunofluorescence staining, which showed co-localization between endothelial markers and mesenchymal markers. BMP7 treatment inhibited enlarged left ventricular diameters and improved cardiac function which presented as lower LVEDd and LVESd, as well as higher LVEF and FS (both p<0.05). Virus replication and interstitial fibrosis in cardiac samples after CVB3 injection were surprisingly decreased by BMP7 intervention. Double immunofluorescence staining demonstrated that ameliorated myocardial fibrosis was consistent with the decrease expression of Endo-MT. Moreover, western blot displayed that both TGF-β and β-catenin signaling pathways were activated in VMC, which were downregulated after BMP7 supplement. Co-IP illustrated that CVB3-induced formation of a protein complex between β-catenin and smad3, which further promoted the Endo-MT in injury cardiac samples. BMP7 intervention attenuates Endo-MT by breaking down these protein complexes and then inhibiting TGF-β and β-catenin signaling pathways.

**Conclusion:** Endo-MT was crucial in CVB3 mediated myocardial remodeling and BMP7 attenuated cardiac fibrosis through inhibiting the interaction between smad3 and β-catenin during Endo-MT in viral cardiomopathy. Conjoint activation of TGF-β and β-catenin pathway may coordinate changes of Endo-MT and promote myocardial fibrosis, which suggest a potential new therapeutic approach during CVB3 myocarditis.

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**P4519 | BENCH**

Human cardiac fibroblasts increase SR-dependency of induced pluripotent stem cell-derived cardiomyocyte calcium handling by modulating SR uptake and SERCA2a expression via direct physical contact

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**Introduction:** Cardiac fibroblasts can influence cardiomyocyte structure and function through direct physical interaction and/or by the secretion of soluble factors. Here we assess the relative importance of these different modalities of interaction in terms of their effects on cardiomyocyte electrophysiology.

**Methods:** Ventricular fibroblasts were isolated from the explanted hearts of di-lated cardiomyopathy (DCM) patients (n=4) and cultured with human induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) at a ratio of 2:1 for 24 hours in three groups: iPS-CMs with fibroblast conditioned medium (CMed), co-cultured in transwells to allow bi-directional paracrine communication but prevent physical contact (CC), and iPS-CMs in direct contact with fibroblasts (DC). iPS-CMs alone were used as control. Ca2+ transients and action potentials were recorded optically using fu4-AM and dI-A-NEPS. Data are presented as percent change from control where appropriate.

**Results:** iPS-CM calcium transient duration was significantly reduced in DC vs control (−8.4±2.2% n=12 p<0.05) while the other culture groups showed no change. Sarcoplasmic reticulum (SR) calcium uptake assessed by caffeine application was highly upregulated in DC (2.07±0.12 s⁻¹ vs 0.63±0.07 s⁻¹ in control n=26 and 23 p<0.001), associated with a significant increase in caffeine-induced transient amplitude (F/F₀: 3.74±0.11 vs 2.97±0.11 in control n=37 < 0.05). iPS-CMs in DC displayed a greater dependence on SR uptake for Ca2+ extrusion than other mechanisms (SR/NCX/Slow: 60.7±3.1% 9.7% vs 23.3±7.9% 9.5% in control). Ca2+ transient time to peak was prolonged by CMed and CC (+12.0±3.4% and +16.9±3.1% n=12 p<0.05) but reduced in DC (−17.5±7.1% p<0.05).

**Conclusion:** DCM fibroblasts influence iPS-CM electrophysiology through different modalities; however physical contact with fibroblasts has effects not seen with soluble mediators alone. This contact-dependent shift towards greater SR-dependency favours a novel effect of fibroblasts on cardiomyocyte calcium handling. Determining whether these effects are mediated through mechanical, electrical or paracrine signalling and will be the focus of future work.

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**P4520 | BENCH**

Reparative fibrosis is impeded in Mks5 deficient mice following myocardial infarction

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**Background:** The adverse cardiac remodelling that occurs following left ventricular myocardial infarction (MI) is complicated by scarring and constriction which presents as lower LVEDd and LVEF and increases in LV end diastolic diameter, myocardial performance index, and wall motion score index in Mks5+/− and Mks5−/− mice compared to their respective wild type controls. In contrast, in the isolated perfused rat heart model during perfusion and scar formation and subsequent cardiac function and scar failure that develops after MI. As Mks5 mRNA is highly expressed in heart and we have shown previously that reactive (interstitial) fibrosis is reduced in heterozygote Mks5−/− mice, Mks5 may play a role in cardiac remodelling. Here we demonstrate that Mks5−/− mice, the infarct size of Mks5−/− mice is significantly reduced and co-ordinated matrix deposition. This reparative fibrosis is a critical component of cardiac wound healing.

**Purpose:** The present study was to determine if reparative fibrosis secondary to MI is impeded by Mks5 haplosufficiency.

**Methods:** Twelve-week-old Mks5−/− and wild-type littermate (Mks5+/+) mice underwent ligation of the left anterior descending coronary artery (LAD). Sham mice underwent the identical procedure but the coronary artery was not occluded. LV structure and function were assessed before and 7 days post-LAD by transthoracic echocardiography (Echo). Scar size was assessed by both magnetic resonance imaging (MRI, before and 8 days post-LAD) and Masson Trichrome staining. Mice were sacrificed 8 or 21 days post-surgery (n=24–34).

**Results:** Eight days post-LAD, survival rates for Mks5−/− and Mks5+/+ mice did not differ significantly. In contrast, survival rates did differ over 21 days: the median survival of Mks5−/− mice was 9 days post-LAD. Echo revealed similar increases in LV end diastolic diameter, myocardial performance index, and wall motion score index in Mks5+/− and Mks5−/− mice compared to their respective wild type control mice. In contrast, in the isolated perfused rat heart model during perfusion and scar formation and subsequent cardiac function and scar failure that develops after MI. As Mks5 mRNA is highly expressed in heart and we have shown previously that reactive (interstitial) fibrosis is reduced in heterozygote Mks5−/− mice, Mks5 may play a role in cardiac remodelling. Here we demonstrate that Mks5−/− mice, the infarct size of Mks5−/− mice is significantly reduced and co-ordinated matrix deposition. This reparative fibrosis is a critical component of cardiac wound healing.

**Conclusion:** The present study was to determine if reparative fibrosis secondary to MI is impeded by Mks5 haplosufficiency.

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**P4521 | BENCH**

VC74P6: a cardioprotective adenosine receptor agonist with minimal haemodynamic effects


Adenosine receptor (AR) activation provides powerful cardioprotection. However, it is also associated with adverse effects in the form of profound heart rate (HR) and blood pressure (BP) reduction which has hindered the transition of AR agonists into the clinic. The aim of this study was to determine the effect of VC74P6, a novel AR agonist on infarct size (IS), HR and BP and compare it to other adenosine agonists, 5'-N-Ethylcarboxamidoadenosine (NECA) and 5-Cyclopentyl/1-adenosine (CPA). Two animal models were used: (1) a Langendorff-perfused isolated rat heart model subjected to 30 min/60 min ischaemia/reperfusion (IR). Heart weights were incubated in 1% 2,3,5-triphenyltetrazolium chloride (TTC) to determine IS. 2) An acute myocardial infarction (MI) rat model subjected to 30 min/120 min of IR. Hearts were then infused with 5% Evans Blue followed by incubation in 1% TTC to determine IS. IS was reduced in the isolated rat heart with VC74P6 treatment (1 μM) and CPA (100 μM) at reperfusion compared to the vehicle-treated group (14.7±2.6% vs 10±1.7% vs 32±1.4% of area at risk (AAR), respectively; n=5, P<0.05). HR in hearts treated with VC74P6 at reperfusion were unaltered (203±5 vs 219±9 BPM; n=5; P<0.05), unlike in CPA-treated hearts (707±7 vs 219±9 BPM; n=5, P<0.05). In MI rats, IS was reduced following VC74P6 (80 μg/kg) and NECA (10 μg/kg) treatment at reperfusion compared to the vehicle group (Table; n=6–8, P<0.05). The infarct sparing effect of VC74P6 was abolished by an A1AR antagonist, 8-Cyclopentyl-1,3-dipropylxanthine (DPCPX 100 μg/kg). VC74P6 had no effect on HR and mean arterial pressure (MAP; Table; n=6–8, P<0.05 vs vehicle) while NECA significantly reduced HR and MAP (Table; n=6–8, P<0.05 vs vehicle). The results suggest that unlike CPA and NECA, VC74P6 has a minimal haemodynamic effect at doses that are cardioprotective, displaying a desired effect without the adverse effects. The infarct-sparing effect of VC74P6 is also likely to be mediated through the A1AR.

**Table 1: Effect of adenosine agonists and antagonist on infarct size and haemodynamics in MI rats**

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>DPCPX (100 μg/kg)</th>
<th>VC74P6 (80 μg/kg)</th>
<th>NECA (10 μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (BPM)</td>
<td>405±17</td>
<td>465±15</td>
<td>408±16</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>99.1±6.4</td>
<td>91.5±2.6</td>
<td>107.2±8.9</td>
</tr>
</tbody>
</table>

*P<0.05 vs vehicle; n=6–8; mean ± SEM.
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Background: In this study we assessed whether remote ischemic preconditioning (RIPC) may reduce platelet activation during coronary angiography (CA) and/or 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) the day before the procedure. Patients were randomized to RIPC, induced by 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 MPA gate and platelet CD41 and CD62 in the platelet gate, without and with ADP stimulation.

Results: Basal values of platelet variables were similar in the two 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=0.005) 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.

P4524 | BENCH
High-density lipoproteins increase myocardial salvage and attenuate microvascular obstruction by modulating toll-like receptor innate immune signaling
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Background and introduction: The protective role of HDL in cardiovascular disease has been questioned because of the failure of large intervention trials with CETP-inhibitors, which raise HDL-cholesterol levels, to reduce clinical event presentation in patients who had suffered an acute coronary event. Although some cardioprotective effects had been reported in mice, the mechanisms of action of HDL on the heart are largely unknown.

Purpose: Here we investigate the clinical and molecular effects of apoA1-rich HDL (aHDL) on a preclinical experimental model of acute myocardial infarction (MI).

Methods: Pigs were randomized to 2 intravenous infusions 3 days apart of aHDL (15mg/kg) or vehicle-saline. One day after the last dose all pigs underwent a 60 min closed-chest coronary balloon occlusion followed by reperfusion (experimentally induced MI). Left ventricle pressure and areas of the myocardial infarction were analyzed.

Results: aHDL-recipient animals showed, compared to vehicle, a 2-fold improvement in myocardial salvage index (0.43±0.04 vs 0.18±0.02; P<0.05) and 42% reduction in infarct size (13.8±2.1% vs 23.9±1.6% LV; P<0.05) despite comparable myocardial-at-risk (15.1±1.4% vs 21.3±1.4% LV). MVO was attenuated in HDL-recipient animals (P<0.05 vs vehicle) and directly correlated with the extent of necrosis (P<0.05; R=0.63). LV volumes improved by 14% in HDL-recipient animals (P<0.05 vs vehicle). HDL-infusion significantly reduced neutrophil recruitment to the infarcted myocardium which, in turn, was associated with the attenuation of myocardial TLR signaling (both, Myd88-dependent and TRIF-dependent pathways) and the prevention of MI-induced TLR activation in PBMC. aHDL also exhibited antioxidant effects and modulated the SAFE- and TRIF-signaling pathways.

Conclusion: In the onset of coronary ischemia, aHDL attenuates the deleterious effects of myocardial infarction by increasing myocardial salvage and improving cardiac perfusion. aHDL exerts cardiomyocyte protection by modulating neutrophil infiltration through TLR signaling.

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P4525 | BENCH
Calpastatin overexpression impairs post-infarct scar healing in mice by compromising reparative immune cell recruitment and activation
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Background: In myocardial infarction (MI) the calpain system is activated. Calpastatin is the natural endogenous inhibitor of calpains. The impact of calpain inhibition by calpastatin overexpression on post-MI scar healing and left ventricular (LV) remodeling is elusive.

Methods and results: Mice ubiquitously overexpressing calpastatin (TG) and wild-type (WT) controls underwent an anterior coronary artery ligation. A higher incidence of cardiac rupture in TG (54% vs 14% in WT, p<0.05) at the first week post-MI was responsible for an increased mortality in 6 weeks in TG (44% vs 24% in WT, p<0.05) despite comparable infarct size, LV dysfunction and dilatation. Calpain activation post-MI was blunted in TG myocardium. In TG mice inflammatory cell infiltration and activation were reduced in the infarct border zone (BZ), particularly affecting M2 macrophages and CD4+ T cells, which are crucial for scar healing. To elucidate the role of calpastatin overexpression in macrophages, we stimulated peritoneal macrophages obtained from TG and WT mice in vitro with IL-4, yielding an abrogated M2 polarization in TG cells, but not in WT cells. Lymphopoeitic Rag1−/− mice receiving TG splenocytes prior to MI demonstrated decreased T cell recruitment and M2 macrophage activation in the BZ at day 5 post-MI, as compared to those receiving WT splenocytes.

Conclusion: Calpastatin overexpression impairs post-MI scar healing and promotes cardiac rupture. Defective scar formation is associated to decreased CD4+ cells and M2 macrophages recruitment and activation when calpastatin is overexpressed.

Conclusion: Administration of DPP-4 inhibitors attenuated MI-induced cardiac remodeling in DPP-4 deficient rats via DPP-4-independent pathways.
P4526 | BENCH
Cardioprotective effect of cgmph induction by sgc activator, bay60-2770, in ischemia-reperfusion injured rat heart
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Objective: Mitochondria play critical roles in both the life and death of cardiac myocytes. During ischemia and reperfusion (IR) injury, cGMp-mediated alterations of mitochondrial protein level by sGC activator have not been assessed up to now.

Methods: Ischemic reperfusion (IR) injured hearts have some limitations under the pathological conditions which are reduced NO generation and oxidized heme in sGC. To prove the cardio protective effect of NO-independent and haem-independent sGc activator, which potenalizes NO/cGMP signaling, we treated Bay60–2770 (4-(((4-carboxybutyl)-2-(5-fluoro-2-(4-fluoromethy)phenyl)ethyl)amino)methyl)benzoic acid) in IR injured rat heart. IR injury was established by occlusion of LAD for 40 min and reperfusion for 7 days, and the effect of sGC activator (5 mg/kg, Bay 60–2770) on myocardial protection in the IR injury was assessed by echocardiography and TTC staining.

To investigate the novel cardiac protective mechanism of sGC activator, 5 mM and 5 μM of Bay 60–2770 were perfused into isolated rat heart in Langendorff system. After 10 or 30 min reperfusion with Bay 60–2770, cGMP and CAMP concentration and PKG and GSK3β activation status were examined. In addition, 1 μM KT5823, 100 μM 5-HD and 200 μM L-NAME were perfused with 5 mM Bay 60–2770 to explain the mechanism of sGC-activator mediated alterations of mitochondrial protein levels.

Results: In IR injured rat heart, sGc activator limits infarct size (53.0±11.3% in IR vs. 17.9±6.6% in Bay 60–2770 treated). Echocardiography shows that the reduced ejection fraction (89.5±2% vs. 77.3±6.8% in normal and IR hearts, respectively) by IR was recovered by sGc activator (84.4±2.2% in Bay 60–2770). Tissue samples from Bay 60–2770 (5 mM and 5 μM) perfused heart had cGMP levels about 2-fold higher than IR (17.2±7.6 μM in IR vs. 32.8±13.6 μM in 5 mM vs. 38.4±10.95 fmol/mg tissue in 5 μM) without any alteration of CAMP concentration. PKG activity in myocardium after reperfusion was increased by sGc activator. The decreased protein level of cG-P by Bay 60–2770 administration was abrogated by KT5823 in isolated myocardium.

Conclusion: Our results suggest that infarct size limitation by Bay 60–2770 was associated with elevated cGMP levels and further alteration of PKG-mediated mitochondrial protein status. Thus we propose that sGc activator protects mitochondria against IR injury.

P4527 | BENCH
Cardioprotective effects of inorganic phosphate in an ischemia-reperfusion model
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Objectives: Ischemia-reperfusion damage (IR) has been explained by overload of calcium (Ca2+) and overproduction of reactive oxygen species (ROS). Inorganic phosphate (PO4) can complex Ca2+ and preserve cardiac function. We found biochemical evidences of protection at mitochondrial level and we decide to search if they were accompanied by improvement in clinical parameters like electric stability, myocardial mobility index, ventricular systolic function and survival.

Methods: We used 3 groups of 10 rats each (control, PO4 and non-PO4). PO4 group received 60μl of 10mM PO4 five minutes before coronary occlusion. Electrical activity and haemodynamic stability were monitored. Echocardiographic studies were performed initially, 3 minutes after reperfusion and at 20 minutes. At the end of the study we collected the heart and through centrifugal differentiation, we obtained mitochondria. In them we measure free Ca2+, Ca2+ transport and lipoperoxidation.

Results: PO4 group had better survival (80% vs. 10%), mobility index during ischemia and 3 minutes reperfusion (2.71±0.756 vs. 1.50±0.837 and 4.0± vs. 1.67±1.9), and a better ejection fraction during ischemia, 3 min. and 20 min. after reperfusion (62.1%±19.2 vs. 28.3%±14.2; 85.2%±6.3 vs. 43.1±11.3 and 71.9%±31.8 vs. 25.7%±39.8). We also found that free Ca2+ levels were similar between control and PO4 groups (196±47 mM and 179±58 mM) in contrast to non-PO4 where Ca2+ was higher (305±14 mM).Preserved function of Ca2+ transport and an almost absent lipoperoxidation were observed.

Conclusions: Pre-treatment with PO4 decrease life threatening arrhythmias, mobility alterations and reperfusion damage. For the first time, it is demonstrated besides biochemical measurements its functional effects.

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 (IR) 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 hearts were perfused in isolated Langendorff system, and were exposed to 40 min of ischemia followed by 60 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-cellular Signal–Regulated Kinases 1/2 (ERK1/2). Furthermore, we used isolated cardiomyocyte subculture to assess the effects of Ucn-1 on survival after IR. Ucn-1 regulation of cardiac myocyte survival.

Results: We found that Ucn-1 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 augmentation of cell survival and the decrease of cell necrosis. Ucn-1 stimulated the increase of the expression of BAD, CD40-ligand and XIAP proteins that are implicated in apoptosis and cell survival. Finally, we determined that Ucn-1 regulated CD40 ligand and XIAP through Epac and ERK 1/2 activation, meanwhile it preserved BAD expression independently of ERK 1/2 signaling pathway.

Conclusions: Our data confirm that Ucn-1 efficiently preserved hearts hemodynamics and survival by the regulation of signaling pathways involved in cell survival and apoptosis which include recovery of heart contraction, prevention from intracellular Ca2+ overload and cardiac cell death. Likewise, eryRNA was released from cardiomyocytes under ischemia and protection.
hypoxia and subsequently induced TNF-α liberation by activation of TNF-α converting enzyme (TACE) and provoked cardiomyocyte death. Conversely, TNF-α promoted eRNA release especially under hypoxia, feeding a vicious cell damaging cycle during I/R. Administration of RNase1 or TAPI (TACE-inhibitor) prevented cell death and myocardial infarction. Likewise, RNase1 significantly reduced TNF-α-mediated energy exhaustion, opening of mitochondrial permeability transition pores as well as oxidative damage in cardiomyocytes. Finally, a dramatic increase of endogenous vascular RNase1 in human subjects was achieved by inducing non-invasive intermittent limb I/R using an external occluder, thereby supporting the impact of the eRNA/RNase system in remote ischemic preconditioning. Together, RNase1 as well as inhibition of TACE provide novel therapeutic regimen to interfere with the adverse eRNA-TNF-α interplay and significantly reduce or block a pro-inflammatory outcome of ischemic heart disease. The uncovered fundamental pathomechanisms are likely operative in other organs and tissues as well, such that the proposed interventions offer new concepts for general cytoprotection in medicine.

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 explore 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 a 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, the two 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 determine mRNA expression of inflammatory and anti-inflammatory M2 macrophages in hindlimb quadriceps muscle. Flow cytometry was employed to analyse blood circulating monocyte subsets (Ly6Chigh inflammatory monocytes versus Ly6Clow resident monocytes).

Results: Maximal walking distance and time until 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 muscle significantly increased (3.6-fold versus non-ischemic muscle at week 5 post-arterial ligation). In WR mice, mRNA expression of M2 marker CD206 in ischemic muscle significantly increased (+40%) at week 3, (+50%) at week 4 and (+28%) at week 5 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 mice significantly increased the resident monocyte Ly6Clow subset in the circulation (~45% versus SED mice at week 5 post-arterial ligation).

Conclusion: PE prior to peripheral arterial stenosis ameliorates impaired walking capacity subsequent to arterial stenosis. Underlying potential mechanisms include increased myocardial perfusion, the ischemic 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.

P4531 | BENCH
Novel mechanisms promotes adaptive cardiac remodelling through enhancing fatty acid oxidation in the murine heart
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Methods: Mice were kept sedentary (SED) for 5 weeks before unilateral iliac artery ligation. Thereafter, the two 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 determine mRNA expression of inflammatory and anti-inflammatory M2 macrophages (M1 versus anti-inflammatory M2 macrophages) in hindlimb quadriceps muscle. Flow cytometry was employed to analyse blood circulating monocyte subsets (Ly6Chigh inflammatory monocytes versus Ly6Clow resident monocytes).

Results: Maximal walking distance and time until 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 mice significantly increased the resident monocyte Ly6Clow subset in the circulation (~45% versus SED mice at week 5 post-arterial ligation).

Conclusion: PE prior to peripheral arterial stenosis ameliorates impaired walking capacity subsequent to arterial stenosis. Underlying potential mechanisms include increased myocardial perfusion, the ischemic 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.

METABOLISM AND METABOLIC SYNDROMES

P4532 | BDESIDE
Cystatin C is not causally associated with diabetes or the metabolic syndrome
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Background: We recently reported a relationship between plasma levels of cystatin C and the risk of incident diabetes (Diabetes Care 2011; 34:985-9). In the present study we aimed to investigate the association between plasma cystatin C and incident diabetes (Diabetes Care 2011; 34:985-9) and thereafter examine the association between plasma cystatin C and the metabolic syndrome (MDC-CC-re-examination of 1153 subjects who participated in the re-examination study of the population-based Malmö and Diet Cancer Cardiovascular cohort (MDC-CC-re-exam). In this study we aimed to replicate these results and also investigate if cystatin C was causally associated with MetS and diabetes.

Methods: We estimated the effect size of the strongest genome wide association study derived cystatin C SNP (major allele of rs13083305) on plasma cystatin C in the now completed MDC-CC-re-examination (n=3,365) and thereafter examined the association between plasma cystatin C as well as rs13083305 with incident diabetes (436 cases of diabetes and 2840 controls). The association of rs13083305 and incident MetS (610 cases of MetS and 2300 controls) was similarly investigated in the whole MDC-CC-re-exam. We also attempted to replicate our previously shown association of cystatin C with incident MetS in subjects from the MDC-CC-re-examination (147 cases and 709 controls) that were not included in our previous report.

Results: In the entire MDC-CC-re-exam, the total number of cases of MetS was increased by 0.20 standard deviation (SD) higher plasma concentration of cystatin C (p=8.9E-12) in age and sex adjusted analysis. Cystatin C in the now completed MDC-CC-re-examination (n=3,365) and thereafter examined the association between plasma cystatin C as well as rs13083305 with incident diabetes (436 cases of diabetes and 2840 controls). The association of rs13083305 and incident MetS (610 cases of MetS and 2300 controls) was similarly investigated in the whole MDC-CC-re-exam. We also attempted to replicate our previously shown association of cystatin C with incident MetS in subjects from the MDC-CC-re-examination (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 associated with poor cardiovascular outcomes. Increased visceral fat mass is a rapidly growing public-health problem worldwide and significantly associated with poor cardiovascular outcomes. Increased visceral fat mass is a rapidly growing public-health problem worldwide and significantly associated with poor cardiovascular outcomes.

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P4533 | BEDSIDE
Platelet to lymphocyte ratio as a novel indicator of inflammation is associated with the presence and severity of metabolic syndrome
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Background: Metabolic syndrome (MetS) as a cluster of several cardiometabolic components is rapidly growing public-health problem worldwide and significantly associated with poor cardiovascular outcomes. Increased visceral adiposity activates the important pathways connecting low-grade chronic inflammation, cardiovascular stress and insulin resistance. Recently, platelet to lymphocyte ratio (PLR) has been considered as a novel indirect inflammatory marker. Therefore, for the first time, we aimed to investigate the association of PLR with both the presence and severity of MetS.

Methods: Within our previously reported study (J Diabetes Complications and Care 2015; 29:134-143), 121 patients were included to determine the association of PLR with MetS. The study included 121 patients, of whom 53 had MetS (n=53). The association of PLR with MetS and diabetes was evaluated in the entire cohort (n=121) and thereafter examined the association of PLR with MetS in patients with diabetes (n=23) and in those without diabetes (n=98). In our previous study. The association of PLR with MetS was measured and diabetes was confirmed by HbA1c (n=23) and in those without diabetes (n=98). In our previous study.

Results: In our study, a total of 1146 participants were enrolled (n=539 with MetS and n=607 without MetS). MetS was defined according to NCEP-ATP III criteria. Independent predictors of MetS were determined by logistic regression analysis. PLR was calculated from complete blood count.
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 increasing 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). A multivariable regression analysis, serum YKL-40 level [1.033 (1.020–1.047), p<0.001], age and BMI were remained as independent predictors for the presence of MS. In the ROC curve analysis, using a cut-off level of 145.5, YKL-40 well predicted the presence of MetS.

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
FactorXa inhibits brown adipose tissue function and induces systemic metabolic dysfunction in obesity
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Brown adipose tissue (BAT) is a highly-vascularized organ abundant with mitochondria that produce heat through uncoupled respiration. Obesity causes BAT dysfunction, but the mechanism is largely unknown. We have recently reported that obesity causes capillary rarefaction and functional hypoxia in BAT, leading to a BAT "whitening" phenotype that is induced by mitochondrial dysfunction and lipid droplet accumulation, contributing to impaired systemic glucose metabolism. Coagulation factorXa (FXa) is the activated form of FX and has a pivotal role for the regulation of coagulation system. There is evidence that FXa is involved in inflammatory responses, via the activation of its receptors, proteinase-activated receptor1 (PAR1) and PAR2. Increasing evidence shows that PAR1 contributes to tissue remodeling in various models such as liver fibrosis, restenosis and neo-intima formation in response to vascular injury, fibrotic lung disease, kidney fibrosis, and cardiac remodeling. Here we show the previously unknown role of FXa in promoting systemic metabolic dysfunction via the inhibition of BAT function in dietary obesity. We generated an obesity model by imposing a high fat high sucrose (HFHS) diet on C57BL/6Ncr mice. Mice fed the HFHS diet for eight weeks since four weeks of age showed a marked increase in circulating FXa level. To test the specific roles of FXa in obesity, we treated the mice with an FXa inhibitor. Treatment with the FXa inhibitor led to a non-significant reduction in body weight in both the chow and HFHS fed groups and improved systemic insulin resistance upon dietary obesity. The addition of FXa into brown adipose cell-line markedly increased mitochondrial reactive oxygen species (ROS) and reduced mitochondrial membrane potential. FXa treatment also inhibited mitochondrial respiration and induced apoptosis. The inhibition of PAR1 ameliorated FXa-induced mitochondrial ROS production. These results suggest that increased production of FXa associated with obesity promotes systemic metabolic abnormalities by inducing BAT dysfunction. The maintenance of BAT homeostasis via the inhibition of FXa-PAR1 signaling would become a new therapeutic target for obesity and diabetes.

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 pathophysiological role of cyclic guanosine monophosphate (cGMP) signalling has been extensively investigated in DM. Vardenafil, an oral PDE5 inhibitor, has 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 (fa/fa)) and Zucker lean (ZDFL) rats served as controls. Animals received either vehicle (ZDFL, ZDF) or 10mg/kg BW vardenafil per os (ZDFL/Vard, ZDF/Vard) 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 micromanometer system. Gene expression analysis of atrial natriuretic factor (ANF; qRT-PCR), cardiomyocyte diameter/tibia length (CD/TL) and Masson’s staining (fibrosis score (FS)) were used to prove pathological myocardial hypertrophy.

Results: Cardiac hypertrophy (echocardiography; LV anterior wall thickness in systole (LVAWs); 2.81±0.1 mm; relative wall thickness (RWT); 0.49±0.02; LVmass/TL; 0.30±0.01 g/cm; CD/TL: 3.53±0.02 μm/cm; ANF; 3.04±0.26 vs ZDFL (LVAWs; 2.53±0.04 mm; RWT; 0.42±0.02; LVmass/TL; 0.23±0.004 g/cm; CD/TL; 3.98±0.02 μm/cm; ANF; 0.92±0.17); p<0.001, ANF and CD/TL were remained as independent predictors for the presence of MS. In the ROC curve analysis, using a cut-off level of 145.5, YKL-40 well predicted the presence of MS with a sensitivity of 79% and specificity of 75.8% (AUC: 0.843; 95% CI: 0.806–0.880). We reported that chronic administration of vardenafil prevents DM associated myocardial dysfunctions. 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 dysfunction 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 development of systemic metabolic dysfunction in obesity.

We generated an obese mouse model by imposing a high fat/high sucrose (HFFS) diet on C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant increase in the BAT GABA level in the dietary obese model. Addition of GABA into diet C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant increase in the BAT GABA level in the dietary obese model. Addition of GABA into diet on C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant increase in the BAT GABA level in the dietary obese model. Addition of GABA into diet.
but not for TNF=α (all 4 μg/kg) administration. Using IL-1-Receptor- and IL-6 KO mice we found LPS-mediated GIP secretion to selectively dependent 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 insulin secretion (not depicted). Glucagon, GLP-1, and GLP-2 were found neither in LPS nor IL-6 treated mice (not depicted).

To confirm the role of GIP in glucose metabolism in vivo we performed a knockdown in neonatal rat cardiomyocytes with siRNA for TPC1, TPC2 and TPC1/2 KO mice vs. wt.

Purpose: 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 insulin secretion (not depicted). Glucagon, GLP-1, and GLP-2 were found neither in LPS nor IL-6 treated mice (not depicted).

Conclusions: GIP provides a novel link between the immune system and the gut. Although GIP seems to hold minor relevance for glucose metabolism under inflammatory conditions it acts as an anti-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 activated by NAADP. There are two different subtypes in human and rodents: TPC1 and TPC2. Dysfunctional ion concentrations are deleterious to cardiac cells and 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: For maintaining a proper cardiac function a continuous production of energy is critical. Our aim is to go further into cardiac metabolic alterations in TPC1 and TPC1/2 KO mice vs. wt.

Methods: To identify the proteins deregulated by the lack of TPC1 and TPC1/2 we carried out a proteomic study in male left cardiac ventricles of TPC1 and TPC1/2 KO mice by LC-MALDI-TOF/TOF. We validated FABP3 by western 2-DE. Finally, we performed a knockdown in neonatal rat cardiomyocytes with siRNA for TPC1, TPC2 and TPC1/2 and we measured glucose uptake.

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 KO and 129 in wt KO mice; 22 unique were found in TPC1 KO mice, 15 unique in TPC1 wt and 71 in both conditions. In TPC1 KO vs. wt mice, 149 proteins were identified; 43 unique proteins were found in TPC1 KO; 98 common proteins between both conditions and 8 found only in TPC1 KO. The 2-DE western blot for FABP3 in left ventricular tissue of wt, TPC1 KO and TPC1/2 KO showed two spots, one of them downregulated in KO mice.

The majority of proteins deregulated in TPC1 KO and TPC1/2 KO seemed to be key in glucose metabolism. Downregulation of TPC1, TPC2 and both increased 2-deoxy-D-[3H]-glucose uptake by primary cultured neonatal rat cardiomyocytes significantly (p < 0.01, n=5).

Conclusion: The results showed an alteration in the proteins that are implicated in glucose and fatty acid metabolism. In this sense, by 2-DE western blot we confirmed the downregulation of FABP3, a key fatty acid transport. Also, we corroborate in vitro that a downregulation of TPC1, TPC2 and TPC1/2 increased 2-deoxy-D-[3H]-glucose uptake by primary cultured neonatal rat cardiomyocytes. These results highlight the potential role of TPCs in cardiac metabolism.

P4542 | BENCH
Teteniligil ameliorates hypertensive cardiac remodeling via angiotensin-II-mediated cardiac sodium-proton exchanger1 pathway
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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 teneliligil (TEN) on BP and HF using preclinical hypertensive HF models.

Methods: Spontaneously hypertensive rats (SHR; 10 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 cardiomyocytes were monitored by its specific fluorescence indicator (pHrodo, Life Technologies) and live cell imaging using Confocal Scannary Unit (CSU-X1-Yokogawa Electric Corporation) and fluorescence microplate reader (Infinite, TECAN).

Results: Cardiac catheterization revealed that TEN ameliorated hypertension of SHR-CON (Fig. 1). The maximum dP/dt of SHR-CON was elevated (10452±539 for SHR-CON and 5739±599 for WKY-CON), which was reduced by TEN (8033±656 in SHR-TEN) without affecting heart rate. Diastolic indices (minimum dP/dt and tau) were ameliorated by TEN. SHR-CON exhibited increased in heart and body weight (BW) ratio, left ventricular (LV) wall thickness, cardiomyocyte hypertrophy and fibrosis, which were attenuated by TEN. Elevated lung weight and BW ratio and circulating BNP level of SHR-CON were ameliorated by TEN. Cardiac and circulating DPP4 activities of SHR-CON were elevated, which was suppressed by TEN. 

Conclusion: TEN ameliorates cardiac remodeling by downregulating key DPP4 substrate. TEN may have potential for the treatment of cardiac remodeling.

P4543 | BENCH
The effects of age on ovine atrial conduction
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Background: The incidence of atrial fibrillation (AF) has a steep relationship with age, with prevalence in persons aged over 85 exceeding 15%. The susceptibility of the atria to fibrillation in the elderly is incompletely understood. Atrial conduction velocity (CV) has been shown to inversely correlate with vulnerability to AF. CV has also been reported to decrease with age. A determinant of CV is the peak sodium current INa. We investigated how CV and INa changed with age in a species that becomes sensitized to AF.

Methods: Young adult (~18 months) and aged (~8 years, last quintile of life) sheep underwent electrophysiological studies under general anaesthesia. A catheter with 32 bipolar electrode pairs recorded electrogamms from the right atrium (RA) during stimulation at 2Hz. Pacemakers were implanted and AF was induced by using 90Hz burst pacing to the right atrium in conscious subjects. 6 lead ECGs were recorded at the time of surgery during sinus rhythm and were used to calculate p-wave duration. Animals were euthanized with Phenobarbitone and myocytes were isolated from the left atrial appendage. INa was recorded using the whole cell patch clamp technique at room temperature with 3mM extracellular sodium.

Results: Aged sheep were more vulnerable to AF than young sheep in terms of the proportion of bursts that elicited AF (36.3±3.7% vs 22±4.3%, p < 0.05). Circulating angiotensin II (ANG II) was elevated in SHR-CON (19±2±4 vs 12±1±3, p < 0.05). P-wave duration was 14% longer in aged animals (48±1±5ms vs 42±1±4ms, n=22, p < 0.05). In contrast to other models of ageing, RA axial CV was increased by 36% in aged compared to young animals (1.0±0±04 m/s vs 0.74±0±6 m/s, n=11 animals, p < 0.05). Circumferential CV showed similar changes. The anisotropic ratio (circumferential CV/axial CV) did not change with age. Increased CV was associated with a 29% age dependent increase in INa (−26.5±−2.5 pA/pF vs. −24.9±2.3 m/s, p < 0.05). In contrast to other models of ageing, RA axial CV was increased by 36% in aged compared to young animals (1.0±0±04 m/s vs 0.74±0±6 m/s, n=11 animals, p < 0.05). Circumferential CV showed similar changes. The anisotropic ratio (circumferential CV/axial CV) did not change with age. Increased CV was associated with a 29% age dependent increase in INa (−26.5±−2.5 pA/pF vs. −24.9±2.3 m/s, p < 0.05).

Conclusion: Ageing was associated with increased vulnerability to AF and longer p-wave duration, suggesting a prolongation of atrial depolarization. Surprisingly CV increased with age possibly due to increased INa. Increased CV in the aged atria could represent a physiological adaptation compensating for atrial dilatation.

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losplenic axis has not been evaluated before. We aimed to investigate the link between inflammation and fibrosis, in the context of a vasculopathic axis in an experimental type II diabetes model, the ob/ob mouse, and evaluate whether an increase in high density lipoproteins (HDLs), known for their immunomodulatory properties, could affect this axis.

Methods: Ob/ob (B6.V-Lepob/Jr) and C57BL/6 mice were sacrificed at 15 weeks (w) of age. Gene transfer with human apolipoprotein (apo) A-I, the main apo of HDL, was performed in 8 w old ob/ob mice and mice were sacrificed 7 w later. After sacrifice, spleens were isolated, characterized by flow cytometry and their impact on collagen production under coculture with fibroblasts evaluated. Furthermore, the aorta was isolated for mRNA expression analysis. Blood was withdrawn at different timepoints for glucose and human apo A-I measurements. Results: The % of fibrocytes in splenocytes from ob/ob mice was 3.5-fold (p < 0.001) higher compared to those in C57BL/6 mice. There was a 13%, 18%, and 18% increase in the activation/proliferation state of total mononuclear cells (MNCs), CD4 cells, and CD8 cells, respectively, in ob/ob versus C57BL/6 mice (p < 0.05) in the absence of differences in T regulatory cells. The % of TGF-ß expressing MNCs was 18% (p = 0.0571) higher in ob/ob versus C57BL/6 mice. Co-culture of splenocytes from ob/ob, but not from control mice, with murine fi broblasts induced the collagen content in fibroblasts by 57% (p < 0.001). In line with this link between immune activation and fibrosis, aortic collagen I, III, and a-SMA mRNA expression was 5.6-fold, 4.2-fold, and 2.6-fold induced in ob/ob versus C57BL/6 mice (p < 0.01). A-1 transfer leading to persistent human apo A-I levels during the experimental timeframe and to a 1.8-fold (p < 0.05) increase in HDL-cholesterol compared to ob/ob mice at the day of sacrifice, exerted immunomodulatory effects in ob/ob mice. In contrast to splenocytes from ob/ob mice, splenocytes from ob/ob Ad apo A-I mice did not induce collagen content in fibroblasts upon co-culture. Finally, aortic collagen I, III, and a-SMA was 2.5-fold, 3.1-fold, and 1.6-fold lower in ob/ob Ad apo A-I versus ob/ob mice (p < 0.05).

Conclusion: The vasculopathic axis exerts strong pro-fibrogenic effects in a murine model of type 2 diabetes mellitus, which are counteracted by HDL-raising transfer.

**CHRONIC PULMONARY HYPERTENSION**

P4545 | BENCH

A role for tenascin-C in the development of pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease entailing a deteriorating pulmonary vasculopathy with obstruction of small pulmonary arteries, smooth muscle cell hypertrophy and intimal fibrosis. It has been proposed that Tenascin-C (TnC), a key mediator of smooth muscle cell behaviour, has a crucial role in the development of pulmonary arterial hypertension. We aimed to investigate the effect of TnC inhibition by direct gene manipulation on the development of PH.

Methods: We utilized mice with a homozygous TnC knock-out (TnC KO) and A/J wild types (WT). Both TnC KO and WT littermates were held in an environmental chamber with FIO2 of 10% or under normoxia for 4 weeks. We investigated the effect of TnC deletion and chronic normobaric hypoxia on parameters of pulmonary vascular resistance such as right ventricular systolic pressure (RVSP) and right ventricular hypertrophy (Fulton Index/right to left ventricular ratio). To assess the degree of smooth muscle cell hyperplasia, alpha-smooth muscle actin antibody staining was performed.

Results: TnC KO mice showed significantly increased right ventricular pressures after 4 weeks under normoxic conditions, compared with wild type controls (15.2 vs. 21.95 mmHg, p < 0.001). Under 4 weeks hypoxic breeding TnC KO mice revealed significantly higher right ventricular pressures (27.3 vs. 34.9 mmHg, p < 0.001), and Fulton indices than controls (0.43 vs 0.50, p < 0.001). Under both normoxic and hypoxic conditions TnC KO mice revealed significant increased medial thickness (Fig.1).

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.

P4546 | BENCH

Response to fluid challenge test in normal subjects and in a heterogeneous population with pulmonary hypertension

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Background: Hemodynamic assessment after fluid challenge test (FCT) has been proposed for identifying heart failure with preserved ejection fraction (HF-PEF). Limits of normal of FCT are unknown so far. Aim: To explore the hemodynamic response to a FCT in normal subjects and in patients with different forms of pulmonary hypertension (PH).

Methods and results: Seventy subjects underwent right heart catheterization in conditions and after FCT (volume loading with rapid saline infusion of 7 mL/kg in 10 min). At baseline, 20 showed normal pressures (healthy controls), 15 post-capillary and 35 pre-capillary PH. Right atrial pressure (RAP), systolic, mean and diastolic pulmonary arterial pressure (SPAP, MPAP and DAP), pulmonary arterial wedge pressure (PAWP), cardiac index (CI), diastolic pulmonary gradient (DPG) and pulmonary vascular resistance (PVR) were calculated at baseline and immediately after FCT.

Conclusion: Rapid volume loading resulted in a significant increase in RAP, PAWP, MPAP and CI in all groups, yet DPG and PVR remained unchanged.

The difference (△) between basal and FCT is reported in table 1: RAP increased more in pre- and post-capillary PH than in controls, PAWP and MPAP increased more in post-capillary PH than other groups and CI increased more in control subjects. Six out of 70 analyzed patients, 3 apparently normal at baseline and 3 considered having pre-capillary PH, were considered at risk for HFpEF after FCT due to a steeper increase in PAWP (>10 mmHg increase reaching an absolute value >20 mmHg).

Table 1. Difference between basal and FCT

<table>
<thead>
<tr>
<th>Normal</th>
<th>Post-PH</th>
<th>Pre-PH</th>
<th>p</th>
<th>p</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>△RAP (mmHg)</td>
<td>3.2</td>
<td>5.2</td>
<td>5.2</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>△PAWP (mmHg)</td>
<td>4.3</td>
<td>9.3</td>
<td>9.3</td>
<td>&lt;0.01</td>
<td>ns</td>
</tr>
<tr>
<td>△MPAP (mmHg)</td>
<td>4.4</td>
<td>9.5</td>
<td>9.5</td>
<td>&lt;0.05</td>
<td>ns</td>
</tr>
<tr>
<td>△CI (l/min/m2)</td>
<td>0.10</td>
<td>0.20</td>
<td>0.20</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>△DAP (mmHg)</td>
<td>-11</td>
<td>-21</td>
<td>-11</td>
<td>&lt;0.05</td>
<td>ns</td>
</tr>
<tr>
<td>△PVR (WU)</td>
<td>-11</td>
<td>-51</td>
<td>-11</td>
<td>&lt;0.05</td>
<td>ns</td>
</tr>
</tbody>
</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 patients and allows unmasking patients at risk for developing HFpEF.

P4547 | BENCH

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 inflow 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 BR-VI: the angiographic findings of extravasation with
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<0.0001). 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 affect the incidence of PI after BPA, while improving RV fractional area change. Additionally, the PAAT/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.

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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**Hospital Bicetre, AP-HP - Service de Pneumologie et Soins Intensifs, Université Paris-Sud, Le Kremlin-Bicetre, France

Background: Heart failure with preserved ejection fraction (HFpEF) is a frequent cause of pulmonary hypertension (PH) that may be difficult to differentiate from pre-capillary pulmonary hypertension (PrePH), particularly in elderly.

Conclusions: To Single out 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 with or without invasive pulmonary vascular resistance (PVR) ≥ 3 WU. Clinical heart failure 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.

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), higher BMI (32.75 ± 26.6, 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 lower cardiac output than PH-UT, but had higher right atrial pressure (15±5 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 g/m², p<0.01), 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) diastolic area (21±7 vs 24±8 cm², p<0.001) and RV 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).

In contrast, daily treatment with CO2 mist extended the survival period of rats in that group. At 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 hypertrophy of PI-BG impaired RV fractional area change. Additionally, the PAAT/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.

P4550 | BEDSIDE
Genetics of pulmonary arterial hypertension in a Spanish cohort. P0549: First results of the Spanish multicentric study of genetics of HPAH/IPAH
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Recent advances in gene sequencing have led to discovery of new genes related to pulmonary arterial hypertension (PAH) other than BMPR2. Scarce information about genetics in PAH Spanish patients (pt) is available.

Aims: To Describe presence of known PAH related genes and characterize the phenotype of idiopathic PAH pt versus Heritable PAH pt in Spain.

Methods: An Spanish Multi-centric study of genetics of HPAH/IPAH is ongoing since 2011. All pt were screened for BMPR2, KCNK3 and TBX4. After genetic analysis pt were assigned into 2 groups: a group referring to family history and genetic findings: IPAH group (no family story/no mut) and Heritable PAH group which included: PAH with positive family story but no detected mut, PAH with positive family story with detected mut and sporadic cases with detected mut. Clinical data were obtained from Spanish Registry of PAH (REHAP).

Results: 117 pt were studied: 104 with negative family story and 13 with positive family story.Mutations (mut) were found in 22 pt (18.8%): 18 mut in BMPR2 (53.84% of PAH with positive family story and 10.53% of sporadic PAH), 2 mut in TBX4 in two non-related sporadic PAH pt (1.9%) and 2 mut in KCNK3: one sporadic PAH pt (0.96%) and one PAH pt with positive family story (7.6%). Final distribution was: 90 pt with IPAH (76.9%), 22 pt with positive family story and detected mut (18.8%) and 5 pt with positive family story but no detected mut (4.3%). Baseline characteristics in Chart 1.

Baseline characteristics

<table>
<thead>
<tr>
<th>Trait</th>
<th>Heritable (n=27)</th>
<th>Idiopathic (n=90)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35±13.73</td>
<td>40±8±14.21</td>
<td>0.0509</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>37.03%*</td>
<td>15.55%*</td>
<td>0.0001</td>
</tr>
<tr>
<td>% NYHA III / IV</td>
<td>51.9%*</td>
<td>44.96%*</td>
<td>0.036</td>
</tr>
<tr>
<td>O2sat during 6MWD (meters)</td>
<td>64.4%*</td>
<td>39.1%*</td>
<td>0.0001</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>63.4±15.54*</td>
<td>7.1±7.03</td>
<td>0.0051</td>
</tr>
</tbody>
</table>
| mPAP, mean pulmonary artery pressure; mmHg, kilometers of mercury; PVR, pulmonary vascular resistance; AVT, acute vasodilator test.

Conclusion: PAH pt tend to be younger with slightly more severe hemodynamics, better 6MW and less response in AVT. Prevalence of TBX4 and KCNK3 is low. BMPR2 mut were found in a smaller proportion of Heritable PAH than previously reported. Further research is needed to find new PAH related genes that may play a role in Spain.

P4551 | BEDSIDE
The assessment of exercise tolerance and oxygenation after balloon pulmonary angioplasty for patients with inoperable chronic thromboembolic pulmonary hypertension
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Background: Balloon pulmonary angioplasty (BPA) could be effective for inoperable chronic thromboembolic pulmonary hypertension (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±11.6 years old) who underwent BPA were enrolled. We evaluated hemodynamics, arterial blood and mixed venous oxygen 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 arterial pressure; 38±4.6 mmHg to 20.8±5.3 mmHg, p<0.001, pulmonary vascular resistance; 727±136 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±3.6 mmHg, p=0.87, respectively). BPA also greatly improved exercise tolerance of 6MWD (288±97 mm to 397±117 mm, 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 diffusion 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 diffusion 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.

P4552 | 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 patient 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 diagnostic impact of each PH in patients with dialysis.

Results: Eight hundred ninety patients were examined. Twenty eight hundred eighty two patients (25%) had PH. The prevalence of group 5 was 48% (5) and group 2 were 180 patients (20%). Left ventricular ejection fraction (LVEF) was significant differences among the group (non-PH: 48±12%, group 5: 44±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 (2.28, 95% CI: 1.66–3.06, p<0.001). On multivariate analysis, both group 2 and group 5 were significant factors on mortality after adjusting for 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.

P4553 | 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 (Δ) 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 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 ΔS, ΔTAPSE, ΔPASP, ΔSV and ΔPASP, but increased TAPSE-PASP at peak exercise. Aging was associated with decreased ΔS, ΔTAPSE, ΔPASP, ΔSV and TAPSE-PASP Changes in S, TAPSE-PASP and SV were directly correlated to workload.

Conclusions: These results provide age- and sex-related limits of normal RV contractile reserve as assessed by stress echocardiographic PASP, TAPSE, S and TAPSE-PASP. Right ventricular contractile reserve, however measured, correlates with exercise capacity.

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 center.

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 31th, 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 estimated diagnostic work-up in the everyday clinical practice of a regional hub center.

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 finding TR, and 2827 (20%) mentioned no PAPs at all. In the group of patients with high echocardiographic likelihood 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-
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, and clinical events including aortic valve replacement, heart failure requiring hospitalisation, 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-all admission, acute coronary syndrome and syncope, were measured as main outcomes.

**Conclusion:** Increased levels of bone turnover biomarkers were found in AS with potential target for therapeutic actions.

**P4556 | BEDSIDE**

Impact of pulmonary arterial pressure on long-term survival in patients with aortic stenosis and preserved left ventricular ejection fraction


**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 with preserved LVEF.

**Methods and results:** Between 2000 and 2010, 749 patients (74±8 years, 57% of males) with preserved LVEF (>50%) and severe AS (aortic valve area ≤ 1.0cm²) were included. 31 healthy people as a control (57.6±0.8 yrs; m:f 1:1.2) were examined. Serum osteoprotegerin (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:**

**Conclusion:** Pulmonary pressures were higher in patients with higher TR grades. 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 24 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=0.0199 adjusted for age, sex and censored 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. 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.

**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.

**References:**


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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 valve replacement criteria were included. Moderate 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 patients by TR severity into 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.

**Conclusion:** In patients with severe AS and preserved LVEF, PH was an independent predictor of mortality (hazard ratio=1.5, 95% CI: 1.1–2.1, p=0.037). Using quartiles of mean PAP, only patients with most elevated PAP showed significant reduced survival in patients with PH (10-year survival= 41±8 vs. 61±3%, p < 0.0001). Likewise, the mortality analysis focusing on patient with AVR showed significant reduced survival in patients with PH (10-year survival= 45±8 vs. 65±4%, p < 0.0001). In multivariate analysis, after adjustment for all cofactors, PH was an independent predictor of mortality (hazard ratio=1.5, 95% CI: 1.1–2.1, p=0.037). Using quartiles of mean PAP, only patients with most elevated values (Q4: 27–67mmHg) have significantly reduced survival, as compared to the three other quartiles (all p < 0.0001). By opposition, there was no significant difference in term of survival between Q1, Q2 and Q3. Similar results were found when patients with preserved LVEF and AVF were performed with standard PAP instead of mean PAP resulted in similar findings.

**Conclusion:** In patients with severe AS and preserved LVEF, PAP is an independent predictor of both 30-day and long-term mortality. Nevertheless, only severely elevated PAP seems 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 important 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 LVEF were obtained quantitatively by 2D speckle tracking and automated functioned image (AFI) 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 non-remodeling in severe MR with normal LVEF was −20.5% of 2D mid-layer GLS (sensitivity 0.70, specificity 0.75). Patients were divided into two groups by the baseline global GLS −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.

Table 1. Multivariate 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>0.351 (0.067–1.583)</td>
<td>−0.153</td>
<td>0.178</td>
</tr>
<tr>
<td>Post OP E/e’</td>
<td>0.860 (0.935–1.919)</td>
<td>0.060</td>
<td>0.585</td>
</tr>
<tr>
<td>Baseline mid-layer GLS</td>
<td>2.440 (1.259–4.729)</td>
<td>0.803</td>
<td>0.009</td>
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</tbody>
</table>

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. LVGLS (%) was measured off-line from the three apical views by 2D-STE using EchoPac 110 workstation. Parameters were calculated. Global and regional LS were obtained quantitatively by 2D speckle tracking and automated functioned image (AFI) technique.

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 pathophysiologic 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.

Conclusions: 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

<table>
<thead>
<tr>
<th>Variable</th>
<th>MR</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>65.04±6.88</td>
<td>61.67±6.06</td>
<td>0.028</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>53.22±18</td>
<td>47.30±3.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVGLS (%)</td>
<td>−17.73±6.06</td>
<td>−20.43±3.33</td>
<td>0.023</td>
</tr>
</tbody>
</table>

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.

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 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 98 patients (mean age 55.3±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 (0.8±1.7 vs 6.2±1.1, 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 HSR has 72.9% 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.

P4562 | BEDSIDE
The overlooked parameter of shear stress in mitral annular calcification: Whole blood viscosity
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Introduction: Endothelial insult prompted by an increased mechanical stress has been postulated as the initial step in the pathogenesis of mitral annular calcification (MAC). Increased whole blood viscosity (WBV), can aggravate endothelial disruption via enhanced mechanical stress. Therefore, we aimed to assess the relationship between MAC and WBV.
**AORTIC VALVE DISEASE II**

**P4564 | BEDSIDE**

The prognostic significance of post-MitraClip vena contracta area in heart failure patients with functional mitral regurgitation

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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+), with a statistically significant difference in success rate observed between the 13 patients with intact leaflets at the time of the repeat intervention and the 8 patients in whom leaflet tear/PCD was present (11/13 [85%] vs. 2/8 [25%], respectively; p=0.0176). Thus, leaflet tear/PCD was strongly predictive of repeat procedural failure (odds ratio 16.5 [95% confidence interval 1.8–149]; p=0.012).

The 21 pts were followed for a median of 8.5 (interquartile range 2.3–18.6) months; 13 pts (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 with satisfactory leaflet/clip integrity. Leaflet tear/PCD at the time of 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 Schaerfer have received research grants from Abbott Vascular, Inc.

**P4565 | 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).

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Conclusions: Repeat MC intervention for significant MR in elderly patients deemed inoperable or at high surgical risk appears to be a viable therapeutic approach with satisfactory leaflet/clip integrity. Leaflet tear/PCD at the time of 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 Schaerfer have received research grants from Abbott Vascular, Inc.
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 accordingly. EuroScore was used to determine operative risk and Charlson Comorbidity Index to measure comorbidity. The McNiemar-Bowers 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.

Conclusions: Current international class Ia indications for symptomatic patients guarantee a good long term survival. Class Ia indications for asymptomatic patients with reduced LVEF are associated with poor long term survival. Present findings suggest the need of critical revision of surgical indications for this specific group of patients.

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 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 3 months (the opening group, Fig A), had improved LV contractility during exercise over those with closed native AV irrespective of exercise (the closed group) (p=0.05 for all). The opening group suffered no AI at the 6 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).

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.

P4568 | BEDSIDE

Long term survival after aortic valve replacement: role of European and American guidelines adherence

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Background: ESC and ACC/AHA guidelines recommend aortic valve replacement (AVR) with class I indication only for patients with symptomatic severe aortic valve stenosis (SSAVS) and asymptomatic patients with depressed left ventricular ejection fraction (LVEF <50%).

Purpose: We examined the influence of International guidelines adherence on long term survival.

Methods: 604 patients underwent isolated AVR for SAVS between January 2001 and December 2012. The population was first divided in two groups based on preoperative LVEF (< 0.50). A second step analysis was performed based on presence or absence of symptoms (NYHA ≤ II respectively).

Results: Median follow-up time was 5.75 years (3.24–8). Patients with LVEF <0.50 presented higher long term mortality (p=0.015). Presence of symptoms had not a significant negative impact on mortality (p=0.201) (panel A). The combined analysis (panel B) showed that preserved LVEF is a protective factor for mortality in asymptomatic patients (class IIb) and asymptomatic patients with reduced LVEF presented higher risk of mortality (HR 1.32, CI 95%, 0.12–14.17). LVEF did not play any role in mortality for symptomatic patients (class Ia) (HR 0.41, CI 95%, 0.18–0.95). At multivariate analysis the independent risk factors for death were age (HR 6.46, CI 95%, 2.22–18.76) and presence of atrial fibrillation (HR 1.07 CI 95%, 0.57–2.04) or new permanent pace-maker (HR 1.21, IC95%, 0.44–3.32) at discharge.

Conclusions: Current international class Ia indications for symptomatic patients guarantee a good long term survival. Class Ia indications for asymptomatic patients with reduced LVEF are associated with poor long term survival. Present findings suggest the need of critical revision of surgical indications for this specific group of patients.

P4569 | BEDSIDE

Exercise hemodynamics in symptomatic patients with low grade 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 radial artery 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 (SVRI) decreased (~227 dynes/s/cm² per mL/kg/min of VO2). Multivariate 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 major 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 P590/02602, RD12/0042 and CM12/00273 from the Instituto de Salud Carlos III, Spain.
Echocardiographic and MRI assessment of myocardial strain and strain rates using speckle tracking and feature tracking in asymptomatic aortic stenosis

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Background: Myocardial deformation analysis allows detection of subclinical myocardial dysfunction, which may have prognostic value in aortic stenosis (AS). Speckle tracking Echocardiography (STE) is the most widely used technique for strain assessment, while Feature tracking (FT) is a novel technique on magnetic resonance imaging (MRI).

Purpose: To compare MRI-FT and STE in patients with AS and healthy controls (HC).

Methods: 138 Patients with 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.

Results: 72 AS patients (age 65±12.9 years, 72% male, aortic valve area 1.15±0.34 cm2, mean pressure gradient 34.47±12.24 mmHg) and 16 HC (mean age 68±8.24 years, 75% male, mean AVA 3.49±0.86 cm2) were included. There was no significant difference in PSS between the two groups, but with poor agreement. There was a significant positive bias for FT strain rates which was particularly marked for peak early diastolic strain rate with poor agreement between techniques. This finding likely results from poor speckle tracking during diastole.

Conclusion: 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/rate can be useful in the management of asymptomatic patients with AS.

Acknowledgement/Funding: National Institute Health Research, Universities Hospital of Leicester, Cardiovascular Biomedical Research Unit Glenfield Hospital.

P4571 | BEDSIDE

The relationship between aortic valve weight and hydraulic vascular load in patients with severe isolated aortic stenosis who underwent surgical aortic valve replacement

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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 patients with isolated severe AS who underwent surgical AVR between 2010–2014 and had AV weighed, 649 (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 (Za) could be measured in 276 pts. 4 hemodynamic subgroups were analyzed using cut points of stroke volume index (SVI) and mean gradients (MG) of 35 ml/b/m² and 40 mmHg, respectively. One-way dynamic subgroups were analyzed using cut points of stroke volume index (SVI) dynamic profile. Systemic vascular resistance (SVR), systemic arterial compliance (SAC) and global LV afterload (Za) could be measured in 276 pts. 4 hemodynamic subgroups were analyzed using cut points of stroke volume index (SVI) and mean gradients (MG) of 35 ml/b/m² and 40 mmHg, respectively. One-way dynamic subgroups were analyzed using cut points of stroke volume index (SVI) dynamic profile.
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 paravalvar AR immediately after deployment of the transcatheter heart valve but not with the final result after corrective measures such as postdilation (Figure) and did also 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 paravalvar AR: perimeter (79.2±8.4 vs. 73.6±6.4 mm; P=0.005), area (480.5±90.5 vs. 421.7±73.4 mm², P=0.01), ellipticity index (1.3±0.10 vs. 1.2±0.11, P=0.001), and PLR index (9.1±3.8 vs. 8.5±1.9, 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 paravalvar 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


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Aims: Usefulness of exercise-stress echocardiography for risk stratification of asymptomatic patients with aortic stenosis (AS) is still debated (Class IIb recommendation). The exercise-induced increase in transvalvular gradient has been proposed as a new marker for severe AS, 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 death 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 patients (mean [quartiles]; age 67 [57–75] years, 68 male, mean gradient 46 [25–52] mmHg, aortic valve area 0.97 [0.82–1.11] mm²) had a normal exercise test and 39 (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 [0.29–1.65]) 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 additional value and therefore the use of exercise-stress echocardiography for risk-stratification of asymptomatic patients with AS.

AORTIC VALVE INTERVENTIONS

P4575 | BEDSIDE

Improvised management of left-sided infective endocarditis not accompanied by lower mortality

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Introduction: Despite continued progress in the management of infective endocarditis (IE) this entity continues to have an in-hospital mortality of 20–30% which has remained steady over the past 2 decades.

Objective: The aim of this study is to determine if there is a relationship between a worsening epidemiological profile and the lack of improvement in mortality rates over the past 18 years in IE.

Methods: We prospectively collected all IE episodes diagnosed in three tertiary hospitals from 1997 to 2014. A global cohort of 969 left-sided IE episodes was divided into three six-year periods over time: 259 episodes (26%) diagnosed from 1991 to 1997, 335 (35%) from 2003 to 2008 and 375 (39%) from 2009 to 2014. A multivariate logistic regression model for mortality was developed for the first group of patients and then was tested on predicting death in the second and third periods.

Results: Female sex (46% vs 29%, p=0.010), mean age (63 vs 58, p=0.007), cancer (12% vs 4%, p=0.012), Staphylococcus aureus (31% vs 12%, p=0.001), vegetations on echo (91% vs 80%, p=0.025), heart failure (75% vs 50%, p=0.004), re-admission after 1 year (66% vs 34%, p=0.001), shock (36% vs 3%, p=0.001) and persistent infection (49% vs 22%, p=0.001) were related with a higher mortality in the first period of time (1997–2002). Multivariate analysis revealed age (OR 1.024, 95% CI: 1.01–1.047), Staphylococcus aureus (OR 2.486, 95% CI: 1.130–5.469), vegetation on echo (OR 3.518, 95% CI: 1.340–9.240), persistent infection (OR 2.314, 95% CI: 1.202–4.452), heart failure (OR 3.091, 95% CI: 1.563–6.113) and renal failure (OR 2.021, 95% CI: 1.076–3.798) as independent predictors of mortality. A logistic equation including the coefficients of the regression analysis was generated. Predictive accuracy of the model and validation was measured (CPC area under the curve: 0.805). This model was applied to the second and the third periods. Expected mortality for the second period (2003–2008) according to the model was 32.1% whereas observed mortality in the cohort was 28.1% (12.5% of reduction). Expected mortality for the third period (2009–2014) was 15.2% and observed mortality was 33.8% (21.6% of reduction).

Conclusions: Although the crude in-hospital mortality rate of IE has remained unchanged over the past 18 years, there has been a reduction in observed mortality compared to the expected mortality according to the prognostic risk profile of the patients.

P4576 | BEDSIDE

Changes in clinical, epidemiological and prognostic profiles in native left-sided infective endocarditis without underlying heart disease


Introduction: Native left-sided infective endocarditis (NSLEI) 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 aims are 1) to compare NSLEI profile between patients with (UHD) and without (NUHD) underlying heart disease and 2) to describe changes in this profile in NUHD patients.

Results: From 1967 to 2014 a consecutive series of 254 patients diagnosed with NSLEI was retrospectively analyzed. Among the 121 patients enrolled, 35 (29%) had an abnormal exercise test (91% vs 80%, p=0.025), a higher elective rate of surgery (48% vs 15%, p=0.004) and persistent infection (30.7% vs 15.5% of reduction, p=0.001). The comparison of the three periods (1988–2000, 2001–2008 and 2009–2014) showed that the crude in-hospital mortality rate of IE has remained unchanged over the past 18 years, there has been a reduction in observed mortality compared to the expected mortality according to the prognostic risk profile of the patients.

Conclusions: Although the crude in-hospital mortality rate of IE has remained unchanged over the past 18 years, there has been a reduction in observed mortality compared to the expected mortality according to the prognostic risk profile of the patients.
in-hospital mortality with a sensitivity of 78% and specificity of 61%. In multivariate 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 mortality in patients with IE.

**Figure**

Conclusion: Our study findings showed that on-admission PLR value well predicted in-hospital mortality in IE. Thus, the PLR, as a simple, easily available and promising biomarker, help us in identification and risk stratification of high-risk IE patients for early aggressive management strategies to prevent in-hospital mortality.

**P4579 | BEDSIDE**

The impact of a second mitral valve surgery after repairing a rheumatic mitral valve


**Background:** The repair of rheumatic mitral valves (MV) is not consensual based on the less favourable reports concerning the immediate rate and shorter durability of mitral valve repair (MVR).

**Purpose:** We proposed to analyse MV reoperations in this setting and the impact of a second mitral valve intervention after repairing a rheumatic MV.

**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 second surgery with those who did not (log-rank).

**Results:** The mean age was 60.6±10.5 years, female gender prevailed (73%), the majority of patients were in NYHA class III–IV (63.3%), 52.8% were in atrial fibrillation and 53.6% had isolated mitral stenosis (MS). The majority of the operated patients had a stenotic component in the first surgery and only 8.1% had isolated mitral regurgitation (MR). The main indications for the second surgery were MR, as a mixed lesion (46%) or “pure” MR (29.8%), and only 24.2% had isolated MS.

**Conclusion:** Our findings showed that in-hospital mortality in patients with IE.

**Methods:** Prospective cohort study of high-risk Indigenous Australian children. Cases had Borderline RHD or NSVAs on prior echocardiography. Controls had a normal echocardiogram. Follow-up echocardiography was performed 2.5–5 years later to assess for progression of valvular lesions and development of Definite RHD. Risk of progression and Definite RHD was assessed. Baseline echocardiograms were re-read by an independent cardiologist and sensitivity analysis undertaken.

**Results:** 442 individuals were enrolled. Classification of participants based on initial reading of baseline echocardiograms was: 55 Borderline RHD, 62 NSVAs, 325 Normal. Cases were at significantly greater risk of progression (RR 3.36, 95% CI 1.90–5.94) and development of Definite RHD (RR 20.8, 95% CI 1.8–89.7) than Controls.

Subsequent re-reading of baseline echocardiograms demonstrated concordance in 351 (79%), Inter-rater reliability using linear weighted Kappa was 0.656 (p<0.001, 95% CI 0.592–0.721). After reclassification of participants the assessment of risk was largely unchanged with Cases remaining at a greater risk of progression (RR 3.17, 95% CI 1.69–5.94) and Definite RHD (RR 24.9, 95% CI 3.2 to 190.7).

**Inter-rater concordance**

<table>
<thead>
<tr>
<th>Classification based on initial reading</th>
<th>Normal</th>
<th>NSVA</th>
<th>Borderline RHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>279</td>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>NSVA</td>
<td>41</td>
<td>33</td>
<td>5</td>
</tr>
<tr>
<td>Borderline RHD</td>
<td>4</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Definite RHD</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

Percentages show concordance of subsequent reading with initial reading.

**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 Research 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 auscultation skills at an annual cardiology meeting (American College of Cardiology) over a period of two years from 2011 to 2014. Cardiologists chose to be tested on a set of basic murmurs including Aortic Stenosis, Aortic Regurgitation, Mitral Stenosis, Mitral Regurgitation or a set of advanced murmurs including Bicuspid Aortic Valve, Mitral Valve Prolapse, combined Aortic Stenosis and Regurgitation and combined Mitral Stenosis and Regurgitation. Cardiologists could choose to be tested on both modules. Before a pre-test, all subjects listened to 400 repetitions of each murmur while viewing cardiac images including phonocardiograms relevant to that lesion. The training time averaged 90 minutes for each set of murmurs. Immediately following the training, there was a post-test of the respective murmurs in a randomized order. The test murmur samples were from different patients than the training murmur samples.

**Results:** On the basic murmurs, 980 cardiologists scored 47.6±12% on the pretest which increased to 88.4±15% on the posttest (p<0.001 by paired t-test).

On the advanced murmurs, 932 cardiologists scored 65.8±13% on a pretest which improved to 92.7±16% on a post test (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 repetition training in a short time frame.

**P4581 | BEDSIDE**

Aortic valve replacement with or without concurrent coronary artery bypass grafting in octogenarians: 8-year cohort study


**Background:** The introduction of transcatheter aortic valve implantation...
P4582 | BEDSIDE
Impact of direct transcatheter aortic valve implantation on final device position and paravalvular leak. Is it beneficial?

Background: Transcatheter aortic valve implantation (TAVI) may be limited by paravalvular leak (PVL) related to malpositioning of the bioprostheses. 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. The potential effect of BAV in the implantation depth (ID) and consequently in post-TAVI PVL is not known.

Methods: We reviewed the characteristics and outcomes of octogenarians undergoing isolated AVR and AVR+CABG at our centre.

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 when TAVI was 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=0.018), higher STS score (6.9% vs 4.9%, <0.001) and higher 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 someone from undergoing cardiac surgery.

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±1.4 mm, P=0.005, respectively). Implantation of a TAVI was performed successfully in all patients with AR and the post-procedure aortic reguritation grade was: absent in 5 patients, middle-moderate in 4 patients, and moderate-severe in one patient.

The NYHA functional class improved from 3.2±0.6 to 1.6±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=0.037 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 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.

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.

(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) particularly in high-risk patients to inform 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 analyses.

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 when TAVI was 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=0.018), higher STS score (6.9% vs 4.9%, <0.001) and higher 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 someone from undergoing cardiac surgery.
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 speckletracking echocardiography.

Results: GLS of three-layer cardium in DM patients are lower than those of normal 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±5.78, 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 three-layer 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: Relevant to anakinra administration in patients with recurrent idiopathic pericarditis published up to October 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 12 citations retrieved, nine reports (four case series and five case reports with 34 patients, 20 men, mean age 26.8 years) were assessed.

The mean disease duration was 31 months and the number of recurrences 8.2.

Anakinra was administrated as a daily subcutaneous injection of 100 mg or as a single loading dose of 1.1 mg/kg in weight-adjusted regimens. The mean full-dose duration was 9.2 months. C-reactive protein normalized within 7.1 days, and steroids were withdrawn within 62 days. Dose tapering was adopted in 64.7% of patients, leading to recurrence in 26% of cases. In a 28.3-month follow-up, eight out of 34 patients (23.5%) were disease free without treatment, after receiving anakinra for 10.4 months overall. Anakinra was proved well tolerated, with mild local reactions being reported in 44% of patients.

Conclusions: Anakinra is a highly effective, rapidly acting, well-tolerated and steroid-sparing agent. Recurrences after drug discontinuation are a matter of concern. Randomized trials are required to confirm these findings and address the most effective treatment protocol.

P4587 | BEDSIDE
Lipoprotein-associated phospholipase A2 (Lp-PLA2), a vascular inflammation marker, is frequently increased in patients presenting with acute pericarditis
A. Izhaki1, M. Boaz2, T. Chaizy1, Y. Abuhav1, J. Roitelman2, Y. Rozenman1.

Introduction: Lp-PLA2 plays a causal role in the development of atherosclerosis and contributes to plaque instability through pathways related to non-atherosclerotic 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 (Plac 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 p</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-Reactive Protein</td>
<td>8.4 (7.3) mg/L</td>
<td>0.441 0.011</td>
</tr>
<tr>
<td>TR</td>
<td>3.4 (3.2) ng/ml</td>
<td>0.399 0.037</td>
</tr>
<tr>
<td>CPK</td>
<td>324 (287) units</td>
<td>0.329 0.044</td>
</tr>
<tr>
<td>WBC</td>
<td>10.6 (4.5)103 cells/L</td>
<td>0.02 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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Objectives: Levels of Lp-PLA2 in AP, a nonvascular inflammation, should be greater than normal.

Intravenous human 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 systematic 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 19.6 months (range 3.3 months to 20 months) in 20 of the 30 patients cases 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 effective steroid-sparing agents in refractory recurrent pericarditis after failure of conventional therapies.

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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 phenotypes 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 polyneuropathy. Cardiac assessment included a clinical examination, electrocardiography (ECG), echocardiography (Echo). The mean age (range) of the patients was 58.6±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 Ser52Pro 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.
(septum:18.1±3.4mm, posterior wall:17.1±2.5mm, right ventricular free wall: 8.1±2mm). A varying degree of diastolic dysfunction was found – mild in 17 (37.8%) patients, moderate in 10 (22.2%) and severe in 18 (40%) patients. Reduced LV ejection fraction was found in 8 (17.8%) patients. Significantly reduced mitral annular myocardial velocities (s:av.-5.9±2.1 cm/s, e:av.-5.1±1.7 cm/s) were present. Periparic effusion was evident in 14 (31.1%) patients. Pathological ECG was present in 40 (88.9%) of the evaluated patients and the most common findings were low voltage in 16 (35.6%), A-V block first degree in 12 (26.7%), left anterior fascicular block in 12 (26.7%), pathological Q wave in 13 (28.9%) patients.

Conclusion: 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.

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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 (TTE), a diagnostic criterion is met if RVOT dilation in addition to RV wall abnormalities is present. Recent studies questioned the diagnostic performance of TTE in comparison to cardiac magnetic resonance (CMR). Therefore, we investigated the reproducibility of TTE 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.

Conclusion: Measuring 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 abnormalities 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 notch-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% 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. 92±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±4.2 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 diluted 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.

Conclusion: There is a need for more studies and further evaluation in patients with end-stage HCM.
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 performed. There were 72 (37%) patients with PLN R14del mutation, 100 (51.3%) patients with other cardiomyopathies (ICMP), and 24 (12.3%) patients with normal hearts. LGE was quantified and expressed as percentage of myocardial mass.

Results: The amount of LGE was significantly higher compared with DCMP group without active inflammation: relatively 1,8 [0,0; 3,2] (p < 0,0001) and 1,3 [0,6; 2,0; 3,0] years and 40 years of FU. Survival was significantly lower in infracardiac type (p < 0,001). Overall 131 patients survived of whom 84.7% are in NYHA class I with none ongoing cardiac medication. Pulmonary pressure levels range within normal value in 109 cases (83%), grade I PHT persists in 9 (7%).

P4594 | BEDSIDE
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Correlation LV-LGE and LVEF (n=160)
Introduction: Obstruction of the left ventricular outflow tract (LVOT) and resultant sub-aortic stenosis (SAS) may represent an acquired condition since it is rarely recognised 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 retrospectively reviewed. Parameters (n=18) were compared between two groups; those who underwent recurrent 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 utilised 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) (33.5±9.0 vs 39.0±9.4, p=0.027), steeper aortoseptal angle (130.5°±8.5° vs 136.1°±8.3°, p=0.006) and smaller mitral valve annulus diameter (15.6±5.9mm vs 20.2±6.4mm, 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±2.3mm vs 6.9±1.4mm, p=0.008 and 4.5±2.2mm vs 6.7±2.4mm, p=0.006). Post-operative residual SAS with higher peak and mean trans-aortic gradients (28.7±15.1mmHg vs 20.1±10.5mMHg, p=0.003 and 15.5±3.8mMHg vs 10.2±2.5mMHg, p=0.002) was more common in patients with recurrent SAS. These patients had higher mean HR: 107.5±24.89 (group A); 100.95±10.97 (group B) (p=0.024); minimum HR: 116, 5±26.05 (group A); 101.95±10.97 (group B) (p=0.012). Duration SNRT before atropine: 1272.78±303.3 msec (group A); 1560.08±275.84 msec (group B) (p=0.04). We also identified a significant difference in duration of the interval PQ, QRS, SNRT after atropine, cSNRT, WP.

Conclusions: Among children with hypervagotonidc BD progression of the disease is observed in 21% of the children. All children need following examination in order to determine the progression of the disease.

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Follow-up of children and teenagers with paroxysmal supraventricular tachycardia but without preexcitation syndrome


Background: With the development of ablation techniques, the natural follow-up of preexcitation syndrome (PS) became difficult to assess. Several authors have reported that recurrent preexcitation syndrome (PS) can be associated with atrial fibrillation (AF). The purpose of this 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±5 years) 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 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 syncype 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±73 bpm vs 190±63 bpm in CS) (0.6). The FS (beta=−0.124, p=0.044), the aortoseptal 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.
oventricular (AV) nodal re-entrant tachycardia (RT) (AVNRT) in 118 children, ei-
ther typical (n=104) or atypical (n=14), to an AVRT related to a concealed acces-
sory pathway (AP) in 44 patients (27%). Radiofrequency (RF) of slow pathway
(n=69) or AP (n=19) was performed in absence of general anaesthesia in 88 pa-
tients (54%) from 1 month up to 13 years after initial evaluation (mean ±2.5±3 years).
Failure of ablation (frequently for refuse to continue) was frequent and occurred in
17 children (26%), 7 with AVNRT (10%), 10 with AP (53%) (0.001). Recurrence of
SVT in patients with apparently successful ablation occurred in 17 patients (24%),
4 (6%) with real recurrence of SVT and 13 (18%) with only sinus tachycardia-
related symptoms. One teenager required atrial fibrillation ablation 11 years later.
In 13 children treated by antiarrhythmic drug (AAD) or beta-blockers, SVT recurred
in 4 children; 2 children presented AAD-related syncope. 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 de-
velopment 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 abla-
tion but false recurrences are frequent (18%). In absence of ablation, one third of
children had a spontaneous favourable evolution. However in symptomatic chil-
dren with frequent SVT’s despite antiarrhythmic drugs or beta-blockers, ablation
should be indicated to avoid drugs-related adverse effects.

P4601 | BEDSIDE

Soluble suppression of tumorigenicity 2 (sST2) time-course in pediatric patients with heart failure supported by ventricular assist device implant

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Background: VAD utilization is increasing in children with heart failure (HF) un-
responsive to medical therapy allowing for bridge to transplantation. Circulating
biomarkers have an important role in the diagnosis and prognosis of HF in adults,
with early indications for their use in pediatric population. Soluble suppression of
tumorigenicity 2 (sST2) is considered an emerging marker of cardiovascular
stress with clinical value for predicting HF in adults.

Purpose: The aim of this study was to evaluate in pediatric patients whether sST2
is associated with the presence of HF and if its plasma levels are modified after
VAD therapy.

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 Mechani-
cally Assisted Circulatory Support (INTERMACS) profiles 1/2] were studied. In-
cluded were patients (54%) from 1 month up to 13 years after initial evaluation (mean ±2.5±3 years). Cardiac events occurred in 43 pts as shown here by groups.

Results: Before VAD implant, sST2 levels are highest in HF compared with healthy
children (p<0.0001 newbons 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).

Conclusion: In pediatric population, circulating levels of sST2 were associated
with presence of HF and were modified by LVAD implant. These data stimulate
to evaluate the impact of inflammatory signals on patient outcome, suggesting a
role for sST2 in a more integrated management of HF in children.

P4602 | BEDSIDE

Double outlet right ventricle with non-committed ventricular septal defect

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Objective: The management of Double Outlet Right Ventricle (DORV) associated with anatomically non-committed Ventricular Septal Defect (NCVSD) constitutes a surgical challenge. The limits for, and the specific outcomes after anatomical versus univentricular repair still remain to be established.

Methods: Between 1993 and 2013, 200 patients presenting with DORV/NCVSD and 2 adequately sized ventricles were included into the study at two centers forming the National Referral Center. The selection criteria included the absence of outflow tract VSD: 21 inlet (4 complete atrio-ventriculare septal de-
fekt (AVSD)), 9 muscular and 5 perimembranous. RVOTO was present in 18/35
(51%). Twenty patients had undergone 25 initial palliative procedures.

Results: Anatomical repair by means of intraventricular baffle construction was performed in 23 (Group I) at a median age of 10.5 months. VSD was surgically
enlarged in 11 (48%). An associated RVOT reconstruction was required in 11
and Arterial Switch Operation (ASO) was done in 5. The remaining 12 patients
underwent univentricular palliative repair (Group II). There were 4 hospital deaths
(11.4%): 3 in Group I and one in Group II (p=0.06). 8/20 survivors of group I
patients underwent 13 reoperations after a median delay of 24 months, with
subaortic stenosis being the main cause for reoperation (6). There was one
late death in group 2. At last visit, all survivors were in NYHA class I/II. Ten years
actuarial survival rate and freedom from reoperation were respectively 74.7±5% and
58±5% in Group I and, 80±7% and 71±7% in Group II. Univariate analy-
sis showed that AVSD and/or isolated mitral cleft were associated with death
(p=0.04) and need for reoperation (p=0.038).

Conclusions: Despite the need for complex procedure and the high incidence
of reoperation for subaortic obstruction, our results suggested the long-term ad-
vantages of anatomical repair in DORV with NCVSD. The presence of associated
AVSD and/or isolated mitral cleft was the only risk factors for mortality and reop-
eration.

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
and after medical therapy (AMT). Risk stratification for patients with CAA in the acute phase.

Methods: We reviewed the outcome and incidence of cardiac events in 214 pa-
tients (159 male 55 female) who had CAA 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: 8mm≤
<6.0 mm when BSA ≤0.50, 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 or <0.5 or ≥0.50. Cardiac events (CE)
included death, acute myocardial infarction (MI) and coronary artery revascular-
ization. CE free rates were analyzed by Kaplan-Meier method.

Results: The follow-up period in respective groups were 182±10, 168±8 and 111±7
years (mean±SD). Cardiac events occurred in 43 pts as shown here by groups.

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 ≥8.0 mm when BSA ≤0.50 in the acute phase’ in the patients with bi-
ateral large CAA, incidence of cardiac events were 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 calcifica-
tion is an active, regulated process similar to osteogenesis, relating to the chronic
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 blood samples were collected at the time of hospitalization. Patients with CALs (−) group took no medicine and those in CALs (+) group were under antiplatelet and/or anticoagulant therapy, particularly, those with calcification were additionally administrated statin or ARB.

Results: Values of %FMD in CALs(+) group were significantly lower compared with those in CALs(−) group (p < 0.05). The breakdown was 19 patients without CALs and 29 with CALs. Patients in CALs (−) group took no medicine and those in CALs (+) group were additionally administrated statin or ARB. Values of hs-CRP levels in CALs(+) group were significantly lower than those in CALs(−)(p < 0.05). The breakdown was 19 patients without CALs and 29 with CALs; 16 without calcification and 13 with calcification. Values of hs-CRP, procalcitonin, and urinary 8-OHdG as oxidative stress markers, and BMD. Patients in CALs(−) group took no medicine and those in CALs(+) group were additionally administrated statin or ARB.

The BMD in CALs(+) group tended to be lower with the age-matched reference values (88.1±7.1% of normal). Values of hs-CRPs in CALs(+) group were significantly lower compared with those in CALs(−) group (p < 0.05). Values of hs-CRPs in CALs(+) group were significantly lower than those without calcification (p < 0.05). Values of hs-CRPs in CALs(+) group were significantly lower than those in CALs(−) (p < 0.05). 8-OHdG values as oxidative stress marker in CALs(+) group were significantly lower than those in CALs(−)(p < 0.05). The breakdown was 19 patients without CALs and 29 with CALs; 16 without calcification and 13 with calcification. Values of hs-CRP levels in CALs(+) group were significantly lower than those in CALs(−)(p < 0.05). BMD in CALs(+) 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 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. 

P4606 | BEDSIDE
New concept for left ventricular training in corrected transposition of the great arteries: the double switch operation
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Purpose: Patients with corrected transposition of the great arteries (ctTGA) beyond the neonatal 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 improve pre- and afterload is presented that is evaluated in regards of effectiveness, numbers of re-operations necessary and the outcome of DS.

Methods: We report on six consecutive patients with ctTGA 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. One patient showed good LV function (ejection fraction of 55%) 1 year after surgery. The other five patients showed a normal LV function after 1–2 years follow up period of 1.5 years (7.2 patient’s years) unrestricted cardiac function and percentage of ejection fraction of 60% or more.

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.

P4608 | BEDSIDE
Outcome of blalock taussig 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 patient 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 over a 4 year period. Inclusion criteria included all newborn infants with age of 28 days or less diagnosed with pulmonary atresia who underwent 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 incidence 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 developing appropriate management of patients who develop early shunt occlusion. We recommend to ligate PDA at the time of mBTS to prevent shunt occlusion 6 weeks after surgery.

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 supple-mentation. Traditionally, diagnosis of iron deficiency has been based on the as-sessment of low transferrin saturation (Tsat) and reduced serum ferritin. However, these standard measures of iron status seem unreliable, especially in acute clin-ical settings. There are pathophysiological premises that soluble transferrin recep-tor (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 hepcidin, 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). Functional iron deficiency 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-serum sTfR). Serum hepcidin was measured using a newly available ELISA (DRG). Serum sTfR was measured using an immunosay (Roche Cobas). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarc-tion (MI).

Results: During a median follow-up of 4.6 years, 5.5% of all subjects died. Both, low hepcidin 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 with unstable angina pectoris (SAP), functional iron deficiency as defined as a concomitance of depleted body iron stores (demonstrated as low-serum hepcidin) and insufficient iron levels in metabolizing cells (demonstrated as high-serum sTfR). Serum hepcidin was measured using a newly available ELISA (DRG). Serum sTfR was measured using an immunosay (Roche Cobas). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction (MI).

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 plaque 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 factor 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 TCFAs than patients without in vivo TCFAs (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=0.42, 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.

P4609 | BEDSIDE

**Relations of estradiol, total testosterone and sex-hormone binding globulin to 11-year cardio-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 changes of long-term individual cardio-metabolic risk factors in postmenopausal women.

**Objective:** We investigated relations between estradiol (E2), 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 blood pressure, body mass index 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 in serum total cholesterol and with a corresponding annual decrease of 0.28 mg/dl in glucose level.

**Conclusion:** One unit increase in estradiol level was associated with an annual rise in serum total cholesterol and with a corresponding annual rise in glucose level.

P4610 | BENCH

**Can copeptin assist the diagnosis of acute kidney injury in breathless patients?**


**Aim:** We assessed the potential of plasma Copeptin to detect acute kidney injury (AKI) defined by the 2012 KDIGO criteria as either 1) a rise in serum creatinine of >26.5μmol/L within 48 hours or 2) a creatinine rise ≥1.5 times baseline, known as an AKI (n=94) that occurred within 7 days of presentation.

**Methods:** This study group is a prospective, ED based population of 364 consecutive patients presenting to a hospital with the primary complaint of acute breathlessness. Copeptin measurements were made on a BRAHMS Kryptor analyser. Serum creatinine was measured by routine hospital core biochemistry laboratory (standard method). The normal range of plasma copeptin was established in 150 healthy volunteers. Statistical assessment was made using SPSS v22 (IBM). Data for copeptin and creatinine were treated as continuous variables and were presented as median (interquartile range, IQR). Groups were compared by Mann-Whitney U test. The diagnostic performance of copeptin and creatinine was assessed using receiver operator curve (ROC) area under the curve (AUC) analysis. For ROC curve generation and comparisons, data were analysed as descriptive standardised variables (z-scores).

**Results:** In 150 healthy volunteers (median age 47, IQR: 32–67, 51% female) copeptin was detectable in 46/150 samples (31%). The median value was 7.4pmol/L (interquartile range (IQR): 5.6–10.3). The 99th percentile limit was 16.4pmol/L. Median serum creatinine was 85μmol/L (IQR: 77–90, n=150). The 99th percentile of serum creatinine was 115μmol/L. The median age of the breathless cohort was 73 (IQR: 63–81, 42% female). In total, 6.9% of the 364 patients met the criteria for AKI. Copeptin levels in AKI patients were higher than non-AKI (AKI (n=25) median 56.7μmol/L, IQR: 29.7–238.2 vs. non-AKI (n=339) median 14μmol/L, IQR: 7.2–61.7, P < 0.001). Creatinine was also higher in AKI than non-AKI individuals (median AKI = 142μmol/L, IQR: 110–196 vs. non-AKI median 96μmol/L, IQR: 82–116, P < 0.001). Assessment of presentation creatinine to diagnose present or impending AKI generated an ROC AUC of 0.79 (95% CI 0.69–0.88, P < 0.001) at a cut-off of 15μmol/L. In comparison, presentation copeptin generated an AUC of 0.810 (95% CI: 0.734–0.886, P < 0.001) at a cut-off value of 18.5pmol/L. Adding creatinine to copeptin produced an AUC = 0.856 (95% CI: 0.787–0.926) which was significantly better than creatinine alone (P=0.048).

**Conclusion:** Addition of copeptin significantly improved creatinine based detection of AKI in a group of ED breathless patients at the time of presentation. Further studies of the utility of copeptin to assist AKI detection in larger, more general risk populations are warranted.

Acknowledgement/Funding: Health Research Council of New Zealand - Public funding
Results: and reflection index (RI), assessed using PulseTrace PCA2, at baseline and at 12 months. Secondary assessments included the effects of any dose of vitamin D versus placebo on 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 plasma 25(OH)D levels at 12 months between the two active doses.

Methods: 1421 consecutive patients referred to rest/bicycle myocardial perfusion SPECT were recruited. We included patients who undergoing exercise stress testing at our Centre before stress testing. 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 end-point of myocardial ischemia was evaluated by myocardial perfusion SPECT and coronary angiogram, if available. Areas under the receiver operating characteristics curves (AUC) were calculated 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 = 0.006, 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 ratio, 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.

Conclusions: 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. Larger trials using 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 peptidase 4 and its relation to endothelial biomarkers in patients with stable coronary artery disease

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Background: Dipeptidyl peptidase 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 seems to be new possibilities for treatment of cardiovascular diseases by using therapeutical options which may reduce DPP4 activity.

Purpose: To investigate the effects of regular exercise training on DPP4 and relationship between changes in DPP 4 and circulating blood markers of endothelial function: 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±6.8 years, 14men) and 19 healthy controls (C group; 55.1±8.0 years, 11 men) were studied. At baseline in all pts and controls, values of DPP4, NOx and XOD by peripheral ven 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±260.08 to 573.1±173.83 μg/l, 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=0.0095) 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=0.652, 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 between decrease in XOD and decrease in DPP4.
Background: High red cell distribution width (RDW) values have been shown to be associated with poor long-term clinical outcomes in patients with cardiovascular diseases. Also, RDW was associated with incidence of atrial fibrillation. However, little is known about the impact of RDW on the prognosis in patients with paroxysmal atrial fibrillation (AF).

Purpose: 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 (<12.8% vs. 13.9%). Progression into persistent AF was increased in a stepwise manner as an increase of RDW 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 varied significantly according to sex, age groups (CI, 15–18 ng/l for men and 17 (95% CI, 15–18) ng/l for women) 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-cTnI increased with age, and most prominent in the stratum ≥65 years.

Conclusion: 99th percentile values for hs-cTnI assays are strongly sex- and age-dependent. Side by side comparison reveals remarkably similar 99th percentiles for hs-cTnI and hs-cTnT. However, highest RDW quartile was associated with higher incidence of atrial fibrillation as well as the composite of death, hospitalization due to heart failure, new onset stroke (log-rank p=0.032), the composite clinical outcomes (log-rank p=0.001). The 2185 pts were divided into two groups. Group I: cTn values ≤10 ng/L (n=453), and group II: cTn values >10 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 cTn values >10 ng/L had a significantly better survival than pts with cTn 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).
P4619 | BEDSIDE

Paroxysmal versus non-paroxysmal atrial fibrillation in Europe: the EORP-AF General Pilot Registry


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-year 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 vs. paroxysmal AF; however, the higher mortality risk became non-significant (OR 0.948, 95% CI 0.547–1.642, p=0.8477) after adjustment for clinical variables known to potentially affect the outcome.

Conclusions: In a real-world observational registry, patients with non-paroxysmal AF have a worse outcome, in terms of all-cause mortality, which was related to a more severe clinical risk profile. The risk of stroke at 1 year was relatively low, perhaps reflecting the high rates of anticoagulation use in this cohort.

P4620 | BEDSIDE

Beyond Framingham risk equations: how can cardiovascular risk be improved in the real world?

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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 (e.g. statins) during follow-up, raising questions about the validity of contemporary data to create risk tools for primary prevention. We investigated the impact on effect estimates (hazard ratios, HR) of updating treatment status.

Methods: A large primary care database of routine CV risk assessments dated the predictive value of the SAME-TT2R2 score for discriminating those who 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.

Conclusions: In our population the GS improved 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.

P4621 | 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-year 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 vs. paroxysmal AF; however, the higher mortality risk became non-significant (OR 0.948, 95% CI 0.547–1.642, p=0.8477) after adjustment for clinical variables known to potentially affect the outcome.

Conclusions: In a real-world observational registry, patients with non-paroxysmal AF have a worse outcome, in terms of all-cause mortality, which was related to a more severe clinical risk profile. The risk of stroke at 1 year was relatively low, perhaps reflecting the high rates of anticoagulation use in this cohort.

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. Stable anticoagulation was considered if patients that were admitted to hospital, as this would influence achievement of stable anticoagulation.

Results: During 2013, 719 patients with non-valvular AF were initiation on OAC

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 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.

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Improving risk scores in the real world 803
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 was 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 2.10 (95% CI 1.44–3.06, p = 0.001) for those patients with a SAME-TT2R2 score >2.

Conclusions: In a prospective real world AF cohort of patients initiating oral anticoagulation with acenocoumarol, we have validated the clinical value of the SAME-TT2R2 score, for the identification of which patients would have poor quality 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 benefit from additional strategies for improving anticoagulation control with VKA or alternative oral anticoagulant drugs.

P4623 | BEDSIDE
External validation of prediction models for the diagnosis of coronary artery disease
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Background and introduction: Prediction models for estimating probability of coronary artery disease (CAD) are crucial in guiding diagnostic decision making in patients presenting with chest pain. The Diamond and Forrester prediction model was developed in a high-risk population referred for invasive coronary angiography. The expected need to overestimate the probability of CAD within low-risk populations. Current European Society of Cardiology guidelines on stable CABG recommends use of a revised version of the Diamond Forrester model.

Purpose: We performed an external validation on previously published prediction models developed for estimating the probability of CAD in low-risk populations.

Methods: We analyzed 1,506 patients, referred from a cardiology outpatient department for coronary CT angiography (CCTA). Inclusion criteria where: age ≥40 and stable chest pain. Scans were performed between December 2007 and December 2012 using 64-slice multidetector (Brilliance 64; Philips Healthcare) or a dual-source CT-scanner (Somatom Definition Flash, Siemens). CAD was defined as >1 vessel with ≥50% luminal stenosis on CCTA. Three prediction models were calculated: 1. basic model: age, sex, chest pain symptoms, 2. clinical model: basic model + diabetes, hypertension, dyslipidemia, smoking. 3. extended model: clinical model + coronary calcium score. Diagnostic performance of the prediction models were quantified by calculating the area under the receiver operating characteristic curve (c-statistic). Calibration was assessed using calibration-in-the large and calibration plots.

Results: The area under the receiver operating characteristic curve was 0.69 (95% CI: 0.67–0.72) for the basic model; 0.70 (95% CI: 0.68–0.73) for the clinical model; and 0.86 (95% CI: 0.84–0.88) for the extended model. Calibration-in-the large showed that the average predicted probabilities of the prediction models were lower to the observed probability of obstructive CAD but were comparable for patients presenting with typical chest pain. The calibration plots showed some underestimate of the prediction models.

Conclusions: Updated prediction models, developed for low-risk populations, show a more accurate estimation of the likelihood of CAD than the commonly used Diamond and Forrester model.

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P4624 | BEDSIDE
Accuracy of statin assignment according to the European vs. American guidelines - a coronary CT correlation study

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 CCTA for suspected 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%)

Results: The median risk of events was 9.7% according to the AHA/ACC calculator, and 2.6% according to the European SCORE (fatal events only). Compared to SCORE, the AHA/ACC calculator showed greater discriminatory power for identifying 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 according 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 – no visible plaque) were more likely to receive statins if managed according to the European guidelines.

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
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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 of the AF 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 July 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.

**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. Cumulative events during follow-up were as follows: stroke in 60 (4%), and death in 231 (15%), respectively. On multivariate analysis, advanced age (<75 years) (hazard ratio (HR): 1.69, 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/SE/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 AF patients. There is good prediction for endpoint of death/stroke/SE using these 6 variables in patients without OAC, as well as those with OAC. **Acknowledgement/Funding:** Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daichi-Sankyo, Novartis Pharma, MSD

**P4627 | BEDSIDE**

**Accuracy of 10-year risk calculation for first atherosclerotic cardiovascular event from new pooled cohort equations and WHO risk calculation in EGAT population**

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**Background:** The World Health Organization (WHO) and American Heart Association (AHA) recommended using Pooled Cohort Equations to estimate the atherosclerotic cardiovascular risk (ASCVD). The World Health Organization (WHO) also issued guidelines for assessment and management of cardiovascular (CV) risk factors, and psychological factors previously associated with CV risk (Type D personality, Alexithymia and depression). There also underwent ultrasound for carotid plaques (CP) detection, defined as a focal thickening ≥1.5 mm. The risk estimate for 20-year cognitive decline has been performed with the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) risk score, based on cognitive reserve, physical activity, anthropometric and cardiometabolic variables. Vascular events, including myocardial infarction, stroke or transient ischemic attack, critical limb ischemia, were recorded during follow-up.

**Results:** A cohort of 198 subjects (75.2% male, age 47.6±6.9 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 7.4±2.5 (mean risk 3.7±3.2%), with 20.6% presenting a CAIDE risk >7.4%. At baseline, significant associations between CP and age (p=0.001), lipodystrophy (p=0.02), lipodystrophy (p=0.001), HeartScore (p=0.001), CAIDE risk score (p<0.001), at multivariate analysis only increasing age (OR=1.10 [95% CI: 1.0–1.2]; p=0.023), and CAIDE risk score (OR=1.16 [95% CI: 1.0–1.3]; p<0.001) remained significantly associated with CP. 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 mid-life 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.

**P4628 | BEDSIDE**

**CAIDE risk score predicts atherosclerosis and vascular events in HIV patients.**

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**Background:** With the increased survival in HIV-infected patients in the highly active antiretroviral therapy (HAART) era, other comorbidities, particularly cardiovascular disease, have emerged as major causes of morbidity and mortality. Cognitive impairment, ranging from mild deficits to severe dementia, remains prevalent in about half of HIV patients, and seems to be more closely associated with the presence of cardiometabolic than viroimmunological factors of HIV progression.

**Purpose:** To evaluate the determinants of accelerated atherosclerosis and 2.5-year median follow-up vascular events and to assess their relation with late-life 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). They also underwent ultrasound for carotid plaques (CP) detection, defined as a focal thickening ≥1.5 mm. The risk estimate for 20-year cognitive decline has been performed with the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) risk score, based on cognitive reserve, physical activity, anthropometric and cardiometabolic variables. Vascular events, including myocardial infarction, stroke or transient ischemic attack, critical limb ischemia, were recorded during follow-up.

**Results:** A cohort of 198 subjects (75.2% male, age 47.6±6.9 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 7.4±2.5 (mean risk 3.7±3.2%), with 20.6% presenting a CAIDE risk >7.4%. At baseline, significant associations between CP and age (p=0.001), lipodystrophy (p=0.02), lipodystrophy (p=0.001), HeartScore (p=0.001), CAIDE risk score (p<0.001), at multivariate analysis only increasing age (OR=1.10 [95% CI: 1.0–1.2]; p=0.023), and CAIDE risk score (OR=1.16 [95% CI: 1.0–1.3]; p<0.001) remained significantly associated with CP. 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 mid-life 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: Thirteen variables were predictors of Non-PCI and used to build the score: unstable angina (vs NSTEMI), female gender, age > 80, no PCI, previous 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±7.7 vs. 55.8±9.8, p=0.218, respectively). Total Ca-score was assessed 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 (SSS: sum of all stenoses, minimal ≥ 1, mild ≥ 2, moderate ≥ 3, severe ≥ 4). SSI index (SSSI) was calculated by SSSI/total segment number. SISI index (SISI) was calculated by SISIS/total segment number. Concordance between MZ and DZ pairs were 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 SSSI were positive in 55.6% of MZ and in 55.9% of DZ twins. The median SISI of MZ versus DZ twins was 0.2 (IQR: 0.1–0.4) versus 0.3 (IQR: 0.1–0.7), 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 (SSSI: h²=0.632 and SISI: 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.

P4632 | BEDSIDE
Cardiac function-specific risk factors for one-year mortality in patients admitted with acute coronary syndromes
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Introduction: Risk stratification in acute coronary syndromes (ACS) is based on clinical and laboratorial values. LVEF is a strong predictor of mortality in coronary disease.

Purpose: 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.

Methods: Demographic, clinical, laboratory and echocardiographic data of 8,974 patients enrolled in the Acute Coronary Syndrome Israel Surveys 2000–2010 were obtained. Multivariate cox proportional hazards regression model was used to identify cardiac function-specific risk factors for 1-year mortality in cardiac function groups defined as: severe LV dysfunction (LV dx ≤30%), moderate LV dx (30–49%), preserved LV (>50%).

Results: Through 2000 to 2010 more patients were admitted with preserved LV and less with LV dx. Patients with severe LV dx had high mortality rates at 1-year (38%) as compared with patients with mild/moderate LV dx and preserved LV (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 LV 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 using predetermined need of statin prescription as a cut-off

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 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, 60–90, 30–59, 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-GC was lower than those of eGFR MDRD-4 and eGFR CKD-EPI for both in urban residents and outpatients, and in China. For all patients, however, moderate renal dysfunction (eGFR <60 ml/min/m²) by eGFR-GC was higher than those by eGFR MDRD-4 and eGFR CKD-EPI (43.1% vs. 25.1% vs. 23.4%, p<.0001). Multivariable analysis showed that 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-GC (area under the curve [AUC] 0.688, 95% confidence interval [CI] 0.67–0.71, p<.0001) and eGFR CKD-EPI (AUC 0.688, 95% CI 0.67–0.71, p<.0001) was higher than that with eGFR MDRD-4 (AUC 0.684, 95% CI 0.66–0.70, p<.0001). Predictability for one-year mortality and MACEs with eGFR-GC 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<.001; AUC for MACEs: 0.619 vs. 0.602 vs. 0.615, p<.001] Net reclassification index for improvement in risk classification using PCE for different MHC population eGFR-GC was 16.8%, 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 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 ACC/AHA guidelines on cardiovascular disease prevention introduced a new tool for risk assessment, the Pooled Cohort Equations (PCE).

Purpose: In a multicentric case-control study population, we evaluated whether the predictive value of apoB/apoA1 ratio is independent of the cardiovascular risk assessed by PCE risk model 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 originating from different 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±47.4 mg/dl vs. 230±50.2 mg/dl, p<.0001; HDL-C 41.4±9.7 mg/dl vs. 45.8±12.8 mg/dl, p<.0001). The predictive value of apoB/apoA1 ratio is independent of the cardiovascular risk assessed by PCE risk model in different ethnic populations. The accuracy of PCE risk score was comparable between ethnicities [AUC (95% CI), European (0.70, 0.71)] vs. Asian (0.69, 0.70), p<.0001.

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.

P4635 | BEDSIDE

Association of creatinine clearance with clinical outcomes in patients with atrial fibrillation: The Fushimi AF Registry

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Background: The adequate antithrombotic therapy including non-vitamin K 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 obtained in 3,390 patients enrolled from March 2005 to December 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 in groups 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.
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, >10, >400). The area under curve (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 receiver 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 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) has been increased owing to improved perioperative management procedures. The second target for successful long-term LVAD treatment was to reduce readmission especially 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 (44–50 Pt), and high risk group (<44 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.
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 is also notable. The major bleeding in Japanese patients with atrial fibrillation.

Purpose: To study whether established cardiovascular risk scores such as the Framingham risk score (FRS) and the Heart Score of the European Society of Cardiology (HS) predict colorectal neoplasias in a large asymptomatic screening cohort.

Methods: We investigated 2138 subjects (59.6±10.2 years, 50% males, BMI 27.2±4.6 kg/m²) that underwent simultaneous cardiovascular risk evaluation and colonoscopic examination. The FRS and HS were calculated for each subject. Colonic findings were classified as: normal (0); advanced adenoma (1), polyps (2), carcinoma (3). The cut-off points were: FRS ≥10%, HS ≥2.0. Results were compared to 1436 control matches.

Results: Of 2138 screened subjects, 1427 (66.7%) had a low FRS (0–10), 572 (26.8%) an intermediate FRS (11–20) and 139 (6.5%) a high FRS (≥21). Subsequently, the results of the screening colonoscopy were correlated to the FRS and HS in each subject. In both scoring systems, the correlation with the number of advanced neoplasias increased from normal (0), to polyps (2), to carcinoma (3). Specifically, the points +0.05, p<0.001) for FRS and r=0.18 (p<0.001) for HS. This linear association was stronger for FRS (r=0.24, p<0.0001) than for HS (r=0.15, p<0.0001) for FRS and r=0.09, p=0.001) for HS. This linear association was stronger for FRS (r=0.24, p<0.0001) than for HS (r=0.15, p<0.0001).

Conclusions: 7 genetic variants were significantly associated with CAD in our population and independent of traditional RF. The utility of genetic scoring in a multi risk locus approach may be useful to further stratify patients.

References:


4. Multiplicative (all genes)
3. Multiplicative (7 risk genes)

Conclusions: In a large asymptomatic screening cohort, subjects with high cardiovascular risk had a significantly higher probability of early and advanced colorectal neoplasia, presumably due to shared risk factors. Our data provide compelling evidence for considering screening colonoscopy particularly in subjects with high cardiovascular risk in order to detect potentially treatable colorectal neoplasia.

P464 | BEDSIDE
What is the best genetic score to predict the risk coronary disease?
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Introduction: Several genetic polymorphisms have been associated with coronary artery disease (CAD) by genomic association studies. However, the individual predictive value of each polymorphism is limited and the approach for the incorporation of these in risk stratification has evolved in the form of "scores". The method for performing a genetic risk score (GRS) which is more discriminative for CAD risk is still not clear.

Aim: Evaluate the discriminative ability of various models of GRS as predictors for CAD.

Methods: Case-control study which included 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. Using specific primers, we evaluated 29 genetic polymorphisms: ACE I/D, AGT235 T/C, AGT235 A/C, AT1R A/C, AT1R C/T and 1298 A/C, PON1 A/G, PON1 Q/R and 1148 A/G, FTO A/C, AGT235 A/C, APOL1 G/T, MTR A/G, MTHFR C/T and 1298 A/G, FTO A/C, AGT235 A/C, APOL1 G/T, MTR A/G, MTHFR C/T and 1298 A/G, FTO A/C, AGT235 A/C, APOL1 G/T, MTR A/G, MTHFR C/T and 1298 A/G, SLC30A8 C/T, TCF7L2 C/T, HNF4 C/G, FTO A/C, ADIPOQ C/G. Subsequently, a logistic regression was done in order to select the predisposing factors of CAD, including the TRF and the GRS.

Criteria. A multiplicative genetic risk score (GRS) was calculated based on the multiplicative value independent of the well-known traditional risk factors (TRF).

Conclusions: Our population, the multiplicative GRS model was found to be preferably used to determine the coronary risk than using only a particular polymorphism.

P464 | BEDSIDE
Genetic polymorphisms and gender - 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.

Methods: A case-control study was performed with 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. The TRF (arterial hypertension, dyslipidemia, smoking, obesity, sedentary lifestyle and family history) were defined according to the International criteria. A multiplicative genetic risk score (GRS) was calculated based on the multiplicative value independent of the well-known traditional risk factors (TRF).

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.

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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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Elevated serum triglycerides have been treated as independent cardiovascular disease (CVD) risk factor, but, their net effect on 10-year CVD risk development has evolved in the form of “scores”. The most widely used. However, non-valvular atrial fibrillation (NVAF) patients with a CHA2DS2-VASc score = 1 is a heterogeneous group. We sought to investigate whether patients with a CHA2DS2-VASc score = 1 have the same risk of developing stroke or death when considering each of the parameter.

Methods: Between 1998 and 2011, among 1,212 consecutive NVAF patients, hospitalised for AF, 246 had a CHA2DS2-VASc score = 1. 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 55.5±10.8 years. At baseline, the distribution was the following: female (n=70), hypertension (n=60), diabetes (n=17), age 65–75 years (n=44), heart failure (n=37), VASc (n=18). At 1 year, stroke or death occurred in 2 (2.9%), 1 (1.7%), 0 (4.6%), 4 (10.8%) and 1 (5.6%) patients, respectively. A CHA2DS2-VASc score = 1 is associated with a stroke and deaths rate of 2.92 per 100 person-years (95% CI = 1.12–5.92) at one-year.

Conclusion: These results suggest that a CHA2DS2-VASc score = 1, associated with a high risk of stroke and death, is not influenced by the presence of any parameter defining this score.

P464 | 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?

Purpose: Stroke risk stratification is based on different clinical markers and traditional risk factors. The appropriate use of the available stroke risk stratification schemes the CHA2DS2-VASc score. This is the most widely used. However, non-valvular atrial fibrillation (NVAF) patients with a CHA2DS2-VASc score = 1 is a heterogeneous group. We sought to investigate whether patients with a CHA2DS2-VASc score = 1 have the same risk of developing stroke or death when considering each of the parameter.

Methods: From May 2001 to December 2002, 1514 men and 1528 women (> 18 years) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011–2012, 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 increased triglycerides increased 10-year risk (Relative Risk (RR) per 1 mg/ml = 1.005, 95%Confidence Intervals
Background: Despite patients with coronary artery calcification (CAC) score zero are considered as low risk of coronary events, however they may carry non-calcified coronary artery plaques in patients with CAC score zero.

Material and methods: A total of 469 consecutive patients (61±2 years, 44.3% males) with intermediate pretest probability of coronary artery disease (CAD), referred for coronary computed tomography angiography (CCTA) between September 2010 and October 2012, were analysed. Coronary artery plaques were evaluated in the whole study group. CAC score was calculated by Agatston method. Serum Lp-PLA2 mass was assessed by PLAC6 test.

Results: CAC score zero was found in 215 (45.8%) of the patients. In this group coronary artery plaques were present in 153 (71.2%) subjects. Multivariate logistic regression analysis revealed that Lp-PLA2 concentration (OR 1.02, 95% CI 1.01–1.04, p<0.0004) was an independent predictor of non-calcified coronary artery plaques in patients with zero CAC. In the ROC curve analysis Lp-PLA2 of 166 mg/ml presented as the optimal cut-off point for discriminating coronary artery plaques presence in patients with CAC score zero (sensitivity: 0.74; specificity: 0.73; AUC 0.734;p<0.0001).

Conclusions: The majority of patients with intermediate pretest probability of CAD and CAC score zero may carry coronary artery plaques, and Lp-PLA2 concentration is independently correlated to their presence.

P4650 | BEDSIDE

Lipoprotein-associated phospholipase A2 as an independent predictor of atherosclerosis among patients with zero coronary artery calcium score

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Background: The majority of patients with intermediate pretest probability of coronary artery disease (CAD) considered 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 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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Background: Studies in mostly Western populations have shown that both short and long sleep duration are associated with increased risk of ischaemic heart disease (IHD), but little is known about these associations in Asian populations. We examined the association of sleep duration with IHD incidence in the China Kadoorie Biobank (CKB) study.

Methods: The CKB study is a prospective study of 512,891 adults aged 35–79 years who were recruited during 2004–8 from 10 diverse locations in China. Sleep duration was recorded by interviewer-administered questionnaires at baseline. During 7 years of follow-up, there were 3361 incident cases of new onset IHD. Cox regression was used to estimate risk ratios (RRs) for IHD incidence versus short self-reported sleep duration after adjustment for confounding factors among individuals without prior cardiovascular disease. The variance of the log risk in each group was used to calculate the confidence interval (CI) for each RR including the CI used as the reference group.

Results: Overall, mean daily sleep duration was 7.38 hours (men: 7.4 hours; women: 7.3 hours); 54% reported snoring and 39% reported daytime napping. Sleep disorder was reported in 17%, and was slightly higher in women than in men (19% vs 14%). There was a U-shaped association between sleep duration and IHD incidence with people sleeping 7–7.5 hours having the lowest risk. The adjusted RRs (95% group-specific CI) were 1.33 (1.14–1.54), 1.18 (1.04–1.34), 0.96 (0.88–1.05), 1.00 (0.93–1.08), 1.06 (0.99–1.12), 1.07 (0.97–1.19) and 1.20 (1.05–1.37) for those who had reported sleeping ≤4, 5, 6, 7, 8, 9- and ≥10 hours per day, respectively. The U-shaped association was seen in both men and women and among people with different ages.

Conclusion: Among adult Chinese men and women, both short and long sleep duration was independently associated with moderately increased risk of IHD.
P4653 | BEDSIDE
Increased maternal complications in pregnant ladies with Elevated brain natriuretic peptide plasma level as a marker of 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 normal pregnancy 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 ladies 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 the Bruntiner Institute for Cardiovascular Research, Holon, Israel

Background: Lipoprotein associated phospholipase A2 (Lp-PLA2), was linked to circulating lipids 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 Infraction 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 tertile (<202.0 mmol/min/ml; p<0.001). Lp-PLA2 correlated with HDL-C (-0.44), non HDL-C (0.37) and fibrinogen (0.12) but was only weakly correlated with C-reactive protein.

Over median follow-up of 7.4 years, 554 patients died. The 3rd Lp-PLA2 activity tertile was associated with greater mortality risk, age-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-CL. This suggests a role in underlying hemodynamic. The high-density lipoprotein (HDL) provides 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 measured with a validated in vitro system.
P4657 | BEDSIDE
Plasma hydroxyanthranilic acid and incident type 2 diabetes in patients with stable angina pectoris
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Background: The tryptophan metabolite hydroxyanthranilic acid (HAA) has been related to ischaemic heart disease and atherosclerosis. 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 1.57 (95% CI: 1.01–2.41), P < 0.05. Further adjustment including serum apolipoprotein A1, triglycerides, 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 [95% CI: 1.06–1.71], P < 0.05). Moreover, HAA significantly improved risk classification for T2D (NRI [95% CI]: 0.19 [95% CI: 0.07–0.38], P < 0.05).

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-lipoxygenase 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 atherosclerotic 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 fibrinogen (FIBTEM) pathways in the presence 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. Clotting time 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: Our work identifies increased concentrations of the ALOX15 product 15-HETE in human ischaemic heart biopsies 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.

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P4659 | BEDSIDE
Relationship between serum beta-2-microglobulin and cardiovascular risk factors
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Background and purpose: Serum beta-2-microglobulin (β2M) 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 β2M with age, BMI, blood pressure, glycemia, lipids, inflammation, liver and renal function were studied. Where appropriate, data were log-transformed.

Results: Serum β2M 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), A1C (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). In the fully adjusted model, serum β2M remained positively associated with systolic blood pressure (p=0.11, 95% CI: 0.04 to 0.18); AST (p=0.14, 95% CI: 0.10 to 0.18), ALP (p=0.10, 95% CI: 0.07 to 0.13), and CRP (p=0.05, 95% CI: 0.04 to 0.07), and negatively associated with HDL (p=0.11, 95% CI: 0.07 to 0.15) and eGFR (p=0.83, 95% CI: 0.60 to 0.69) (all p-values<0.001).

Conclusions: The association of serum β2M level with Framingham risk factors 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: 0.022±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 RCRI score 0 and ≥2 were 0 (n=0 of 30), 28.2% (n=22 of 78) and 34.4% (n=21 of 61), respectively. Multivariate logistic analysis revealed that heart failure was independently associated with myocardial injury (P=0.001 OR 5.779).

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.
P4641 | BEDSIDE
Asymmetric dimethylarginine (ADMA) - intermediate phenotypes and atrial fibrillation in the general population
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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 asymmetrical -arginine metabolites 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: Blood was determined L-arginine and its metabolites asymmetric dimethylarginine (ADMA), L-N-monomethylarginine (NNMA) and symmetric dimethylarginine (SDMA) in a large population-based study (n=5000), mean age 55±11 years, 51% men, in association with intermediate phenotypes of AF such as electrocardiographic and echocardiographic measures and manifest AF.

Results: Individuals with AF (N=161), 71% men, were older, mean age 64.9±8.3 years. In Bonferroni-corrected multivariable-adjusted regression analyses we observed moderate inverse associations for L-arginine, SDMA and ADMA/ ADMA ratio with ventricular heart rate, and for L-arginine and L-arginine/ADMA ratio with QTc. L-arginine was correlated with QRS duration. In echocardiographic analyses, ADMA was related to left atrial diameter, deceleration time and left ventricular ejection fraction, ADMA and NNMA were correlated with left ventricular mass. ADMA (odds ratio [OR] 1.21, 95% confidence interval [CI] 1.04–1.40, P=0.009) and NNMA (OR 1.16, 95% CI 1.03–1.32, P=0.02) were related to prevalent AF. L-arginine/ADMA ratio was inversely associated (OR 0.8, 95% CI 0.65–0.98, P=0.03). Results were similar after adjustment for creatinine.

Conclusions: In our large, population-based cohort, we observed moderate associations of L-arginine metabolites and intermediate electrocardiographic and echocardiographic variables and AF. Our findings support further investigations to define the role of L-arginine derivatives in AF and their clinical utility.

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P4642 | BEDSIDE
Neutrophil/lymphocyte ratio predicts cardiovascular risk. The PREDMED trial
Background: Increased evidence support that neutrophil/lymphocyte ratio (NLR) is a good predictor of future adverse cardiovascular outcomes, but most of the previous studies have been conducted in patients with symptomatic cardiovascular disease. We sought to evaluate the predictive ability of NLR for cardiovascular disease (CVD) in an asymptomatic population sample at high cardiovascular risk.

Methods: Participants were recruited from seven PREDMED study centers, where information about white blood cells count was collected. Our primary end point was a composite of myocardial infarction, stroke, and death from cardiovascular causes. The predictive ability for our end point in the highest quintile versus lowest quintile NLR, and total leucocyte, lymphocyte, neutrophil, monocyte, basophil and eosinophil counts were assessed using Cox regressions.

Results: A total of 4336 participants were included. The median of follow-up was 4.4 years and Cox regression. NLR (OR 1.37, 95% CI 1.03–1.82) and percentage of neutrophils were related with our primary end point, both of them in an unadjusted model (HR for NLR: 1.62; HR for percentage of neutrophils: 1.62) and in a model adjusted for sex, age and baseline risk factors (HR for NLR: 1.67; HR for percentage of neutrophils: 1.69). Similarly, NLR was related with cardiovascular death in the unadjusted (HR: 4.67) and the adjusted model (HR: 5.67), absolute number of neutrophils was related with cardiovascular death in the unadjusted model (HR: 3.24), and percentage of lymphocyte was inversely related with cardiovascular death in the unadjusted (HR: 0.25) and the adjusted model (HR: 0.23).

Conclusions: NLR was a strong predictor of cardiovascular disease in a selected population sample free of symptomatic cardiovascular disease at baseline, but at high cardiovascular risk.

P4663 | 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 may be used to detect cardiovascular disease. However, it is currently uncertain whether subclinical clinical cardiac alterations are involved in QT interval determination among young and healthy adults.

Methods: Healthy adults aged 25–44 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 of ≥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 analyser 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 425±48 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 −0.08 (−1.15; 1.00), p=0.09 per pg/ml increase in hs-cTnI.

Conclusions: There is a strong consistent 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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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.

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**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, aortic 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/endo-vascular) 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 44,200 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 decrease 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.

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**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 (CAD) was assessed from the number of significantly (>50%) stenosed coronary arteries. Patients were divided into four groups: no stenosis, single-, double- and triple-vessel disease group. They were secondarily divided into four groups: no stenosis, single-, double- and triple-vessel disease group. These groups were then subdivided into positive and negative groups for selective LAD (left anterior descending), LCX (left circumflex), RCA (right coronary artery) or LMCA (left main coronary artery) stenosis.

**Results:** Smoking proved the most important CAD predictive factor (p<0.001), 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 status. Obesity 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.

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**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=0.033) and eGFR<60 ml/min (HR=1.97, 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).

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**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 analysis for 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 PRA 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. In addition to NIRS imaging, a 2D imaging map of basal stO2 was acquired from 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) and time to maximum stO2 during hyperaemia (63±38 vs 58±49 sec, p<0.05). Patients with SSc had lower basal stO2 compared to pts without diabetes mellitus (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 anomalies 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 (19% 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
Faces 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 hypertensive patients (51±14 year, 55% male). Diabetic individuals and those with overt cardiovascular or renal disease were excluded. The evaluation of target organ damages (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 SDH 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. Multinominal 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.

<table>
<thead>
<tr>
<th>Masked</th>
<th>ISH</th>
<th>IDH</th>
<th>SDH</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age, years</td>
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<td>59±14</td>
<td>44±12</td>
<td>49±12</td>
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<tr>
<td>24-hour systolic blood pressure, mmHg</td>
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<tr>
<td>24-hour diastolic blood pressure, mmHg</td>
<td>70±8</td>
<td>69±9</td>
<td>71±8</td>
<td>79±8</td>
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<tr>
<td>Carotid femoral pulse wave velocity, m/sec</td>
<td>7.8±2</td>
<td>8.8±2</td>
<td>8.0±1.0</td>
<td>8.6±2</td>
</tr>
<tr>
<td>Left ventricular mass index, kg/m²</td>
<td>79.9±15.8</td>
<td>82.8±18</td>
<td>83.8±19.3</td>
<td>88.5±19.8</td>
</tr>
<tr>
<td>Mean common carotid intima-media thickness, mm</td>
<td>0.69</td>
<td>0.72</td>
<td>0.56</td>
<td>0.63</td>
</tr>
<tr>
<td>(0.60–0.82)</td>
<td>(0.63–0.83)</td>
<td>(0.53–0.67)</td>
<td>(0.56–0.74)</td>
<td>(0.60–0.86)</td>
</tr>
</tbody>
</table>

Renal resistive index 0.64±0.06 0.67±0.06 0.58±0.05 0.60±0.06 <0.001

Conclusions: Renal resistive index is closely associated with systolic and diastolic BP and is an independent determinant of hypertension phenotype.

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Correlation between arterial stiffness as measured by progression of cardiac ankle vascular 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 ankle vascular index (CAVI). This index can reflect the stiffness of the aorta and peripheral vessels eg, femoral artery 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. Correlation between status of hypertension during 5-year period and progression of CAVI were statistically analyzed.

Results: 2,956 participants were eligible for analysis (mean age was 57.7 ± 7.4 year, 23.4% was female). Baseline CAVI in 2007–2008 was 7.94, 8.23, 8.50 in normotensives, controlled, uncontrolled/unaware HTN, respectively (p for difference < 0.001). Adjusted for age, gender, BMI, smoking status, DM status and total cholesterol, participants whose HTN status was not controlled during the year of 2007–2008 and 2012–2013 (“Uncontrolled HTN”) group had the greatest progression in CAVI (CAVI change 0.54±0.5/year), followed by that of 0.52±0.5/year and 0.49±0.5/year in “No HTN to Uncontrolled HTN” group and “Previously-controlled to Uncontrolled HTN” group, respectively.

Conclusion: “Uncontrolled HTN” group has significantly higher percentage of CAVI progression than “Controlled HTN” group. These results imply that well control of blood pressure remains important to slow the progression of arterial stiffness which is reflected by CAVI change.

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 complications. 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).

Methods: Sixteen patients, that had undergone MRA of the renal arteries, underwent bilateral renal denervation with 4 different systems: Symplify™ (n=3), Paradise™ (n=5), Once2shot™ (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 8/23 studied vessels. Six-month follow-up by MRA was performed in 6/7 patients (6/6 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±6.9%, and there was no binary restenosis. There was no other lipid-lowering therapies at baseline. Significant positive correlation was observed between age and percentage change in plaque volume (r=0.256, p=0.004). A multivariate reexpression analysis showed that age was a significant predictor of the percentage change in plaque volume during stent therapy (β=0.223, p=0.03).

Conclusions: Coronary atherosclerosis was more advanced and vascular responses to stent therapy were attenuated in the elderly patients compared to the 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). 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).

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 2.55; 95% CI 1.35–4.94; p=0.003).

Among patient with MB, tranexamic acid was most commonly used in patients on NOACs than in those on VKAs (OR 10.95; 95% CI 3.25–36.89; p<0.001).

Conclusions: In clinical practice, bleeding while on NOACs is similar to those on VKAs in terms of bleeding risk factors and outcomes. The residual risk for major intracranial bleeding is higher in patients on VKAs than in those on NOACs.
P4676 | BEDSIDE

Is it necessary to use new antiplatelet agents in patients who are treated with a bioreorbable vascular scaffold?

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Background: During the last months a few cases of late and very late bioreorbable vascular scaffold thrombosis have been reported. Optimal duration and strategy of dual antiplatelet therapy after BVS implantation at immediate and long term follow up.

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 P2Y12 inhibitor, 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 restenoses were treated with BVS. The scaffolded length was 24±12 mm and the mean BVS diameter was 3.14±0.36 mm. Clinical follow up was obtained in patients. After a mean follow up of 15±9 months the cumulative MACE was 5%. There were 5 cardiac deaths (1%), 20 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 iatrogenic 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. Futher and randomized studies are required to establish an optimal strategy and duration of dual antiplatelet therapy.

P4677 | BEDSIDE

Safety and efficacy of secondary prevention medications

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Background: Advanced glycation end-products (AGEs) and their receptor (RAGE) play an important role in the pathogenesis of diabetic vascular complications. The beneficial effects of statin therapy in reducing cardiovascular patho-
genesis, atherosclerosis, and diabetic complications are well known. Although the mechanisms by which statins provide cardiovascular benefits are not fully under-
stood, the recent finding of an increased stabilization of coronary artery plaque are presumed to play an important role in this effect. Although statin has been shown to increase glycation end-products and its association with coronary atherosclerosis.

Methods: During the last months a few cases of late and very late bioreorbable vascular scaffold thrombosis have been reported. Optimal duration and strategy of dual antiplatelet therapy after BVS implantation remain unclear.

Aim: To study the association between the SAME-TT2R2 scheme and the TTR 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 measurement was taken on 12 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 (n=292; see Table). With regard to labile (i.e. TTR <60%) or highly stable (i.e. TTR>95%) INR control, no difference was observed between groups.

Purpose: To study the association between the SAME-TT2R2 score and the TTR in the very elderly.

Conclusions: In this real-world registry of elderly AF patients, a low SAME-TT2R2 score had a statistically significant higher time in therapeutic range. Clin-
ically, however, this score does not allow for discrimination between those with a labile or highly stable INR control.

P4678 | BEDSIDE

Anticoagulation 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 derived from a relatively young population.

Aim: To study the association between the SAME-TT2R2 score and the TTR 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 measurement was taken on 12 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 (n=292; see Table). With regard to labile (i.e. TTR <60%) or highly stable (i.e. TTR >95%) INR control, no difference was observed between groups.

TTR categorised by SAME-TT2R2 score

<table>
<thead>
<tr>
<th>Low risk (0–1 points)</th>
<th>High risk (≥2 points)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=465</td>
<td>N=387</td>
<td></td>
</tr>
<tr>
<td>TTR, median (IQR)</td>
<td>82.3 (72.7–90.0)</td>
<td>80.0 (71.4–88.9)</td>
</tr>
<tr>
<td>Labile INR (TTR &gt;60%, n %)</td>
<td>24 (4.9)</td>
<td>26 (6.5)</td>
</tr>
<tr>
<td>Highly stable INR (TTR &gt;95%, n %)</td>
<td>59 (12.0)</td>
<td>73 (19.2)</td>
</tr>
</tbody>
</table>

TTR, time in therapeutic range; IQR, interquartile range.

Conclusions: In this real-world registry of elderly AF patients, a low SAME-TT2R2 score had a statistically significant higher time in therapeutic range. Clin-
ically, however, this score does not allow for discrimination between those with a labile or highly stable INR control.

P4679 | SPOTLIGHT

Antplatelet drug resistance in Asian 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) patients who consented for the study.

Methods: Anti-platelet drug resistance was evaluated on day seven using Verify now RPFT 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 resistant to Aspirin and 157 patients (78%) are Sensitive to Aspirin. There is significant (P<0.03) difference in male and female patients in Aspirin sensitivity 124/11 (71.42%) and resistant 50/15 (29.58%) patients. There is no significant difference (P>0.450) in Aspirin sensitivity and age distribution. This study did not show any statistically significant (P<0.973) in Aspirin sensitivity/resistance in DM patients. Our study shows 65 patients (32.7%) are resistant to Clopidogrel and 135 patients (68%) are sensitive to Clopidogrel. There is significant difference (P<0.003) difference in Clopidogrel sensitivity/resistance in male/ female patients. Our study did not shows statistically significant (P<0.07) difference in Clopidogrel Sensitivity/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.

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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 anticoagulant effect of dabigatran etexilate (DE). No data currently link any given coagulation test to bleeding outcomes in patients receiving DE for atrial fibrillation (AF).

Purpose: To correlate different coagulation tests to the bleeding outcomes in AF patients receiving DE.

Methods: Non-valvular AF patients receiving DE of 110 mg (DE110) or 150 mg (DE150) were consecutively enrolled. The hemoclot thrombin inhibitor assay (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±10.3 years old, 67.9% male, median follow-up: 364 days). Compared with DE110, the patients receiving DE150 were younger and more often male and had lower HAS-BLED and CHADS2VASc scores and better renal function. Subjects’ HTI levels were very variable (DE110, 10–90th percentile: 20.5–223.9 nm/ml). A receiver-operator characteristic curve gave a median cutoff HTI level of 117.7 nm/ml to predict bleeding events (C-statistics: 0.65; P=0.036), but no cutoff could be determined for PT, INR or APTT. Based on the Kaplan-Meier analysis, a DE level >117.7 nm/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 optimize 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 congenital condition presenting with symptoms of heart failure. There is scant data about transcatheter closure (TCC) of APW. We present the largest series of patients undergoing APW-TCC.

Aims: To assess the outcome of transcatheter closure using the Amplatzer devices. Amplatzer duct occluder I (ADO I) and Amplatzer septal occluder (ASO) in patients with APW defect.

Methods and results: Seven patients, aged 07 months to 11 years (median 07 years) were operated on isolated APW-TCC. Aims: To assess the efficacy and the acute and short-term clinical outcomes of transcatheter closure in four patients with prosthetic paravalvular leak repair.

Methods and results: Percutaneous repair of paravalvaral leaks was at-
P4684 | BEDSIDE
Deficiency of endothelial progenitor cells is associated with subacute thrombosis after angioplasty in hemodialysis patients
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Background: Subacute thrombosis after balloon angioplasty is much more frequent in patients than in non-hemodialysis patients. The pathological process of subacute thrombosis may be related to impaired vessel healing. Circulating endothelial progenitor cells (EPC) play a key role in vascular repair but are deficient in hemodialysis patients. We hypothesized that patients who develop subacute thrombosis may have reduced or dysfunctional EPCs.
Purpose: We aimed to investigate the relation between EPC level and function with the development of subacute thrombosis after angioplasty of venous stenosis in a prospective cohort.
Methods: Patients with venous stenosis of hemodialysis vascular access were prospectively enrolled, after excluding central vein stenosis, failed angioplasty, or recent acute illness. The proportion of peripheral mononuclear cells expressing CD34, KDR, and CD133 markers was evaluated by flow cytometry. Clinical, access, procedural and biochemical data were collected at baseline. Patients were followed prospectively at six month interval.
Results: From Jan 2010 to Jul 2011, 280 patients were prospectively enrolled. The follow-up was extended to Jan 2014 and the median follow-up duration was 36.7 months. Participants were stratified into tertiles according to baseline CD34+KDR+ cell counts. One hundred and twenty-two patients experienced access thrombosis and 52 of them occurred within one month. Patients with subacute thrombosis had lower CD34+KDR+ and CD34+KDR+CD133+ cell counts compared to the late thrombosis group (both p<0.001). The incidence of subacute thrombosis was progressively correlated with access site, Symptomatic THG (Low vs. 30%; middle, 21%; high, 12%; p=0.03) Patients with subacute thrombosis had increased senescence EPCs (65.1±17.7% vs. 37.9±10.3, P<0.001) and apoptosis EPCs (29.6±5.7% vs. 15.9±2.5, P<0.004) in functional studies. In multivariate analysis, older age, diabetes, and eGFR was more treated (53.7 vs 47.9%, p=0.04). Univariate analysis showed that access 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 (6.3 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 group (p=2.2). This significance, however, did not persist at 2 years FU. All-cause mortality was similar in both groups. Multivariate logistic regression analysis comprised several variables with prognostic value (prior neurologic symptoms, prior ACS, dyslipidaemia, 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 groups.
Conclusions: Our data demonstrate that older patients 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.

P4686 | 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 patient cohort with significant comorbidities and surgical risk, CAS remains 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 2003 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 was 33.20±20.5 (BP). Primary endpoint was major adverse cardiovascular events (MACE) which included stroke, acute coronary syndrome (ACS) and cardiovascular death (CVD).
Results: Baseline characteristics were similar in both gps, except for the presence of severe valvular disease (SVD) (gp 1: 0.9% vs 0.01) 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 gps. In gp 2, proximal flow blockage was used in 12.3 vs 15.7% (p=NS), distal protection filter in 87 vs 83.6% (p=NS) and a greater number of the stented segments was more treated (53.7 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 (6.3 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 group (p=2.2). This significance, however, did not persist at 2 years FU. All-cause mortality was similar in both gps. Multivariate logistic regression analysis comprised several variables with prognostic value (prior neurologic symptoms, prior ACS, dyslipidaemia, 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 gps.
Conclusions: Our data demonstrate that older patients 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.
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 (TAPSE 16.4±8.9) and elevated systolic right ventricular pressure (68±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 (46.2%) of the patients had been previously treated medically for pulmonary hypertension. 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 surgery myectomy. 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 alcohol 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 artery 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 artery disease.

Methods: This retrospective study included 143 patients who had underwent 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 (7.6% vs. 6.3%, p=0.75) 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=0.68) 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 artery disease.

P4691 | BEDSIDE

Initial experience with the TightRail rotating mechanical dilator sheath for transvenous lead extraction: safety and efficacy

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Background: Owing to increasing implantation rates and patients’ longer lifetime 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 TightRail™ 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 TightRail™ 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 TightRail™ 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
extractive technique with TightRail™ system is a new useful tool for chronically implanted pacemaker/ICD leads.

P4691 | BEDSIDE
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 with drug is not effective and 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, unfractured heparin, warfarin, Xa inhibitor, urokinase was administered. Before performing endovascular treatment, IVC 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 rosspassed 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 Fontaine-injection 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 the recurrence of thrombosis 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.

P4692 | SPOTLIGHT
Selective stent placement versus balloon angioplasty for renovascular hypertension caused by Takayasu arteritis: two-year results
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Objective: To investigate the long-term clinical outcomes of selective stenting versus percutaneous balloon angioplasty (PTA) in patients with renal artery stenosis caused by Takayasu arteritis (RATA).

Background: Long-term clinical outcomes of selective stenting in patients with RATA need to be clarified.

Methods: We retrospectively analyzed the data of 152 consecutive patients with RATA 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=0.009. Female, active disease in need of immunosuppressive agents, residual stenosis rate and stenting 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 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 RATA, particularly in patients with high risk for restenosis.

P4693 | BEDSIDE
Endovascular treatment of aortic coarctation
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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 emerged as an attractive 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.

P4694 | BEDSIDE
Prognosis and its predictors after endovascular therapy in hemodialysis patients with critical limb ischemia in contemporary practice
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Background: Little is known about the prognosis of hemodialysis (HD) patients with critical limb ischemia (CLI) undergoing endovascular therapy (EVT). The purpose of the present study was to evaluate the prognosis and its predictors after EVT in this high-risk subset.

Methods and results: Mortality and major amputation free survival of 131 consecutive HD patients with CLI undergoing EVT were examined. The mean age was 67±9.4 years old. 77% of them were male, 75% had diabetes, 56% were comorbid with coronary artery disease, 32% had history of coronary intervention and 29% had prior stroke. The results are shown below.

Conclusion: 77% of survival rate and 89% of major amputation free survival rate at 1-year in this high-risk subset was quite acceptable and diabetes was an only independent predictor of all-cause death.

TECHNICAL ASPECTS OF PCI

P4695 | BEDSIDE
Aortic coronary syndromes in women undergoing percutaneous coronary intervention with drug-eluting stents: a patient-level pooled analysis of randomized controlled trials
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Background: The safety and efficacy of new-generation drug-eluting stents (DES) have demonstrated the benefit of endovascular therapy for acute coronary syndrome (ACS) in women. Previous trials were not powered to detect differences in women, particularly among those with acute presentations.

Objectives: We evaluated: (i) the prognostic impact of ACS presentation in
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 was 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: Out of 11,909 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, 3594 (35%) had a UA/NSTEMI and 779 (8%) had a STEMI as clinical presentation. Women presenting with STEMI were younger, more commonly former smokers and with lower prevalence of cardiovascular risk factors. For the purpose of this analysis, we used the modified ACC/AHA classification: lesions were considered as simple (23.4%), and type B2 or C, complex (76.6%) lesions. Complex lesion was more frequent in older patients, women, hypertensive patients, and those presenting with ST-segment elevation AMI. Compared with patients with simple lesion, those with complex lesion were more likely to have lower estimated creatinine clearance, lower left ventricular ejection fraction, lower pre-PCI TIMI grade, and more extensive coronary disease requiring a greater number of stents implanted. During a median follow-up of 365 days, the primary endpoint occurred in 276 (2.0%) versus 55 (1.3%) in the complex and simple groups, respectively (unadjusted hazard ratio [HR] 1.60, 95% confidence interval [CI] 1.20–2.14, p=0.001). After multivariate regression analysis using Cox proportional hazards models, there was a significant trend toward a higher incidence of the primary endpoint of all-cause death in the complex group (adjusted HR 1.39, 95% CI 0.99–1.95, p=0.059). A subgroup analysis showed there were significant interactions between diabetes mellitus, hypertension, or anterior AMI and lesion complexity in terms of 1-year all-cause death.

Conclusions: Type B2 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 adjusting for differences between men and women undergoing PCI. Women in Innovation Initiative of the Society of Cardiovascular Angiography and Interventions.
Background: New-generation drug-eluting stents (DES) are associated with improved outcomes compared with older-generation DES. Whether or not these benefits extend to women with underlying chronic kidney disease (CKD), however, remains unclear.

Objectives: To compare outcomes between old- and new-generation DES in women with CKD undergoing PCI.

Methods: We pooled patient-level data for women enrolled in 26 randomized trials (n=11,557). Study population was categorized according to the presence or absence of CKD, defined as a creatinine clearance (CrCl) <60 ml/min. The primary endpoint was the incidence of major adverse cardiac events (MACE; defined as the composite of death, myocardial infarction [MI], definite or probable stent thrombosis [ST] and target lesion revascularization). Outcomes were reported at 3 years of follow-up.

Results: Out of 4,217 women included in the pooled database for whom estimation of CrCl was possible, 1,414 (33.5%) had CKD. Women with CKD were older, had lower body mass index and a higher prevalence of cardiac and non-cardiac comorbidities. Moreover a higher prevalence of multivessel coronary artery disease and moderate or severe calcifications were present in women with CKD. Following multivariable adjustment for baseline confounders new-generation DES were associated with a significantly lower risk of MACE (adjHR: 0.57; 95% CI: 0.36–0.92; p=0.02), MI (adjHR: 0.50; 95% CI: 0.26–0.95; p=0.03) and death (adjHR: 0.50; 95% CI: 0.27–0.91; p=0.02) in women with CKD. Moreover a trend towards lower risk of ST (adjHR: 0.29; 95% CI: 0.08–1.13; p=0.07) was observed in women with impaired renal function using new-generation DES. The magnitude and direction of the benefit with new-generation DES was consistent between CKD and non-CKD women, without evidence of interaction (p-int < 0.05).

Conclusions: Women with CKD undergoing PCI, use of newer as compared to older generation DES yields significant and uniform clinical benefits over a 3-year period.

Acknowledgement/Funding: Women in Innovation Initiative of the Society of Cardiovascular Angiography and Interventions.

P4700 | BEDSIDE

Impact of successful recanalization of chronic total occlusions using contemporary strategies on long-term clinical outcomes: a meta-analysis


Background: Although coronary stent implantation dramatically reduced the occurrence 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 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) at the longest follow-up.

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 stents deployment appears to be associated with improvement in mortality and reduced needs for CABG as compared with unsuccessful PCI.

P4701 | BEDSIDE

The hybrid toolkit for chronic total occlusions: materials used in the RECHARGE Registry (Registry of Crossboss and Hybrid procedures in FrAnce, the NetheRlands, BelGium and UniTed Kingdom)

J. Maeremans1, A. Avran2, P. Knaapen3, S. Walsh4, C. Hanratty4, B. Faure4, P. Agostino5, J. Spratt6, P. Kayaen7, J. Dens8 on behalf of RECHARGE.

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Background and introduction: The hybrid algorithm is designed to improve both procedural success rates and efficiency in revascularizing chronic total occlusions (CTO). Data on 1000 hybrid CTO procedures are collected.

Purpose: To provide the first report on the equipment and various strategies, used within the framework of the hybrid algorithm for CTO revascularization.

Methods: Patients treated for a coronary CTO were prospectively enrolled in 18 centers. CTOs were classified according to the Japanese score. Data were collected on the various materials and techniques applied during the procedure.

Results: 482 patients have been included from Jan 2014 to Feb 2015 of which 48, 109, 150 and 175 were classified as easy (0), intermediate (1), difficult (2) and very difficult (3) respectively (Table). An average of 1.38±0.64 strategies were used within the framework of the hybrid algorithm for CTO revascularization.

Conclusions: The average number of guidewires, balloons, stents and microcatheters increases. Likewise, the use of the CrossBoss and Stingray systems (for angiography dissection & re-entry) and additional devices also arise.

Table 1: Average number of materials used

<table>
<thead>
<tr>
<th>J-CTO score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>≥3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of # of patients</td>
<td>48 (100%)</td>
<td>109 (96%)</td>
<td>150 (87%)</td>
<td>175 (78%)</td>
<td>482 (87%)</td>
</tr>
<tr>
<td># of techniques</td>
<td>10.08±3.08</td>
<td>1.22±0.53</td>
<td>1.31±0.59</td>
<td>1.62±0.74</td>
<td>1.38±0.64</td>
</tr>
<tr>
<td>Guiding catheter</td>
<td>1.68±0.74</td>
<td>1.89±1.00</td>
<td>1.97±1.00</td>
<td>2.20±1.04</td>
<td>1.99±1.00</td>
</tr>
<tr>
<td>Guidewires</td>
<td>2.38±2.25</td>
<td>3.58±3.29</td>
<td>5.04±4.22</td>
<td>6.52±4.10</td>
<td>5.01±4.04</td>
</tr>
<tr>
<td>Balloons</td>
<td>2.33±1.40</td>
<td>2.77±2.12</td>
<td>3.02±2.56</td>
<td>3.83±3.26</td>
<td>3.19±2.71</td>
</tr>
<tr>
<td>Stents</td>
<td>1.60±0.71</td>
<td>1.93±0.90</td>
<td>2.33±1.12</td>
<td>2.73±1.02</td>
<td>2.28±1.01</td>
</tr>
<tr>
<td>Microcatheters</td>
<td>0.85±0.62</td>
<td>0.91±0.57</td>
<td>1.16±0.60</td>
<td>1.25±0.58</td>
<td>1.10±0.61</td>
</tr>
<tr>
<td>CrossBoss catheter</td>
<td>1 ± 1</td>
<td>16</td>
<td>22</td>
<td>45</td>
<td>84</td>
</tr>
<tr>
<td>Stingray system*</td>
<td>1 ± 1</td>
<td>16</td>
<td>22</td>
<td>45</td>
<td>84</td>
</tr>
<tr>
<td>Additional devices1</td>
<td>0.10±0.31</td>
<td>0.19±0.52</td>
<td>0.21±0.44</td>
<td>0.38±0.58</td>
<td>0.26±0.51</td>
</tr>
</tbody>
</table>

Values are given as n (%), mean or median and SD. *Stingray system consists of Stingray balloon and Stingray needle. 1Additional devices are the Rotablator, Guideliner and/or Tomus system.

Conclusions: Treatment of complex (J-CTO 2) and very complex CTO (J-CTO ≥3) lesions, results in an average use of more than 5 wires, 3 balloons, 2 stents and need of additional materials. This requires specific reimbursement policies.

P4702 | BEDSIDE

Adjunctive balloon post-dilatation in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

P.S. Song1, J.Y. Hahn2, P.K. Song1, S.H. Choi2, J.H. Park2, H.C. Gwon2 on behalf of the Effects of Postconditioning on Myocardial Reperfusion in STEMI in the Effects of Postconditioning on Myocardial Reperfusion in STEMI (EPIC-STEMI) trial.

1 Pusan National University School of Medicine, Inje University College of Medicine, Division of Cardiology, Department of Internal Medicine, Busan, Korea, Republic of; 2 Samsung Medical Center, Cardiovascular Center, Seoul, Korea, Republic of

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-STEMI) 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-
dilatation. Thrombolysis in Myocardial Infarction (TIMI) flow after PCI, myocardial blush grade (MBG), the rate of complete ST-segment resolution on ECG obtained 30 minutes after the procedure. Clinical outcomes were major adverse cardiac events (MACEs: a composite of death, MI, and target vessel revascularization) at 1 year.

Results: Adjunctive balloon post-dilatation was associated with a higher no-reflow (adjusted risk ratios of 3.66, 95% confidential interval [CI] 1.36–9.81, p=0.01), but TIMI 3 flow, MBG 0 or 1, and complete ST-segment resolution after PCI did not differ between procedures with or without adjunctive balloon post-dilatation. An analysis of adverse outcomes observed in the incidence of MACEs between groups (22/197 patients [6.5%] in the adjunctive balloon post-dilatation group and 19/482 patients [5.6%] in the control group, adjusted hazard ratio 1.15; 95% CI 0.49–2.71; p=0.76). The rates of occurrences for individual components of MACEs, stent thrombosis, and heart failure were also similar between groups.

Conclusions: In this post hoc analysis, the risk of no-reflow appeared to be higher with adjunctive balloon post-dilatation. Contrary to our expectation, adjunctive balloon post-dilatation did not impact procedural and clinical outcomes in patients with STEMI undergoing primary PCI with current standard practice. Based on our findings, it is better operators to use this adjunct in primary PCIs of confined lesions in the contemporary era of AMI.

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 previous CABG or did not actually receive PPCI. Logistic regression 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 5.45% (23/422). Logistic regression was used to examine 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, Lop et al. showed that residual SYNTAX score was a simple practical additional factor to help decide whether and when more intervention on the non-IRA is desirable.

P4704 | BEDSIDE
Multivessel disease diagnosed at the time of primary PCI for STEMI: complete revascularization versus conservative strategy
O. Hlomaza¹, L. Groch¹, L. Polovka¹, F. Lehar¹, T. Vekő², M. Griva³, J. Sittar¹, M. Rezek¹, B. Gersh⁴, P. Widimsky¹ on behalf of Prague-13 investigators.

Purpose: To determine the feasibility and safety of percutaneously inserted emergency VA-ECMO support in patients with acute ST-elevation myocardial infarction (STEMI) who were profoundly hypotensive on high inotropic support, and 4 were undergoing CPR.

Results: Of the 422 patients (mean age 59) analysed, 81% were male and 18% had known diabetes. At 12 months, the mortality rate was 5.45% (23/422). Logistic regression was used to examine 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.

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P4707 | BEDSIDE
Natural history of stent malapposition in patients treated by primary percutaneous coronary intervention: Subanalysis of ROBUST trial
M. Jakl1, P. Cervinka2, P. Kala3, J. Kanovsky3, A. Kucpe2, J. Vanek4, K. Tanaka5, S. Nishino5, A. Schnell5, H.G. Bezerra5. 1University of Defense, Faculty of Military Health Sciences, Hradec Kralove, Czech Republic; 2Masaryk Hospital, Department of Cardiology, Usti nad Labem, Czech Republic; 3University Hospital Brno, Cardio-Vascular Department, Brno, Czech Republic; 4Faculty of Informatics and Management of the University of Hradec Kralove, Department of Informatics and Quantitative Methods, Hradec Kralove, Czech Republic; 5University Hospitals Case Medical Center, Cardiology, The Harrington Heart and Vascular Institute, Cleveland, United States of America

Background: Stent malapposition is anticipated to be associated with unfavorable long-term intravascular 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 primary 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 OCTval-Sent 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).

Conclusions: 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 (FMH5).

P4708 | BEDSIDE
Intracoronary nitroprusside versus verapamil for the prevention of no/low reflow phenomenon in patients undergoing primary percutaneous coronary intervention
H. Abdelaziz, S. Khaled, T. Khairy, S. Thabet, W. Elkeelany, T. Rashid. Ain Shams University Hospital, Cardiology department, Cairo, Egypt

Background: No/low 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 nitroprusside in the prevention of the no/low reflow phenomenon in patients with acute ST segment elevation myocardial infarction (STEMI) undergoing primary PCI.

Methods: A total of 60 STEMI patients with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0/1 were randomly allocated 1:1 to receive verapamil (n=30) or nitroprusside (n=30) given distal 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 nitroprusside-treated patients (p=0.009), and for the sum of multiple leads showing ST elevation occurred in in 43.3% and in 13.3% respectively (p=0.04). Angiographic MVO occurred in 10% of verapamil -treated patients and 30% of nitroprusside-treated patients (p=0.04). The mean LVEF was 42.6±4.9 and 40.4±4.7 for verapamil and nitroprusside-treated patients respectively (p=0.086). Likewise, the mean WMIS was 1.43±0.13 and 1.45±0.16 for verapamil and nitroprusside-treated patients respectively (p=0.145). Procedural hypotension occurred in 33.3% and 20% respectively (p=0.04), MACE occurred in 3.3% and 6.6% respectively (p=0.89).

Conclusions: In STEMI patients treated by PCI, intracoronary verapamil achieved a significantly better myocardial reperfusion with a significantly less occurrence of hypotension in comparison to nitroprusside. However, there was no significant difference in MACE at 1 month follow up.

Acknowledgement/Funding: Ain shams university
P4710 | BEDSIDE
Safety and effectiveness of deferring definitive treatment of the culprit lesion in STElevation myocardial infarction
C. Granda Nistal1, B. Rubio Alonso1, A. Jurado Roman2, J. Garcia Tejada3, S. Mayordomo Gomez1, A. Miguel Gutierrez1, E.P. Garcia Martin1, M.T. Velazquez Martin1, F. Hernandez Hernandez1, A. Albarran Gonzalez-Trinidad1,2, University Hospital of Bellvitge, 12 de October, Department of Cardiology, Madrid, Spain; 2Hospital General de Ciudad Real, Ciudad Real, Spain
Background: In selected patients (p) with ST segment elevation myocardial infarction (STEMI), deferring definitive 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,Gr A) versus STEMI p with immediate stenting (Gr B) during primary percutaneous coronary intervention (PPCI). We compare baseline characteristics, peak CK, and incidence of ischaemic MACE (MI, new target vessel revascularization) and major bleeding (BARC ≥3 criteria).
Results: Patients of Gr A were younger than Gr B, with no other difference in baseline characteristics. A high residual thrombus burden was associated to the decision of deferring definitive treatment of the culprit lesion in 74%. Severe coronary calcification was the reason in 17%. Intensive pharmacologic antithrombotic treatment was administered during 8±3 days. The delayed coronary angiogram showed TIMI 3 flow grade in 95% of the p. There was a significant reduction in thrombus burden between the baseline angiography and the delayed one (TIMI thrombus grade 3.50±0.47 vs. 0.50±p<0.01). 52% of p in Gr A did not show significant residual lesion. A delayed stent implantation was needed in 48% of Gr A (rotational atherectomy was performed in 14%). There is a trend of reduction in cardiac injury measured by the peak of CK in Gr A compared to Gr B. There were significant residual lesion. A delayed stent implantation was needed in 48% of Gr A (rotational atherectomy was performed in 14%). There is a trend of reduction in cardiac injury measured by the peak of CK in Gr A compared to Gr B. There were no difference between baseline angiography and the delayed one. In the follow up after 9.5 months, there were no difference either in the ischemic MACE rate or in major bleeding between Gr A and Gr B.
Conclusions: In selected STEMI patients who underwent a PPCI, the deferred treatment of the culprit lesion showed similar results in effectiveness (ischemic MACE) and safety (bleeding) comparing 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 biodegradable polymer coated sirolimus eluting stent in coronary artery lesions (i-TRIAL study)
R.S. Polavarapu1, J. Prajapati2, A. Raheem3, K. Thakkar1, V. Parmiddikulama3, A. Polavarapu1, N. Polavarapu1, S. Chintan1, S. Kothari3, A. Thakkar1, Lailitha Super Specialty Hospital, Department of Cardiology, Guntur, Andhra Pradesh, India; 2Apollo Hospitals International Limited, Department of Cardiology, Gandhi Nagar, Gurgaon, India; 3Yashfeen Cardiac Hospital, Department of Cardiology, Navsari, Gujarat, India; 4Lions Sterling Super Specialty Hospital, Department of Cardiology, Mehsana, Gujarat, India; 5Sahajanand Medical Technologies Pvt. Ltd. Department of Clinical Trials, Surat, Gujarat, India
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, target lesion revascularization (TLR), target vessel revascularization (TVR), myocardial infarction (MI) 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±9.01 mm and 3.2±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 MACE 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 (0.50%) patients. There 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 MACE. Thus, the i-TRIAL study gives an idea about favor- able 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 elevation 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 these, 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: composite of cardiac death, TLR and target-vessel revascularization at 6-month without aspiration vs. 16.5% with aspiration (p=0.03), TLR 3.9% vs. 1.8% (p=0.01) and definite 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 in a propensity score matching analysis. 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 biodegradable 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 biodegradable polymer-coated sirolimus-eluting Supraflex (Sahajanad 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 1.4±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 16 (14.8%) cardiac deaths, 5 (5.0%) 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.
P4714 | BEDSIDE
Safety and efficacy of angio-seal vs exo-seal in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction

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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 reperfusion

tone 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. Age, sex, size, type of PCI, and TIMI flow grade were comparable. The risk of VC was significantly associated with body mass index (BMI) OR 2.1 (95% CI 0.77–0.86, p=0.01), sheath size OR 1.2 (95% CI 0.12–0.84, p=0.04), presence of chronic kidney disease (CKD) OR 1.5 (95% CI 1.1–1.7, p=0.005) and peripheral arterial disease (PAD) OR 3.2 (95% CI 1.78–3.1, p=0.03). There was just a trend to present hematoma (6.6% vs. 3.5%; p=0.4) and arteriovenous fistula (3.3% vs. 1.7%; p=0.05) in Exo-Seal®; pseudoaneurysm (5.2% vs. 1.1%; p=0.3) and recurrent bleeding (2.2% vs 0%; p=0.5) in Angio-Seal®.

Conclusion: VC after femoral approach in patients undergoing primary PCI for STEMI is at 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.

P4715 | 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 2012 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 of pPCI. Predictors were selected between clinical, angiographic and procedural factors with the study endpoint as dependent variable using logistic regression analysis. Relationship between the study endpoint and clinical outcome was analyzed by Cox-regression analysis.

Results: We enrolled 720 patients of whom 192 (26,4%) presenting with MVD. The left anterior descending artery was the target vessel in 76 (44.7%) cases. The mean age was 50.7±10.2 years and 142 (83.5%) of patients were men. 29.4% (50/170) and 25.9% (44/170) of patients had arterial hypertension and diabetes, respectively. Of the lesions treated (n=170), 166 (97.6%) were classified as American College of Cardiology/American Heart Association type C. The left anterior descending artery was the target vessel in 76 (44.7%) cases. The mean lesion stenosis and length and diameter were 30.8±8.4 mm and 3.1±0.4 mm, respectively. The mean number of stents implanted per patient was 1.1±0.4. The in-hospital and 30-day, TLRF rate were 0.6% (1/170) and 0.6% (1/170), respectively. A total of 169 (99.4%) patients followed at the end of 6-month, 1 patient

P4717 | BEDSIDE
Clinical outcomes of successful percutaneous coronary intervention for chronic total occlusion treated with sirolimus-eluting stent: results from the multicenter CTO registry

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Background and introduction: Survival benefits have been reported after successful percutaneous coronary intervention (PCI) in patients with chronic total occlusion (CTO). The development of bioabsorbable polymer on drug-eluting stents (DES) gained interest in CTO-PCI. We aim to analyze the immediate, short and mid-term clinical outcomes of patients with CTO treated with the indolimus bioabsorbable polymer coated sirolimus-eluting stent (SES), from day-to-day clinical practice.

Methods: We analyzed immediate (in-hospital), short (30-day) and mid-term (6-month) clinical outcomes in 170 patients, who underwent successful recanalization of CTO (defined as >3 months’ duration) and received Indolimus SES, at four tertiary care centres in India between April 2012 and June 2014. During 6-month, main clinical outcome parameter was target lesion failure (TLF), a composite of cardiac death, myocardial infarction (MI), or target lesion revascularization (TLR). We also analyzed stent thrombosis (ST) as a safety endpoint during 6-month of follow-up.

Results: The mean age was 50.7±10.2 years and 142 (83.5%) of patients were men. 29.4% (50/170) and 25.9% (44/170) of patients had arterial hypertension and diabetes, respectively. Of the lesions treated (n=170), 166 (97.6%) were classified as American College of Cardiology/American Heart Association type C. The left anterior descending artery was the target vessel in 76 (44.7%) cases. The mean lesion stenosis and length and diameter were 30.8±8.4 mm and 3.1±0.4 mm, respectively. The mean number of stents implanted per patient was 1.1±0.4. The in-hospital and 30-day, TLRF rate were 0.6% (1/170) and 0.6% (1/170), respectively. A total of 169 (99.4%) patients followed at the end of 6-month, 1 patient

Conclusion: Operator fatigue and sleep deprivation does not seem to have 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 TCO with Indolimus SES showed favourable immediate, short and mid-term clinical outcomes.

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**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. (118 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.

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**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 customized figure-of-eight suture introduced at our centre that allows for performance of "Z" stitch or compression group for hemostasis in a 2:1 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.

**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 not measurable with QCA, like chronic total occlusions or ostial lesions, were not included. In-stent restenosis and patients with clinical or hemodynamic lesions were excluded.

**Results:** Baseline characteristics and procedural variables were comparable in both groups. S (n=220) and L (n=229): mean age (66.6±12.6 vs. 67.2±11.2; p=ns), gender (male 71.6% vs. 75.0%; p=ns), diabetes (29.0% vs. 20.3%; p=ns), hypertension (64.2% vs. 59.9%; p=ns), dyslipidemia (43.2% vs. 47.1%; p=ns), smoking (27.8% vs. 33.7%; p=ns), previous myocardial infarction (22.8% vs. 20.9%; p=ns), primary PCI (11.7% vs. 10.5%; p=ns), number of lesions treated (>1 lesion 28.4% vs. 27.3%; p=ns), pre-dilatation (40.0% vs. 41.9%; p=ns), reference diameter by QCA (2.88±0.56 vs. 2.89±0.53 mm; p=ns), and lesion length by QCA (16.60±9.78 vs. 17.27±9.46 mm; p=ns).

**Conclusion:** EAM reconstruction prior LVAR could play important role: 1. arrhythmic surgery by cryo-ablation of very specific substrate leads to dramatic reduction of VTA induction; 2. guide accurate LV reconstruction.
P4724 | 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 cardiovascular 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 < 50%) participated in this study (mean age 58±7 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 dilation (FMD) of the brachial artery was assessed by high resolution ultrasound. Human umbilical vein endothelial cells (HUVEC) were incubated for 72 hours with 20% of 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<0.001) and decreased the level of viable cells (respectively 82% vs 93%, p<0.001). Rate of dead HUVEC cells was similar for serum from patients with ischemic and non-ischemic CHF (respectively 17% and 19%, p=ns). There was a significant inverse correlation between percentage of dead endothelial cells in vitro and endothelium-dependent vasodilation 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<0.05). Cox regression analysis revealed that high cytotoxic serum activity [Exp(B)=0.831, 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. Circulating blood of patients with CHF damages endothelial cells. This action is irrespective of etiology of CHF and related to impaired FMD. This action is irrespective of etiology of CHF and related to impaired FMD. The study aimed to evaluate whether biomarker risk prediction score is powerful tool for risk assessment of three-year fatal and non-fatal cardiovascular events in CHF patients.
Methods: It was studied prospectively the incidence of fatal and non-fatal cardiovascular events, as well as the frequency of occurrence of death from any cause in a cohort of 388 patients with CHF during 3 years of observation. Circulating levels of NT-pro brain natriuretic peptide (NT-pro-BNP), galectin-3, high-sensitivity C-reactive protein (hs-CRP), osteoprotegerin, CD31+/annexin V+ EMPs and CD31+/CD309+ EMPs ratio. Index of cardiovascular risk was calculated by mathematical summation of all ranks of independent predictors, which occurred in the patients included in the study. The findings showed that the average value of the index of cardiovascular risk in patients with CHF was 3.17 points (95% CI = 1.65 - 5.10 points.). Kaplan-Meier analysis showed that patients with CHF and the magnitude of the risk of less than 4 units have an advantage in survival when compared with patients for whom obtained higher values of cardiovascular risk score ranks.
Conclusion: Biomarker risk score for cumulative cardiovascular events, constructed by measurement of circulating NT-pro-BNP, galectin-3, hs-CRP, osteoprotegerin, CD31+/annexin V+ EMPs and CD31+/CD309+ EMPs ratio, allowing reliably predict the probability survival of patients with CHF, regardless of age, gender, state of the contractile function of the left ventricle and the number of comorbidities.

P4725 | BEDSIDE
Prognostic value of cystatin C-derived estimatedglomerular filtration rate in the patients with acute decompenated 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 decompenated status in comparison from creatinine derived GFR.
Methods: This retrospective study included 262 patients with acute decompenated heart failure. Prognostic value of the estimated GFRs, derived from the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation and cystatin C equation, were compared with estimated GFR derived from the classical equations containing only serum creatinine levels (Modification of Diet in Renal Disease (MDRD) equation and CKD-EPI-creatinine equation). GFR was calculated by mathematical summation of all ranks of independent predictors, which occurred in the patients included in the study. The findings showed that patients with CHF and the magnitude of the risk of less than 4 units have an advantage in survival when compared with patients for whom obtained higher values of cardiovascular risk score ranks.
Results: Serum from patients with CHF increased the level of dead endothelial cells when compared with healthy subjects (18% vs 7%, p<0.001) and decreased the level of viable cells (respectively 82% vs 93%, p<0.001). Rate of dead HUVEC cells was similar for serum from patients with ischemic and non-ischemic CHF (respectively 17% and 19%, p=ns). There was a significant inverse correlation between percentage of dead endothelial cells in vitro and endothelium-dependent vasodilation 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<0.05). Cox regression analysis revealed that high cytotoxic serum activity [Exp(B)=0.831, 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. Circulating blood of patients with CHF damages endothelial cells. This action is irrespective of etiology of CHF and related to impaired FMD. Circulating blood of patients with CHF damages endothelial cells. This action is irrespective of etiology of CHF and related to impaired FMD. This action is irrespective of etiology of CHF and related to impaired FMD. The approach was to calculate estimated GFRs, which were derived from cystatin C, predicted the risk more accurately in patients with acute decompenated heart failure, compared to those from creatinine-only equations.

P4725 | BEDSIDE
Right ventricular function is a powerful independent predictor of adverse heart failure outcomes
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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: All patients referred for consideration for heart transplantation at our institution between 2006–2013 were included. Univariate and multivariate analyses were performed to identify indices associated with poor prognosis.
Results: 182 consecutive patients listed for cardiac transplantation were studied. During follow-up, 20 patients died, 62 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 associated 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
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, GFR, albumin (P<0.03 for all). PAWP was associated with sodium (P=0.02).

Conclusion: Haemodynamic 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 GFR 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

Background: Increased heart rate (HR) and low systolic blood pressure (SBP) are independent adverse 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 with AHF following hospital 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 BP and HR 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 (≥0.66, n=2,751, 66.9±14.9 years, 1,465 males) and low HR/SBP ratio group (<0.66, 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 (46.9% vs. 32.4%, p<0.0001), diabetes (66.7% vs. 62.3%, p=0.0001), and ischemic heart disease (76.0% 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/HR 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 early 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 non-invasive 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 (‘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 MetS (n=83) and non-MetS (n=105) groups.

Results: During the follow-up (18.6±6 months) period, 87 patients (47%) had CE. The creatinun level was higher (P<0.01), LV mass index was higher (P<0.001), LA was larger (P<0.001), LV EDD (P<0.001) and LV ESV (P<0.001) were greater, e′ lower (P<0.001), septal MAPSE lower (P<0.001), diabes and MetS more prevalent (P=0.03 and P=0.001, respectively), NYHA ≥2 more frequent (P<0.001), in patients with cardiac events compared to those without. Patients with HF and MetS were older (p<0.008), had larger LA (p<0.04), lower sphericity index (p<0.006, respectively), and reduced LVEF emptying fraction (p<0.01) compared to those with non-MetS. Multivariate analysis identified E/e′ (OR=0.1.121, 95% CI 1.018–1.234; P=0.02) and MetS (OR=3.967, 95% CI 1.673–9.409; P=0.002) as independent predictors of CE.

Conclusion: In medically treated patients with chronic HF, the presence of MetS, 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 MetS.

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 15 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 CS (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: 0.029 to 1.61, p=0.135).

Cox proportional hazards analysis

<table>
<thead>
<tr>
<th>Univariate</th>
<th>Multivariate</th>
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</thead>
<tbody>
<tr>
<td>OR (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td>P</td>
<td></td>
</tr>
<tr>
<td>CRT responder</td>
<td>0.335 (0.134–0.838)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>0.206 (0.026–1.542)</td>
</tr>
<tr>
<td>Over 60 y/o</td>
<td>0.793 (0.326–1.930)</td>
</tr>
<tr>
<td>Male</td>
<td>0.813 (0.331–1.955)</td>
</tr>
<tr>
<td>LBBB</td>
<td>0.722 (0.239–2.181)</td>
</tr>
<tr>
<td>Chronic atrial fibrillation</td>
<td>1.490 (0.608–3.656)</td>
</tr>
<tr>
<td>Appropriate ICD therapy</td>
<td>1.293 (0.530–3.105)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>1.203 (0.159–9.116)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>0.776 (0.308–1.956)</td>
</tr>
<tr>
<td>GPS over 130ms</td>
<td>0.541 (0.196–1.433)</td>
</tr>
</tbody>
</table>

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 transient episodes of arterial hypotension in patients with chronic heart failure (NYHA Class II-III with preserved left ventricular ejection fraction ≥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

Basic mechanisms, ventricular function, prognosis III 831
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 MnSDP-2 and MnSDP-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 16% of arterial systolic arterial 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 M or CVD deaths: 2 – in the group of patients with episodes of diastolic arterial hypertention and 6 - in the group of patients with episodes of 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 ($x^2=0.98, p=0.3$ and $x^2=5.46, p=0.019$, 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 β-D-glucosaminidase (NAG), Neutrophil Gelatinate-Associated Lipocan (NGAL) and II-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:** Measurements of 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

**Octadecatrienal and phosphatidylcholine as a potential new biomarkers in heart failure - novel insights from the analysis of serum metabolome in chronic heart failure patients**

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**Introduction:** Incomplete knowledge of the pathophysiological basis of the heart failure (HF) enforces further exploration of new analytical methods, as well as predictive and prognostic markers that would allow to trace molecular stages of HF development and its progression. Aim: The goal was to determine if new biomarkers and potential molecular mechanisms to identify changes in the blood metabolome profile, occurring as a result of heart failure development.

**Methods and results:** We prospectively studied 36 optimally treated patients with stable chronic HF (61±13.9 years, 58% ischemic etiology, left ventricular ejection fraction LVEF 38±6.3%, NYHA class II/III 47/33%) and 20 age-matched subjects without the disease (60.5±12.8 years, LVEF 64±5.5%). All of the enrolled patients were assessed clinically, biochemically, echocardiographically and functionally. Acute and chronic inflammatory diseases (rheumatoid arthritis, diabetes mellitus, asthma) were excluded. Fasting serum samples were collected and fingerprinted by liquid chromatography-mass spectrometry (LC-QTOF-MS). T-test or Mann-Whitney test were used depending on data distribution and solely statistically significant metabolites ($p<0.05$, corrected with FDR) were selected to draw conclusions. Identification of significant features was performed based on accurate mass measurement of more than 100 metabolites. Statistically significant differences between both groups were observed regarding to over 110 metabolites. Higher level of octadecatrienal ($+385\%$, $p=0.001$, AUC 0.86, $p<0.0001$), uric acid ($+28\%$, $p=0.026$), vitamin E ($+51\%$, $p=0.039$) and lower level of arachidonic acid ($-32\%$, $p=0.001$), linoleic acid ($-44\%$, $p=0.007$), stearic acid ($-51\%$, $p=0.007$), sphenoglycolins ($-29-36\%$, $p=0.005-0.012$), NADPH oxidase were predicted.

**Conclusions:** Measurement of octadecatrienal could be a potential new biomarker of CHF. In the future, potential new markers could be discovered by the analysis of blood metabolome profile in patients with chronic heart failure.
P4732 | BENCH
Adrenergic signaling-induced bone marrow and endothelial cell senescence promotes cardiac remodeling in heart failure
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Activation of the sympathetic nervous system (SNS) occurs as an adaptive response to heart failure, but it has been reported that sustained SNS activation promotes cardiac dysfunction. In addition, adrenergic signaling is known to be involved in regulating bone marrow homeostasis. Although the p53 protein is known to be the guardian of the genome, accumulating evidence has reported that excessive p53 signaling accelerates cellular senescence and would become pathological in aging models such as diabetes and heart failure. Here we show the previously unknown role of adrenergic signaling in inducing bone marrow and endothelial cell senescence in a murine isoproterenol infux model. Inducing isoproterenol via an infusion pump markedly inhibited systolic function and promoted cardiac inflammation in mice. Isoprotenerol significantly increased p53 level in cardiac tissue and bone marrow cells. This treatment also increased the transcript of adhesion molecules in cardiac tissue and bone marrow cells, suggesting that adrenergic signaling in promoting cardiac remodeling by inducing inflammatory responses in heart. To test our hypotheses that cellular senescence of endothelial cells and bone marrow cells contribute to cardiac remodeling, we generated endothelial cell-specific p53 deletion mice by crossing Tie2-Cre x p53flox/flox (Endo p53 KO) mice and bone marrow cell-specific p53 deletion (BM p53 KO) mice by transplanting bone marrow cells extracted from systemic p53 mice into black6 wild type mice after irradiation. Isoproterenol-induced cardiac dysfunction was significantly inhibited in Endo p53 KO and BM p53 KO mice. Our results indicate the previously unknown pathological role of adrenergic signaling in inducing endothelial cell and bone marrow cell senescence in heart failure.

P4734 | BENCH
Differentiation of fibroblasts into myofibroblasts during hypertensive-derived cardiac fibrosis is promoted by alpha-v beta-5 integrin-mediated activation of TGF-beta1
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Introduction - TGF-β1 plays a key role in the hypertension-associated cardiac fibrosis by acting on cardiac fibroblast differentiation to produce α-smooth muscle actin (α-SMA)-expressing myofibroblasts. Integrin-mediated mechanotransduction via TGF-β1 activation plays a role in the cardiac fibroblast differentiation. Methods: Immunochemistry 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 1n). 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 tools targeting 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 left ventricular dysfunction and chronic heart failure (CHF). Apart from the direct effect on membrane bound receptors, 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. In the presented study we evaluated IL-6 signaling, 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±3%, confirmed by echocardiography and 33 healthy age-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 transthoracic 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: 37.6–64 vs 53 IQR: 45–76 ng/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<0.01). Among CPET parameters decreased standard deviation of systolic blood pressure (SDBP), increased standard deviations of mean (SDBP) and systolic BP variability (SBPV) were observed. At 6 months of CRT significant improvement in NYHA class (2±0±4 vs 2±1±4, p<0.005) and improvement of echocardiographic parameters, e.g. EF (23±6% vs 32±10%, p<0.001) and LVESV (193±58 vs 145±68ml, 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 sIL-6R concentration was observed when comparing to nonresponders (±IL-6R: −0.18±7±6 vs 6.97±4±02pg/ml, p=0.029), while IL-6 and sgp130 concentrations did not significantly change. 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.
Acknowledgement/Funding: Scholarship subsidy under the status Leading Research Centre (KBNW) of Medical University of Białystok.
between their expression and the LVEF (r=−0.68; p<0.04) and LVEDV (r=0.61; p<0.04) in TAC-mice. Microarray analysis identified additional 11 genes associated with Wnt-signaling as differentially expressed (TAC vs. Sham, f<0.15) 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- and 1.84-fold for Normo- and Hypo-Endothelin), Wisp2 expression was unchanged in comparison to the control. Re-expression of the EH-myonemisin isoform. Interestingly, this adaptation is only seen in familial and idiopathic DCM samples but not in any of the samples from women with peripartum DCM (PPDC) that were analysed so far. Also cardiomyocyte size changes were less pronounced in PDCM patients.

Conclusion: We conclude that cardiac cytoarchitecture shows similar changes in human DCM compared to mouse models for this disease but that PDCM has to be considered as a separate subgroup of DCM with distinct cell biological characteristics.

P4739 | BEDSIDE
Hepcidin and its regulator molecule hemouvelin in systolic heart failure
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Introduction: Hepcidin (HPC) is a key regulator of iron metabolism. Hemouvelin (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. HVJ serum concentration was never determined in CHF patients.

Aim of the study: The aim of the study was to assess HPC and HVJ 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 HVJ 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. Endpoints 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 hemojuvelin serum level. HPC and HVJ 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 HVJ. None of the studied parameters turned out to be a valuable marker of heart failure exacerbation.

Conclusion: There is no direct association between hepcidin and hemojuvelin serum levels. 2. CHF has no clinically evident impact on HVJ serum level. 3. HPC may be not strongly related to iron status in heart failure but tissue ischemia resulting from heart failure exacerbation may lead to inhibition of HPC production.

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P4740 | BENCH
Fish oils may promote lipostasy 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 phospholamban (PLB) dynamics.

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 (Omacor, 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 quantitative 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.
Cardiovascular Diseases, Heart Transplant Unit, Siena, Italy; 2 Heart Centre

Conclusion: Fish oil incorporation in human cardiomyocyte membrane reduces myocardial fibrosis in patients with advanced heart failure requiring heart transplantation. 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 undergoing heart transplantation. Myocardial fibrosis was assessed using Masson's staining.

Results: Of 106 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<0.001), modestly 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.

Conclusion: LV GLS is the most accurate LV global function measure that correlates with the extent of myocardial fibrosis in patients with advanced systolic HF requiring heart transplantation.

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-syndromic thoracic aortic aneurysm (TAAD) are associated with aortic dilatation and increased aortic stiffness. Previous reports of abnormal left ventricular 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, 33±15 yrs) and TAAD (n=70, 33, 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 (Ea m(mHg/ml−1)) were measured as indices of ventricular afterload; ventricular function was measured by tissue Doppler and calculation of the end-systolic elastance (Ees m(mHg/ml−1)). Ventricular function indices were compared between groups by ANOVA.

Results: Dilatation of the sinuses of Valsalva was similar in MFS and TAAD but not in MFS, Aortic stiffness index was increased in MFS (16.2±11 and in TAAD 11.6±3 vs controls 11.3±4.6; p<0.01). Mean blood pressure was increased in TAAD (96±10 mmHg p<0.05) vs controls (91±10 mmHg), but not MFS (97±9 mmHg). Left ventricular stroke work was increased in TAAD (p<0.01 vs controls), but not in MFS. The Ees in Marfan was reduced (1.9±4.0 vs controls 2.4±0.6 p<0.01) but not in TAAD (2.19±0.6).

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, exercise capacity, and exercise 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 re- jection 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 peak exercise (r=−0.38, p=0.01), even after adjustment of CAV (r=−0.61, p<0.05). At rest microCFR was significantly correlated to LV filling pressure (mean pulmonary capillary wedge pressure: r=−0.43, p<0.01) and right ventricular filling pressure (mean right atrium pressure: RAP: r=−0.42, 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.
P4745 | BEDSIDE
Advanced heart failure with reduced ejection fraction and severe mitral insufficiency is associated with a reduced cardiac output vs oxygen uptake response to maximal exercise
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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 physiological 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: 104 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-invasive 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 (3.8±1 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 82±5 vs 94±10 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±3.3 L/min) and VO2 (1.0±0.3 vs 0.8±0.3 L/min, p=0.011) partially compensated by a greater C(a-v)O2 contribution (15±5 vs 18±5 for A vs B, p=0.047).

Conclusions: Severe MR and consequent partial abnormal CO redistribution to the pulmonary circulation seems to require different physiological mechanisms that limits 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.

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=0.002), respectively (panel B).

Conclusions: In comparison with BiV pacing at any LV site, MPP yielded a small but consistent increase in hemodynamics 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.

P4745 | 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) (Figure 1). 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±15 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.

Conclusions: 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) of the MAM and TAM calculated as first-time-derivatives of the displacement. For MAM assessment, 4-chamber, 3-chamber and 2-chamber views were used and the derived myocardial velocities were averaged. For TAM assessment, only 4-chamber right ventricular lateral site was used. TDI was performed following the standard protocol based on ASE recommendation.

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 MAM assessment, 4-chamber, 3-chamber and 2-chamber views were used and the derived myocardial velocities were averaged. For TAM assessment, only 4-chamber right ventricular lateral site was used. TDI was performed following 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). However, significant but relative weak correlations were found between TAM and MAM velocities (Sm: r=0.30; Em: r=0.65; Am: r=0.40, all p<0.001) from CMR. This may indicate the anatomical and physiological differences between the left and right ventricles.

Table 1. Correlations of myocardial velocities from MAM and TAM between CMR and TDI methods

<table>
<thead>
<tr>
<th></th>
<th>MAM</th>
<th>TAM</th>
<th>r</th>
<th>p</th>
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<tbody>
<tr>
<td>Sm</td>
<td>0.74</td>
<td>-0.001</td>
<td>0.70</td>
<td>-0.001</td>
</tr>
<tr>
<td>Em</td>
<td>0.84</td>
<td>-0.001</td>
<td>0.78</td>
<td>-0.001</td>
</tr>
<tr>
<td>Am</td>
<td>0.70</td>
<td>-0.001</td>
<td>0.81</td>
<td>-0.001</td>
</tr>
</tbody>
</table>

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 protocol who were followed up with FAST and VAS scores simultaneously. The FAST protocol was positive if E/e' was >15 and LUS presented bilateral B-lines (BL) or pleural fluid (PF) right sided or bilaterally. Patients were classified as “responders” if they improved symptomatically 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. 1.10 U, p<0.004) and VAS scores (6.29 vs. 4.19 U, p<0.002) than non-responders during total treatment course. The fastest change among responders occurred during the first 12 hours of treatment (mean ∆ E/e' 2.34 (SD 3.31) and mean ∆ VAS 3.74 (SD 3.13)) compared with a mean ∆ E/e' of 1.77 (SD 2.90) and a mean ∆ VAS of 2.47 (SD 2.58) during the rest of total hospital stay (p<0.001 for mean ∆ U/hour). The mean time 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 foreshadow 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.

Methods: Fifty-four HTx patients underwent coronary angiography. We excluded 11 patients due to significant CAV. The remaining 40 HTx patients underwent 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 versus median CFVR and group B: preserved CFVR > median CFVR.

Results: CFVR was significantly lower in the HTx-group compared to controls (2.8±0.6 versus 3.8±0.8, p<0.0001), and 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 parameters revealed a 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 with reduced CFVR failed to increase LV longitudinal myocardial deformation compared to HTx patients with preserved CFVR (ΔGLS −2.9±2.8% versus −5.4±2.1%, p=0.01) and healthy controls (ΔGLS −2.9±2.8% versus −5.0±2.5%, p=0.01). We found a strong correlation between CFVR and peak exercise GLS in HTx patients (rho 0.71, p<0.001) after adjustment of 16 potential confounders in a multivariable analysis (p<0.001).

Conclusion: HTx patients without severe microvascular CAV had significantly reduced CFVR and reduced LV longitudinal deformation capacity measured by peak exercise GLS 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 (mean 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 ρho –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,
Conclusions: In HFrEF population the assessment of S-D at rest and peak exercise predicts functional status and is related to more advanced hemodynamic impairment compared with 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 [EOA]<1 cm²) 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-to-right atrial gradient during systole and the right atrial pressure. PHT was classified as absent if <35 mmHg and persistent if ≥35 mmHg.

Primary clinical endpoint was the 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 event 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±8 mmHg, 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±8 mmHg, p<0.001). In multivariate regression analysis, persistence of PHT (OR: 3.310, 95% CI: 1.065–1.098, 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

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of; 3 Jeonju Presbyterian Medical Center, Jeonju, Korea, Republic of

Methods: Between 2008 and 2011, 12,557 patients were enrolled in a registry, and patients who had severe left ventricular dysfunction (<40%) with AMI were analyzed. They were divided into 2 groups; treated with statin group (n=337) and untreated without statin group (n=158). To overcome the differences of baseline characteristics and discharge medication between 2 groups, we performed propensity score matched analysis. And 1-year incidence of major adverse cardiovascular event (MACE) and all-cause mortality were analyzed.

Results: In original cohorts, 1-year composites of MACE (all-cause mortality, myocardial infarction and any 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 statically 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 evaluated 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).

Conclusions: 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).

P4753 | BEDSIDE
Preserved ventricular-arterial coupling but more myocardial oxygen consumption and less mechanical efficiency in haemodialysis patients

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Purpose: Ejection fraction is limited to assess contractility in haemodialysis (HD) patients due to its poor correlation. 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=128, 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: The 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-diastolic weight gain, and Kt/V).

Comparisons of cardiovascular function

<table>
<thead>
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<th>Characteristics</th>
<th>Non-HD controls</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>
</tr>
<tr>
<td>Ees, mmHg/ml</td>
<td>4.44±1.83</td>
<td>4.74±1.61</td>
<td>4.96±2.34</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>
</tr>
<tr>
<td>PVA, mmHg ml</td>
<td>7931±2536</td>
<td>8134±2674</td>
<td>10710±4037</td>
</tr>
<tr>
<td>SW/PVA efficiency, %</td>
<td>60±5</td>
<td>60±6</td>
<td>55±4*</td>
</tr>
</tbody>
</table>

Final column reflects overall p, <0.05 versus Non-HD controls; <0.05 versus HD 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.
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). After CRT, the RV pressure increased (p<0.01) but remained below LBBB. LBBB caused a decrease in LV short-axis work from 126±97 to 198±113 mmHg*mmHg (p=0.01), but LV short-axis work decreased (Fig.B). In the RV, LBBB caused opposite changes with preejection shortening of the RV short-axis diameter, and an increase in RV short-axis work. However, in the RV free wall LBBB caused a decrease in longitudinal work from 34±16 to 25±16 mmHg*mmHg (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.

P4756 | BENCH
Computer-controlled infusion system of cardiovascular drugs to automatically optimize hemodynamics in decompensated heart failure

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Purpose: In the management of patients with decompensated heart failure (HF), vasodilators and diuretics are used to relieve congestion. To maintain cardiac output (CO), inotropes are sometimes indicated. These require strict hemodynamic monitoring and frequent adjustments of drug infusion rates, which is difficult and time-consuming, especially in seriously ill patients. To overcome this difficulty, we have developed a computer-controlled drug infusion system for simultaneous control of arterial pressure (AP), CO and pulmonary capillary wedge pressure (PCWP).

Methods: Our system estimates CO (COest) using transathoracic Doppler aortic velocity and peripheral AP contour, and PCWP (PCWPest) from jugular venous pressure corrected by tissue Doppler tricuspid/mitral annulus velocities. Using AP, COest and PCWPest, our system computes arterial resistance (R), stressed blood volume (V) and Frank-Starling slope of left ventricle (S). Our system controls R with nitropusside (NP), V with furosamide (Fur)/dextran (DEX), and S with dobutamine (DOB), thereby controlling the three variables. In 9 dogs, we created HF by chronic right ventricular tachycardia pacing. We then connected the system to HF dogs, and activated it.

Results: Our system immediately started NP and Fur, and if necessary started DEX/DOB, and optimized R, V and S in 30 minutes. Normalization of R, V and S resulted in restoring normal AP, COest and PCWPest with small deviations from targets values (Figure). Pulmonary artery catheterization confirmed optimization of CO and PCWP from respective baseline values (CO, from 1.3±0.5 to 2.8±0.4 L/min/m², PCWP, from 28±7 to 14±2 mmHg).

Conclusions: Our system could be a powerful clinical tool in managing patients with decompensated HF.
LVESVi, increase in TAPSE and lowest RAp) (Table 1), and clinical outcomes were most favourable in these patients (Fig. 1).

**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 adjunctive 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” and “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.

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**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 tomometry 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: 1.04 to 11.72; p=0.04). Moreover, the addition of Galectin-3 resulted in significant net incremental improvement in risk assessment (net reclassification index 0.514, 95% CI 0.078–0.949, p=0.021).

**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.

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**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...
(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 hyponatremia (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 hyponatremia, 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]).

Conclusion: A MELD-XI scoring system could provide the additional long-term prognostic information to hyponatremia in AHDF pts.

P4761 | BEDSIDE
Prognostic impact of plasma phospholipid fatty acid composition and dihomo-gamma-linoleic acid level in patients with acute heart failure
T. Nagai, N. Iwakami, Y. Sugano, T. Shibata, Y. Asaumi, T. Noguchi, K. F. Kusano, H. Ogawa, S. Yasuda, T. Anzai. National Cerebral and Cardiovascular Center Hospital, Department of Cardiovascular Medicine, Suita, Osaka, Japan

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 outcomes 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) 0.9, 95% CI 0.85–0.95, P<0.0001] 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<0.01) 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) than non-obese subjects (BMI<30) but similar levels of GDF-15 (1855±5947 vs. 1792.6±139.0 ng/L, p=n.s.). In Cox univariate analysis, systolic blood pressure (SBP), LVEF, 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 (HR 1.02 per each 100 ng/L, P=0.03), SBP (0.95 per 5mmHg, P=0.04) and sodium (HR 0.90 per 1 mmol/L, P=0.008) 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.

Predictors of mortality in obese patients with systolic HF

Parameter | Hazard ratio | Lower 95% | Upper 95% | p-value
--- | --- | --- | --- | ---
BNP (100 ng/L) | 0.49 | | | 
GDF-15 (100 ng/L) | 1.04 | 1.009 | 1.062 | 0.008 
Systolic blood pressure (5 mmHg) | 0.999 | | | 
Sodium (1 mmol/L) | 0.87 | 0.79 | 0.96 | 0.007 

Conclusion: In obese HF patients, GDF-15 has a potential to replace BNP in prognostication process since it appears to be better predictor of mortality.

P4763 | 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 (EDPR gradient <24 mmHg) 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 gradient 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 (LDD) (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, LDD, LVEF, and tricuspid regurgitation pressure gradient.

Methods: To investigate the PPFA composition and its impact on clinical outcomes in patients with systolic HF (SHF). Delta-6-desaturase activity, and nutritional risk index (P<0.01) in obese BMI(>30) individuals.

Conclusions: A MELD-XI scoring system could provide the additional long-term prognostic information to hyponatremia in AHDF pts.

P4762 | BEDSIDE
Prognostic role of growth differentiation factor 15 (GDF-15) in obese patients with systolic heart failure (HF)
J. Benes1, M. Kocri1, V. Melenovsky1, J. Kautzner1, P. Jarolim2, 1 IKEM, Prague, Czech Republic; 2 Brigham and Women’s Hospital, Department of Pathology and TMI-group, Boston, United States of America

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.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hazard ratio</th>
<th>Lower 95%</th>
<th>Upper 95%</th>
<th>p-value</th>
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<tr>
<td>BNP (100 ng/L)</td>
<td>0.49</td>
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</table>
| GDF-15 (100 ng/L) | 1.04 | 1.009 | 1.062 | 0.008 
| Systolic blood pressure (5 mmHg) | 0.999 | | | 
| Sodium (1 mmol/L) | 0.87 | 0.79 | 0.96 | 0.007 |

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.
BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS II

P4764 | BEDSIDE
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 specific issues and a particular worrisome prognosis.

Aim: Define predictors of prognosis 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 transplantation (HTx) between 2004 and 2014. Clinical, laboratory and hemodynamic data were evaluated. Primary endpoints were time to all-cause death, HTx and hospitalization for HF after reference 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. Half of the pts were in NYHA class IV, with median BNP 605 (IQR 665) pg/dL and median peak VO2 15.6 (IQR 15) mL/kg/min. Hemodynamic baseline 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 3.6) 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 did not impact on the prognosis of these pts. However, after beginning of sildenafil therapy this parameter predicted the occurrence of hospitalization (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 predicted by increase in maxVO2 reduced the probability 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) systemic 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=0.04, HR: 0.9; IC 95% 0.83–0.99). 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% 0.94–0.96).

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.

P4765 | BEDSIDE
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 (HF-PEF) has been shown to be more common among the elderly population. Nevertheless, 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 HF-PEF, as defined by left ventricular ejection fraction (LVEF) ≥40%, were compared to those who were <70 years of age. 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 (63.9% vs 48.6%, p<0.009) and have hypertension (75.2% vs 56.9%, p<0.001), but less likely to have diabetes (35.5% vs 49.5%, p<0.01). At a mean follow-up of 35.8±30.2 months, 175 (38.0%) of those who were >70 years old and 44 (40.4%) of those who were <70 years old died, of whom 12 (24.3%) and 20 (18.3%) of them died of cardiovascular cause, respectively (log rank test p=0.06). Multivariate model showed that age (HR 1.88 per decade, 95% CI 1.45–2.43, p≤0.006), LVEF ≤50% (HR 2.11, 95% CI 1.24–3.59, p≤0.006), systolic blood pressure on admission (HR 0.992, 95% CI 0.986–0.999, p=0.02) and diastolic anticoagulant (HR 5.79, 95% CI 2.09–16.03, p=0.001) independently predicted cardiovascular mortality among those who were ≥70 years old, while only smoking history (HR 3.34, 95% CI 1.39–8.03, p<0.007) was found to be predictive of cardiovascular mortality among those who were <70 years old.

Conclusion: Elderly patients >70 years of age who had HFPEEF showed similar survival to but different predictors for cardiovascular mortality than their younger counterparts, reflecting potentially different contributing factors to cardiovascular mortality between the two groups of patients. Development of risk model that assesses clinical risk factors and effect of treatment specific for this group of patients can improve their management.

P4766 | BEDSIDE
Regression of sokolow-lyon voltage is associated with higher incidence of cardiac events in patients with chronic heart failure
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Background: Left ventricular hypertrophy (LVH) predicts a new onset of heart failure in hypertensive patients. Sokolow-Lyon (SL) voltage is an easily measured electrocardiographic parameter for assessing LVH. However, the impact of SL voltage for the prognosis in chronic heart failure (CHF) due to LVH remains to be determined.

Methods and results: We performed standard 12-lead electrocardiography and calculated SL voltage in consecutive 330 CHF patients with echocardiographic LVH. SL voltage was positively correlated with left ventricular mass index (LVMi) (R=0.37, p<0.0001). However, SL voltage was significantly decreased with advancing New York Heart Association functional class. During median follow-up period of 467 days, there were 100 major adverse cardiac events (MACE). Multivariate Cox proportional hazard analysis showed that SL voltage was an independent predictor of cardiac events (Hazard ratio [HR]: 0.82, 95% confidence interval [CI]: 0.70–0.96, p=0.01). Moreover, patients were divided into two groups according LV geometry defined as follows: concentric hypertrophy (high relative wall thickness [RWT]); and eccentric hypertrophy (low RWT). Multivariate Cox proportional hazard analysis demonstrated that SL voltage was an independent predictor of cardiac events in patients with eccentric hypertrophy (HR: 0.79, 95% CI: 0.62–0.98, p=0.03). In contrast, there was no association between SL voltage and MACEs in patients with concentric hypertrophy.

Conclusion: Sokolow-Lyon voltage can be used to predict MACEs in CHF with LVH, in particular LV eccentric hypertrophy.

P4767 | BEDSIDE
Soluble ST2 predicts cardiovascular events, infectious and all-cause mortality in diabetic hemodialysis patients
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Background: Soluble suppression of tumorigenesis 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 diabetic hemodialysis patients who participated in the German Diabetes and Dialysis Study (4D Study). Hazard ratios (HR) for pre-specified, adjudicated endpoints sudden cardiac death; death due to heart failure; myocardial infarction (fatal and non-fatal); stroke (fatal and non-fatal); combined cardiovascular events (CV death; stroke, myocardial infarction); and death due to infections; and all cause mortality were 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

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(HR: 3.34 (95% CI: 1.15–9.75)) and a doubling of all-cause mortality risk (HR: 2.01 (95% CI: 1.61–2.61)). Similar results were observed for combined CV events (HR: 1.65 (95% CI: 1.23 to 2.19)) and stroke (HR: 1.92 (95% CI: 1.17 to 3.14)) but myocardial infarction risk was not meaningfully affected. Besides CV end points, high sST2 concentrations were associated with a two fold increase in death due to infections (HR: 2.01 (95% CI: 1.2 to 3.37)).

Conclusions: In this cohort of diabetic hemodialysis patients, high concentra-
tions of sST2 were a strong predictor of fatal and non-fatal CV events, death due to infections and all-cause mortality.

Acknowledgement/Funding: Presage ST2 assays were provided by Critical Di-
agnostics.

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 car-
diogenic 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-
Ab ≤ 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-Ab more often pre-
pared with pulmonary oedema on chest X-ray. Low P-Ab was associated with
higher 90-day mortality (48.1% vs. 23.3%, p<0.004). A stepwise increase in 90-
day mortality was observed with lower albumin levels: 23.3% for P-Ab ≤ 34 g/l,
41.6% for P-Ab ≤ 27–34 g/l and 57.1% for P-Ab ≤ 27 g/l (pairwise comparisons
between all groups log rank p<0.05) (Figure 1). Low P-Ab remained predictive of
higher 90-day mortality also in multivariate 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: A low albumin (≤34g/l) at presentation is independently associ-
ated with a worse clinical profile and poor outcome in cardiogenic shock patients
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.

P4769 | BEDSIDE
Is the combination BNP- Six-minute walking test a simple and reliable strategy to define prognosis of patients with chronic heart failure? A.B. Scardovi1, S. Ghio2, P.L. Temporelli3, P. Faggiano4, A. Rossi5, A. Spirito6, W.S. Choe, H.J. Cho, H.Y. Lee, S.E. Lee, B.H. Oh on behalf of KorAHF investigator. Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea

Purpose: The aim of the study is to investigate the differences in short-term out-
comes and predictors of in-hospital mortality between HFrEF and HFrEF 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 ten regionally-representative tertiary university hospitals in Ko-
rea. Clinical characteristics, all cause in-hospital mortality and predictors of mor-
tality were compared between patients with HFrEF (LVEF<50%) and HFrEF (LVEF≥40%). Patients with borderline LVEF (40–50%) were excluded from the analysis because of heterogeneity due to the presence of other causes of heart failure.

Results: 5,627 patients had been consecutively enrolled between March 2011 and
March 2014. 24% of these patients had HFrEF and 57% had HFrEF. The me-
adian age of patients tend to be older in HFrEF than in HFrEF (72 vs 67 years). A
larger proportion of patients were female in HFrEF (81% vs 39%). Valvular heart
disease was the most common cause of heart failure in HFrEF (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
HFrEF. The prevalence of diabetes (17% vs 27%), chronic kidney disease (13% vs
23%), history of myocardial infarction (31% vs 43%) and history of coronary artery bypass graft (17% vs 37%) was higher in HFrEF.

Conclusions: In-hospital mortality in unselected AHF pts remains high. Short
term mortality can be predicted by easily available variables. Referral to heart failure centre should be considered in pts with predictors of higher in-hospital mortality for advanced treatment options assessment.
HAEMODYNAMICS AND AUTONOMIC NERVOUS SYSTEMS IN HYPERTENSION

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), 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), MSI and MI size were determined by T2-weighted and late gadolinium enhanced CMR.

Results: AAR, MI size normalized by LV mass was 36±14% and 27±15%, respectively (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 index (LVMi) and peak CPK level (r=-0.38, -0.40, -0.46, respectively, all P<0.05). The presence of hypertension was a significant predictor of lower MI (p coefficient=-0.34, p<0.05).

Conclusion: The current results demonstrated that myocardial salvage was attenuated in hypertensive patients with acute MI and inversely related with LVMi. 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 myocardial 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 ejection fraction and 15 controls (NT, 43±3yrs, 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 with two MOLLI acquisitions (3–5), before and 15 min after administration of gadolinium (0.1 mmol/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 partition coefficient (GPC) and extracellular volume fraction (ECV), a measure of disease state in the group whose MoCA scores improved compared to those in the non-improved group (Table 1). Noting these worsened clinical indicators in the group with improved MoCA, a multivariate logistic model was tested using these variables. Pre-operative serum sodium levels and history of A. Fib. were found to be independent predictors for improvement in MoCA score after LVAD implantation (OR: 0.84 CI: 0.71–0.99 p<0.02, OR: 0.28 CI: 0.08–1.02 p=0.05, respectively).

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 impact quality of life, functional capacity, and survival. Though the effects of hemodynamic support on cognitive function (CF) remain poorly investigated, a recent study indicated improvement following left ventricular assist device (LVAD) implantation. We investigated pre-operative predictors of improvement in CF following LVAD implantation.

Methods: We used the MoCA (Montreal Cognitive Assessment) to determine if patients prior to and 8 months after LVAD implantation improved in cognitive function. The Montreal Cognitive Assessment (MoCA) was used to evaluate CF in 56 patients following LVAD implantation. When the cohort was subdivided based on change in MoCA score, 20 (35.7%) patients did not improve postoperatively (22.8 vs 25.0, p=0.049). Mean pulmonary artery pressure, serum sodium, albumin, B-type natriuretic peptide (BNP), and incidence of atrial fibrillation (A. Fib.) indicated a trend towards a more advanced disease state in the group whose MoCA scores improved compared to those in the non-improved group (Table 1). Noting these worsened clinical indicators in the group with improved MoCA, a multivariate logistic model was tested using these variables. Pre-operative serum sodium levels and history of A. Fib. were found to be independent predictors for improvement in MoCA score after LVAD implantation (OR: 0.84 CI: 0.71–0.99 p<0.02, OR: 0.28 CI: 0.08–1.02 p=0.05, respectively).

Table 1

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<th>Pre-Implant MoCA</th>
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<td>Pre-Implant MoCA</td>
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</tr>
<tr>
<td>Age (years)</td>
<td>65.05±12.03</td>
<td>56.76±14.05</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.66±16.78</td>
<td>27.67±8.56</td>
</tr>
<tr>
<td>Mean pulm. artery pressure (mmHg)</td>
<td>29.9±10.44</td>
<td>37.95±10.74</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>135.7±3.52</td>
<td>133.21±4.57</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.26±0.50</td>
<td>2.93±0.47</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>35.5±21.32</td>
<td>85.4±162.23</td>
</tr>
</tbody>
</table>

Conclusion: Compared with HFrEF, HFpEF showed better in-hospital outcome and different predictors of mortality.
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 rate (GRSR) with ECV (all p < 0.05).

Conclusion: 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. This finding may have implications for early diagnosis of target organ damage in hypertensive patients.

P4776 | 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. A new cuff-based method (Vicorder [V]) shows promise, but large comparative studies are lacking, especially in the elderly where arterial stiffening is most prevalent.

Purpose: To assess the ability of S and V to obtain pulse wave velocity (PWV) measurements and compare data from both devices.

Methods: We studied 1720 men in the British Regional Heart Study. Carotid (C) to femoral (F) PWV measurements were derived from path length (PL)/transit time (TT) for both devices. For S, PL was calculated as distance from: (sternal notch [SN] to F) minus (SN to C). For V, PL was distance from SN to centre of thigh cuff. TT with S (TTs) was calculated as time from: (ECG R wave to F pulse wave onset) minus (ECG R wave to C pulse wave onset). TTv– was measured between the onsets of the C and F pulse waves in the same cardiac cycle.

Results: Acceptable PWV data were obtained with S (PWVs) in 1180 men (69%) and 1577 (92%) with V (PWVv). In 1122 men with both PWVs and PWVv, mean PWVs was > PWVv (10.3±2.6 m/s vs 10.0±1.7 m/s; p < 0.001) and values were positively correlated (r=0.519, P < 0.001). However, S tended to give faster readings than V at higher PWV and slower readings at lower PWV. The slope of the regression line for F TTs vs TTv was steeper than for C TTs vs TTv for both devices. For S, PL was calculated as distance from: (sternal notch [SN] to F) minus (SN to C). For V, PL was distance from SN to centre of thigh cuff. TT with S (TTs) was calculated as time from: (ECG R wave to F pulse wave onset) minus (ECG R wave to C pulse wave onset). TTv– was measured between the onsets of the C and F pulse waves in the same cardiac cycle.

Conclusions: PWVv can be measured in a greater proportion of elderly men than PWVs. S gives higher values than V at faster PWV and V higher values than S at slower PWV. The subtraction of a progressively greater proportion of carotid from femoral TT when deriving PWVs as TT shortens, (increasing PWV), could account, at least in part, for the tendency for PWVs to exceed PWVv as the aorta stiffens and vice versa.

Acknowledgement/Funding: British Heart Foundation

P4777 | BEDSIDE
An increase in peak excess pressure accounts for the rise in systolic blood pressure along the aorta
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Purpose: The mechanisms driving aortic pressure propagation remain incompletely defined. The reservoir-wave approach may more accurately model central aortic pressure generation however its application at differing aortic locations remains unknown.

Methods: We analysed invasively acquired aortic pressure waveforms from 40 patients undergoing clinically indicated catheterisation. Waveforms were acquired at the level of the ascending aorta, transverse aortic arch, diaphragm, renal arteries and aortic bifurcation using a solid-state transducer. Reservoir-wave analysis was performed to determine reservoir wave pressures and associated parameters. Repeated measures 1-way-ANOVA with Dunnett’s test for multiple comparisons was used to compare parameters at the 5 aortic sites.

Results: Systolic blood pressure generation increases along the 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.

Conclusions: The relationship between right ventricular (RV) mechanics in hypertensive patients with different geometric patterns by increasing from the ascending aorta to the bifurcation. The P4777 | BEDSIDE

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 reservoir (mmHg s)</th>
<th>Excess pressure integral (mmHg s)</th>
<th>Peak excess reservoir pressure (mmHg)</th>
<th>Peak reservoir pressure time (ms)</th>
<th>kS (ms)</th>
<th>kD (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>131.6±27.4</td>
<td>65.5±11.5</td>
<td>20.6±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>
<td>2.6±0.8</td>
</tr>
<tr>
<td>Carotid arch</td>
<td>120.5±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>57.5±7.8</td>
<td>13.9±3.8</td>
<td>2.6±0.8</td>
<td>2.6±0.8</td>
</tr>
<tr>
<td>Daphnog</td>
<td>140.4±23.7</td>
<td>65.4±18.7</td>
<td>19.7±6.3</td>
<td>48.9±16.3</td>
<td>7.0±2.8</td>
<td>33.2±8.8</td>
<td>56.6±4.8</td>
<td>12.1±2.3</td>
<td>2.8±0.7</td>
<td>2.8±0.7</td>
</tr>
<tr>
<td>Renal arteries</td>
<td>138.7±23.2</td>
<td>67.2±9.7</td>
<td>18.5±5.7</td>
<td>46.9±12.2</td>
<td>7.6±2.7</td>
<td>37.0±7.8</td>
<td>54.5±6.2</td>
<td>10.4±1.5</td>
<td>2.9±0.7</td>
<td>2.9±0.7</td>
</tr>
<tr>
<td>Bilfuration</td>
<td>141.3±24.8</td>
<td>67.6±8.6</td>
<td>18.3±5.7</td>
<td>46.9±12.3</td>
<td>8.2±2.8</td>
<td>40.3±9.5</td>
<td>54.6±2.8</td>
<td>9.7±1.4</td>
<td>3.0±0.7</td>
<td>3.0±0.7</td>
</tr>
</tbody>
</table>

kS, systolic rate constant; kD, diastolic rate constant. *P < 0.01; †P < 0.001.

Conclusions: The relationship between right ventricular (RV) mechanics in hypertensive patients with different geometric patterns by increasing from the ascending aorta to the bifurcation. The P4777 | BEDSIDE

Right ventricular mechanics

<table>
<thead>
<tr>
<th>Normal LV geometry remodeling</th>
<th>Concentric LV non-dilated LVH</th>
<th>Eccentric LV dilated LVH</th>
<th>Concentric LVH for trend</th>
<th>Dilated LVH for trend</th>
<th>p value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longitudinal RV strain rate (s⁻¹)</td>
<td>2.3±0.3</td>
<td>2.2±0.4</td>
<td>2.1±0.3</td>
<td>2.0±0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>RV systolic strain rate (s⁻¹)</td>
<td>1.5±0.3</td>
<td>1.5±0.3</td>
<td>1.4±0.4</td>
<td>1.2±0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>RV early diastolic strain rate (s⁻¹)</td>
<td>1.8±0.4</td>
<td>1.7±0.4</td>
<td>1.6±0.3</td>
<td>1.4±0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>RV late diastolic strain rate (s⁻¹)</td>
<td>1.6±0.4</td>
<td>1.6±0.4</td>
<td>1.8±0.6</td>
<td>1.5±0.5</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Dv, left ventricle; LVH, left ventricular hypertrophy; RV, right ventricle.
toxic 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 normal LV geometry patients. 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 straintracking echocardiography assessment 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 compensative mechanism of LV against pressure overload to reduce LV stress and maintain systolic performance. LV endocardial function may be more deteriorated by pressure overload than LV epicardial function. Therefore, we examined the relationship between LV systolic stress and strain in HTN using one-beat real-time 3D-STE with high volume rates and sought to evaluate the impact of LV systolic stress on contractility in HTN.

Methods: A total of 168 subjects (114 patients with HTN and 54 controls (age 69±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 patients with hypertensive heart failure (HHF) (age 71±11). We examined LV longitudinal, circumferential and radial strain peak at endocardium and 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.

Results: LV strain in 3 directions and SR at endocardium were reduced in HTN and further reduced in HHF (longitudinal strain: control = 19±3, HTN without LVH = 17±4, HTN with LVH = 15±4, HHF = 13±3, *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 radial SR during systole at both endocardium and epicardium in total subjects (r=0.28, p=0.001 and r=0.20, p=0.010). There was a significant correlation between LV systolic stress and circumferential strain in HHF (r=0.48, P=0.018), but no relation between stress and longitudinal or radial strain. Significant correlation was not found between LV stress and LV strains in 3 directions in controls or HTN.

Conclusion: LV contractility assessed by LV strain and SR was reduced associated with increased LV stress. Only LV circumferential strain was reduced in HHF 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.

P4780 | BEDSIDE
Myocardial fibrosis correlated with sub-endocardial but not global circumferential strain in hypertension
W.-C. Tsai, L.-T. Yang, W.-H. Lee. National Cheng Kung University Hospital, Tainan, Taiwan ROC

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 two-dimensional speckletracking echocardiography. Myocardial fibrosis was categorized into sub-endocardial, sub-epicardial and transmural sub-endocardial. The two-dimensional speckletracking echocardiography allows a semi-automated determination of myocardial mass. Longitudinal and circumferential strain were calculated from 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 sub-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 mainly in sub-endocardial 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 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 Fe (HTFE+; age 46.9±2.6 yrs, mean±SEM), we measured, along with Fe levels and transferrin saturation, clinic blood pressure (BP), heart rate (HR, EKG), muscle sympathetic nerve traffic (MSNA), HOMA index and glucose. Data were compared to those from 7 untreated male essential hypertensives with normal Fe levels (HTFE-) age matched with HTFE+.

Results: For both HTFE+, HTFE− displayed FE values significantly greater than those seen in HTFE: (44.3±10 vs 13.5±4.9 μg/dl, p<0.05). This was the case also for transferrin saturation (38.9±24 vs 24.2±9.9%). In HTFE+ the increased iron load was accompanied by HOMA index values significantly greater than in HTFE− (2.1±0.4 vs 1.2±0.2 au, p<0.05). This was accompanied by significantly greater values of MSNA, both when expressed as bursts frequency over time (46.3±4 vs 39.7±3.5, *p<0.05) and when corrected for HR (66.4±5.0 vs 61.7±4.1, *p<0.05). In the group as a whole there was a significant relationship between MSNA and FE (r=0.64, 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 HRR and ongoing and incidental hypertension as well as the association of HRR 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=35 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.

In a survival analysis by Cox proportional model of the whole cohort, the HRR was an independent predictor of survival (HR 0.97; CI 0.96–0.98; p<0.01) 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 Läkaresällskapet
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 dipper. 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 routine treadmill Ex-test (Bruce protocol, symptom-limited) were examined and 15 OH (a fall in systolic blood pressure [sBP] at least 15 mmHg; 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 clinical features (body mass index [BMI; kg/m²], low-density lipoprotein cholesterol [LDL-C; mg/dl]) and ultrasound echocardiogram-guided left ventricular diastolic dimension [LVDd:mm] and ejection fraction [LVEF;%]) were compared between OH and control groups. Based on the resting rate, a ratio of HR in each Ex-period was estimated as “Ex/rest”, “peak-Ex/rest” and “recovery (Rec)/rest”, respectively. The degree of a BP fall (ΔsBP) in OH was 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 components [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: 2.±0.4 to 2.±0.4 nM, P<0.05; 900 mM: 1.±0.3 to 5.±1.1 nM, P<0.01). (3) Ouabain significantly increased dialysate ACh concentration (1.2±0.2 to 2.±0.3 nM, P<0.01). (4) Benzamil significantly decreased dialysate ACh concentrations in both baseline and high sodium (900 mM) conditions (ouabain, 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 chemotactic protein 1 (MCP1) levels
H. Lopes1, R.F. Dominguez2, J.G. Santos1, V. Costa-Hong1, L.A. Bortolotto1, F. Consolim-Colombo3, 1 Heart Institute (InCor) - University of Sao Paulo Faculty of Medicine Clinics Hospital (HC-FMUSP), Sao Paulo, Brazil; 2 Nove de Julho University, Medicina, Sao Paulo, Brazil

Introduction: The monocyte chemotactic protein 1 (MCP1) is important in vessels 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 caucasians and 20 non caucasians]. Anthropometric data (weight, height, body mass index, abdominal circumference) and blood pressure, heart rate, heart rate variability, biochemistry data, including norepinephrine and adipocytokines were evaluated.

Results: An association between MCP1 and abdominal circumference (r=0.294, p=0.011), homocysteine index (r=0.323, p=0.005), LDL-cholesterol (r=0.312, p=0.007), norepinephrine (r=0.248, p=0.032), leptin (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 tumor necrosis factor alpha-TNFα (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, adiponectin, retinil, and retinal binding protein 4 (RBP4). In a multiple linear regression stepwise diastolic blood pressure, LF/HF ratio, LDL-cholesterol, PAI1, 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 norepinephrine, IL6, TNFa, and PAI1 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.

Conclusion: Subjects with metabolic syndrome MCP1 is associated with higher blood pressure, LDL-cholesterol, adipocytokines levels, and higher sympathetic activity evaluated by norepinephrine and spectral analysis.