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Abstracts

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Featured Poster Session 1

FP 1-1

Novel regulators of cardiomyocyte proliferation and regeneration in mouse and human

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Background: The adult mammalian heart has little regenerative capacity after myocardial infarction (MI) while neonatal mouse hearts regenerate without scarring or dysfunction. However, the underlying pathways and responsible coding and non-coding transcripts are poorly defined.

Objective: We sought to derive insights into the pathways regulating neonatal development of the mouse heart and cardiac regeneration post-MI.

Methods and Results: Performing RNA-seq on neonatal mouse hearts through the first 10 days of postnatal life revealed changes in the coding and non-coding transcriptome after neonatal MI, with evidence of essentially complete healing by P10. Over two thirds of each of the mRNAs and microRNAs that were differentially expressed in the post-MI heart were also differentially expressed during normal postnatal development, suggesting a common regulatory pathway for normal cardiac development and post-MI cardiac regeneration.

We selected exemplars of miRNAs that were implicated in our data set as regulators of cardiomyocyte proliferation. Several of these showed evidence of a functional influence on mouse cardiomyocyte cell division. In addition, a subset of these microRNAs, miR-144-3p, miR-195a-5p, miR-451a and miR-6240 showed evidence of functional conservation in human cardiomyocytes.

Promising targets of the coding transcriptome were validated in neonatal mice in-vivo using a rAAV9 mediated knock-down system. Candidates like Igf1r, Myl9, Lamc2 and Spp1 were confirmed as potentially important players in the process of neonatal cardiac regeneration.

Conclusions: The sets of mRNAs and miRNAs that we report here merit further investigation as gatekeepers of cell division in the postnatal heart and as targets for extension of the period of cardiac regeneration beyond the neonatal period. Results of rAAV9 mediated knock-down experiments furthermore strengthen the validity and relevance of our screening results in the process of neonatal cardiac regeneration.

FP 1-2

Repeated remote ischemic conditioning preserves systolic left ventricle function and increases NRG-1 expression following myocardial infarction in rats

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Background: Adverse left ventricle (LV) remodelling following myocardial infarction (MI) plays a key role in the progression of congestive heart failure (HF). Recombinant human Neuregulin-1 (rhNRG-1) has been demonstrated to have both anti-fibrotic and anti-inflammatory effects. Chronic administration of rhNRG-1 markedly improved LV ejection fraction (LVEF) and coronary microcirculation in patients with HF. Repeated remote ischemic conditioning (RIC) is considered as a potential clinically approach to improve cardiac function following MI, however the mechanisms are not fully elicited.

Purpose: The aim of the present study was to (1) clarify the effects of a brief period of RIC on LV hemodynamic function and coronary flow (CF) and (2) to assess the expression of NRG-1, ErbB2/3/4 expression following MI.

Methods: Male Sprague-Dawley rats were subjected to permanent left coronary artery (LCA) occlusion and allocated to three groups: (1) MI ($n=13$), (2) MI+RIC ($n=10$) and (3) control group (Sham, $n=6$; without LCA occlusion and without RIC). Repeated RIC was started at the 3rd day after MI once a day for 5 days by 3 cycles of 5 min of unilateral hindlimb ischemia and 5 min of reperfusion. Cardiac functional parameters were assessed by transthoracic echocardiography at baseline and at days 3 and 8 following MI. Coronary flow (CF) and LV systolic pressure (LVSP) were evaluated on an isolated erythrocyte-perfused working heart model at day 8 following MI. The alterations in CF primarily reflect alterations in coronary resistance, allowing evaluation of microvasculature function in this experimental setup. The expression of plasma level of NRG-1 was measured by ELISA and mRNA expression of ErbB2/3/4 was accessed by RT-qPCR.

Results: Short term duration (5 days) of RIC enhanced LVEF as compared to MI group (63 ± 1% vs. 58 ± 2% on day of 8th following the induction of MI, $p=0.074$). This was accompanied by preserved LV systolic function in rats with RIC as compared with MI (LVESD: 5.9 ± 0.06 mm and 6.4 ± 0.2 mm, $p=0.064$). Results were obtained from the isolated working heart system showed that CF and LVSP were markedly enhanced in rats with RIC as compared to MI (CF: 4.3 ± 0.2 vs 3.1 ± 0.2 ml/g heart weight and LVSP: 109 ± 2 mm Hg vs 119 ± 4; mm Hg; $p<0.01$, respectively). Both plasma and tissue expressions of NRG-1 were significantly elevated by RIC in comparison to MI group (plasma: 10.6 ± 1.7 µg/ml vs 19.4 ± 3.3 µg/ml and LV tissue: 0.53 ± 0.09 vs. 3.16 ± 0.9 1/18S; $p<0.05$). Similarly, the mRNA expression of ErbB2/3/4 showed at least partly significant differences between the groups (ErbB2: 1.0 ± 0.2 vs. 2.08 ± 0.4 1/18S, $p<0.05$; ErbB3: 1.07 ± 0.3 vs. 2.4 ± 0.4 1/18S, $p<0.05$; ErbB4: 0.46 ± 0.12 vs. 0.64 ± 0.23 1/18S; n.s.) in LV tissue samples, taken from the infarcted zone.

Conclusions: RIC preserves systolic LV function and markedly enhances basal CF following MI in rats. These results were accompanied by with a marked increase in NRG-1 levels in plasma and myocardial tissue samples indicating enhanced cardioprotection. Therefore, repeated remote RIC is a potential therapeutic approach for improved post-MI remodelling.

FP 1-3

Fibrocytes accumulate at the culprit lesion site in STEMI and are activated by neutrophil extracellular traps

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Background: Inflammation is important in the pathogenesis of ST-elevation myocardial infarction (STEMI).

Neutrophil extracellular traps (NETs) are enriched at the culprit lesion site (CLS) of patients.

Fibrocytes, mesenchymal progenitor cells with both leukocyte and fibroblast properties,

accumulate in cardiac tissue of a murine ischemia/reperfusion model and contribute to tissue repair and Collagen-I deposition. In advanced atherosclerotic plaques, expression of bone morphogenic protein receptor II (BMPRII) is lost. We studied fibrocyte frequencies and their phenotype at the CLS of STEMI patients.

Methods: We drew blood samples from the CLS and femoral site during primary percutaneous coronary intervention from STEMI patients ($n=50$, male = 78%, mean age = 61 ± 13y) and 72 h after STEMI ($n=21$). Healthy controls were recruited as comparators ($n=21$). Fibrocytes were characterized using flow cytometry. Double-stranded (ds) DNA and citrullinated histone H3 (citH3), surrogate markers of NETosis, were measured in plasma. To assess the influence of NETs on their activation, fibrocytes were stimulated in vitro with isolated NETs. Enzymatic infarct size of STEMI patients was assessed using the creatine kinase-isoform MB area under the curve (CK-MB AUC). Left ventricular function at long-term follow-up (LT-FU, $n=23$, 24 ± 8 months) was assessed using Wall Motion Score Index (WMSI).

Results: Fibrocytes were increased two-fold at the CLS and were highly activated compared to femoral blood. No differences were found in BMPRII expression between CLS and femoral blood. dsDNA and citH3 were highly increased at the CLS, and correlated positively with the expression of CD34 on fibrocytes. In vitro treatment of fibrocytes with NETs induced an increase of Collagen-I, BMPRII, CD34 and IL-6. DNase 1, which degrades NETs, failed to abolish this effect. NET burden at the CLS was positively correlated with enzymatic infarct size, BMPRII expression of fibrocytes and WMSI at LT-FU. Furthermore, BMPRII and CD11b expression of fibrocytes were positively correlated with WMSI.

Conclusions: We report the accumulation of fibrocytes at the CLS and STEMI. Furthermore, our data suggest a functional link between NETs and fibrocytes, leading to their activation. NETs might thereby promote pro-fibrotic functions of fibrocytes after STEMI and thus contribute to adverse remodeling.

FP 1-4

Optimized density gradient protocol for the purification of plasma exosomes for proteomic analysis

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Background: Exosomes are 30–150 nm sized extracellular vesicles produced by all living cells which carry out a myriad of important functions in cell biology. Research into exosomes as biomarkers of cardiovascular disease has been rapidly increasing in recent years, yet there is no gold-standard for isolation and purification. Simple ultracentrifugation results in co-isolation of plasma proteins and other microvesicles, which is especially problematic in proteomic analyses. A widely used method for further purification of exosome samples is the use of an isopycnic density gradient run in an ultracentrifuge. Sucrose and Iodixanol are most often used, with Iodixanol being more biologically inert than highly osmotic sucrose. The mixing of a density gradient is time-intensive, and the results can be highly operator dependent. Here we have investigated if a simple freeze-layering technique applicable to sucrose gradients can be used to reliably produce a continuous iodixanol gradient that can be prepared and stored in advance, for reliable plasma exosome purification.

Methods: For these experiments, we used healthy pig plasma exosomes, previously isolated via ultracentrifugation and suspended in PBS. The iodixanol gradient is generated by diluting a stock solution of OptiPrep™ (60% (w/v)) with 0.25 M sucrose, 10 mM Tris–HCl, +20 µl HCl 37.2%, pH 7.5 (40% (w/v), 20% (w/v), 10% (w/v) and 5% (w/v) solutions of iodixanol). For our freeze layering method, the gradient was formed by adding 3 ml of 40% iodixanol solution in an ultracentrifugation tube (12 ml, Polypropylene Centrifuge Tubes, Beckman Coulter), freezing at –80 °C, followed by layering of 3 ml each of 20% and 10% solutions, and 1 ml of the 5% solution, each with a freezing step in between. The freeze-layered gradients were thawed overnight at 4 °C, then used for purification of plasma exosomes. As a control, we used the traditional method of carefully layering the different density solutions on top of each other in liquid phase, creating a discontinuous gradient, which was then immediately used. We used a Sorvall WX Ultra-Centrifuge, a TH-641 rotor at 24,200 rpm (100,000 g) for 18 h. The fractions of the DGs were then carefully collected in 1 ml fractions from the top. The density of each fraction was measured by comparing them to a standard curve of absorption at 340 nm at a 1:4 dilution of 5%, 10%, 20%, 30%, 40% iodixanol. To recover exosomes the fractions were diluted 1:10 in PBS and centrifuged at 120.000 g for 3 hours. The exosomes were then resuspended in 100 µl PBS and a TSG101 Western Blot was performed to visualize the exosome containing fractions.

Results: Density curves measured in 1 ml fractions are shown in Fig. 1 with fraction 1 being at the top of the tube. Fig. 2 shows the TSG101 Western Blot for fractions 7, 8 and 9 which were most enriched with exosomes, with a density between 1.17–1.19 g/ml.

Conclusions: Freeze-layering resulted in a highly consistent continuous density distribution across multiple tubes and operators. Freeze-layering increases ease of use, reproducibility and flexibility in performing density gradient centrifugation,

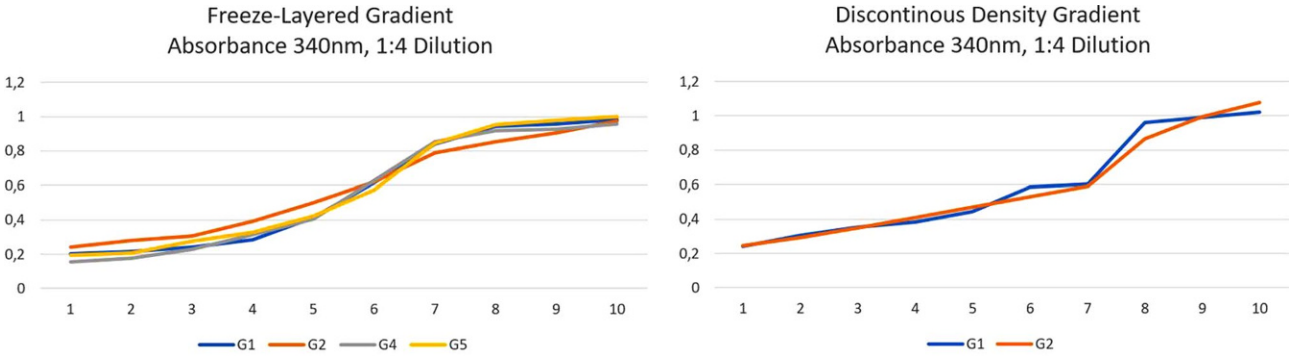

Fig. 1|FP 1-4 Density of fractions measured via Absorbance at 340 nm at 1:4 dilution for freeze-layered and discontinuous gradients

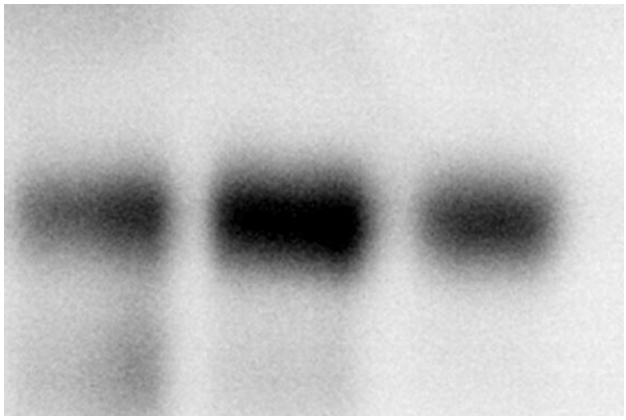

Fig. 2|FP 1-4 TSG101 Western slot of fractions 7, 8, 9

while having no negative effect on the purification of exosomes. We think that this simple protocol will increase access and use of density gradient centrifugation in the investigation of exosomes.

FP 1-5

Ventricular fibrillation during myocardial infarction is associated with increased infarct size—a large scale porcine MRI study

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Background: Primary ventricular fibrillation (VF) is an infrequent, but serious complication in acute myocardial infarction. Even tough VF influences survival of acute myocardial infarction, only little is known about the impact of VF on cardiac function post-MI, measured by cardiac magnetic resonance imaging parameters (cMRI). In this study we analysed the effect of VF or infarct-related other complications on infarct size and LV functional parameter.s

Methods: A total of 166 female pigs underwent acute myocardial infarction induced by percutaneous balloon occlusion of the mid left anterior descending coronary artery for 90 minutes. cMRI was performed on three days and two months post myocardial infarction. Infarction size and left ventricular parameters (left ventricular end systolic volume—LVESV, left ventricular end diastolic volume—LVEDV, left ventricular ejection fraction—LVEF) were assessed. Complications during balloon occlusion and therapeutic interventions were recorded.

Results: In total in 44.6% of all pigs experienced ischemia-related life-threatening complications, such as VF, which could either be terminated by administrating anti-arrhythmic medication or required defibrillation, and/or cardiopulmonary reanimation. VF occurred in 30% of all pigs, mean 27 ± 21 minutes after start of balloon occlusion. Pigs survived the infarction with/without VF were included in the present cMRI analysis. In all animals 3 d LVEF was depressed (39.62 ± 6.09%) and did not change during the 2 months follow up (42.32 ± 4.75%).

Three-day LVEF was significantly decreased in pigs with complication as compared to the other animals (39.12 ± 5.45 vs. 41.21 ± 6.36%, $p = 0.036$). Similarly, infarct size was significantly increased (30.58 ± 12.30 vs. 25.57 ± 7.96%, $p = 0.005$) in pigs with complications. Two months after myocardial infarction onset, LVEF was slightly decreased in pigs with complications (41.56 ± 4.84 vs. 43.24 ± 4.58%, $p = 0.082$) but infarct size remained significantly increased (23.70 ± 6.44 vs. 19.22 ± 7.18%, $p = 0.012$).

For the parameters LVESV and LVEDV, as signs of adverse remodelling, no differences in pigs with or without complications were observed.

Conclusions: This is the first study to demonstrate a clear association between myocardial ischemia-induced life-threatening rhythm complication and worse outcome in terms of reduced LV function and increased infarct size.

FP 1-6

Dysregulated BMPR/TGF-beta impact fibrotic vascular remodeling during thrombosis

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Background: Excessive transforming growth factor (TGF)-β and reduced bone morphogenetic protein receptor (BMPR) signaling have been implicated as key underlying derangements

of pulmonary arterial hypertension (PAH). Fibrotic vascular occlusion is a feature of PAH, but also of chronic thromboembolic pulmonary hypertension (CTEPH). Therefore, we aimed to study the role of BMPR and TGF-β in chronic thrombosis.

Methods: Transgenic mice (BMPR2+/R899X and TBRIIΔk) and wild type controls were subjected to subtotal inferior vena cava (IVC) ligation. Thrombus was harvested on days 3, 7, 14 and 21, and histological and molecular analysis were performed. RNA-seq was employed to study the transcriptome of fibroblasts isolated from pairs of pulmonary artery adventitia and thrombus excised during pulmonary endarterectomy (PEA).

Results: Mice deficient in BMPR2 (BMPR2+/R899X) demonstrated significant increases of thrombus cross sectional area and volume at early time points (days 1, 3 and 7). Compared with wild type controls, transgenic mice also had more fibrin and collagen in their thrombi. In TGF-β overexpressing mice (TBRIIΔk), thrombus burden was significantly greater on days 7, 14 and 21. RNA-seq analysis revealed significant ($P<0.05$) fold differences in 39 genes, with substantial increase of MMP-9 in thrombus fibroblasts. Majority of upregulated genes concerned TGF-β signaling (SMOC1, FERMT3) and endothelial to mesenchymal transition (MMP-9).

Conclusions: Similar to PAH, the TGF-β pathway genes are important for pulmonary vascular remodeling in CTEPH. Our results indicate that BMPR2 deficiency seems to impact early thrombosis, while TGF-β overexpression plays a role in thrombus non-resolution.

FP 1-7

Endothelial cell-specific deletion of vascular endothelial growth factor receptor 2/kinase insert domain protein receptor and proliferative pulmonary vasculopathy

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Background: Pulmonary arterial hypertension is a severe and progressive disease characterized by a negative pulmonary vascular remodeling process with total vessel occlusion and monoclonal expansion of collateral endothelial cells. Endothelial cells are the building blocks of vascular networks that enable oxygen and nutrient delivery throughout a tissue but also serve as a rich resource of factors which maintain endothelial cell integrity in an autocrine fashion. Vascular endothelial growth factor (VEGF) and its tyrosine kinase receptor, VEGF receptor-2, play a central role in angiogenesis, endothelial cell protection, but also in the destabilization of endothelial barrier function. Therefore, we investigated the role of VEGF receptor in the development of pulmonary vasculopathy in human and experimental pulmonary hypertension.

Methods and Results: We performed an endothelial cell-specific conditional deletion of vascular endothelial growth factor receptor 2/kinase insert domain protein receptor in C57BL6 mice (KdrΔend) and held them in an environmental chamber with FiO2 of 10% or under normoxia for 2, 4, and 6 weeks. We found significantly elevated right ventricular pressures and increased Fulton indices, but no change in systemic blood pressure in KdrΔend mice after normoxic and hypoxic exposure. KdrΔend mice showed normal left ventricular function, but impaired right ventricular function (Fig. 1 a–b). Knockout mice exhibited a significant increase in pulmonary arterial wall thickness and muscularization. Furthermore, we observed loss of isolectin-B4 positive microvessels after Kdr knockout. Both in patients and in mice we found a significant up-regulation of VEGF levels after VEGF blockade (Fig. 2 a–f). Lung histologies demonstrated neointimal thickening and vessel occlusions in lungs of KdrΔend mice. We observed a similar proliferative vasculopathy in patients undergoing treatment with anti-VEGF antibodies.

Conclusions: Direct ablative gene manipulation of Kdr in C57/BL6J mice leads to classical pulmonary vasculopathy, similar to that observed in patients with pulmonary arterial hypertension and similar to vascular changes observed in asymptomatic patients receiving anti-VEGF treatments. This murine model could serve to study experimental pulmonary arterial hypertension.

FP 1-8

Potentiated effect of isoprenaline on calcium homeostasis in mouse cardiomyocytes with inhibited autophagy

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Background: Autophagy is a cytoprotective process essential for the maintenance of structural and functional homeostasis in the heart. Cardiac-specific autophagy-deficient mice develop profound left ventricular (LV) dysfunction accompanied with increased cardiomyocyte death upon chronic beta-adrenergic stress. We tested whether loss of autophagy in cardiomyocytes causes impaired subcellular calcium (Ca_{2+}) homeostasis early in life, and if these alterations are potentiated in response to acute beta-adrenergic activation. Such early alterations of intracellular Ca_{2+} handling may contribute to the development of contractile impairment and accelerated remodeling of cardiomyocytes with blocked autophagy.

Methods: Ventricular myocytes were isolated from adult male and female (15–26 weeks old) cardiomyocyte-specific autophagy-deficient mice with an apparently normal phenotype (Atg5-/-, N = 7 mice) and their control littermates (Atg5+/+, N = 8 mice). Nucleoplasmic and cytoplasmic Ca_{2+} transients (CaTs) were recorded using line-scan confocal imaging in electrically stimulated cells (1 Hz) loaded with Fluo-4/AM and perfused with normal Tyrode solution (baseline). A subset of cells was acutely exposed to the beta-adrenergic agonist isoprenaline (10 nM) followed by a rapid caffeine application (30 mM) to assess the sarcoplasmatic reticulum Ca_{2+} load. Hearts from Atg+/+ and Atg-/- male mice (14–16 weeks old, N = 11–13) were retrogradely perfused and fixed using 4% formaldehyde. Heart samples were then processed for electron microscopy. Quantification of LV cardiomyocyte composition was performed using

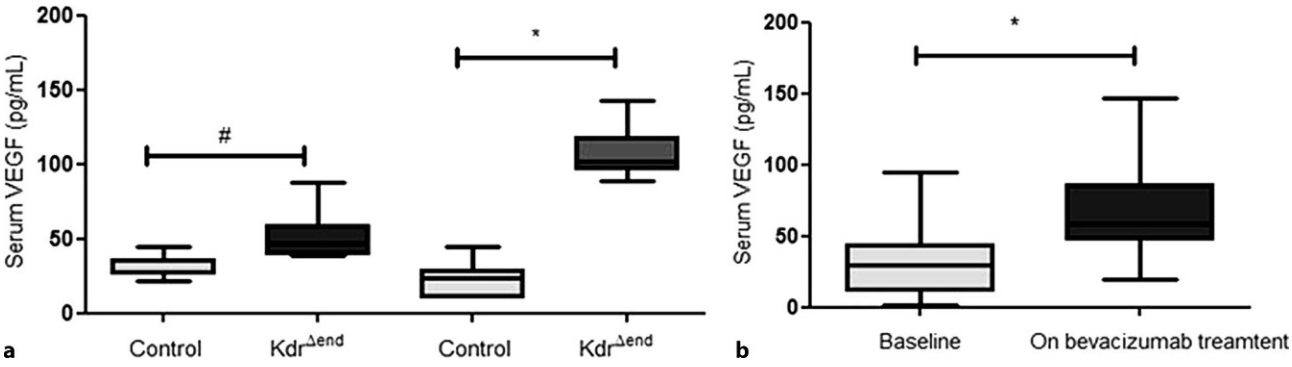
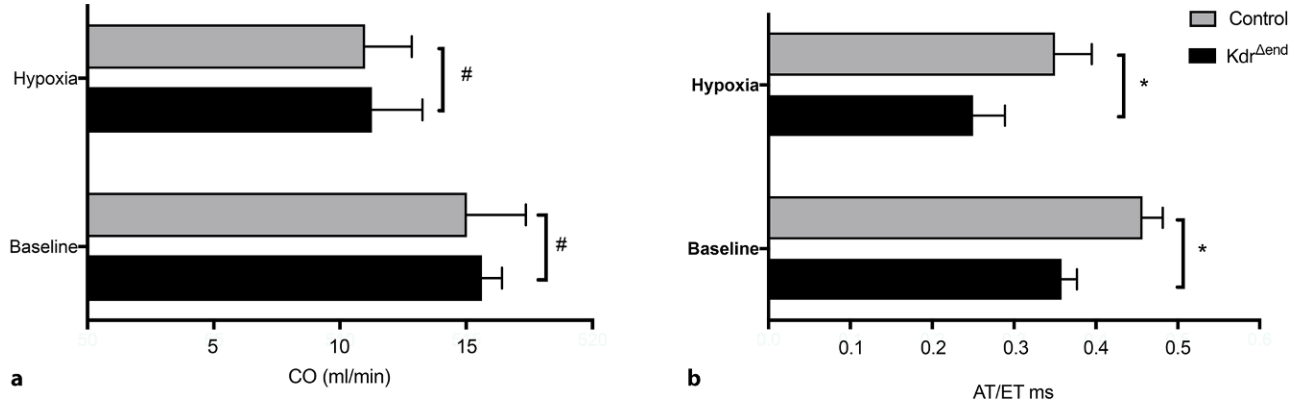
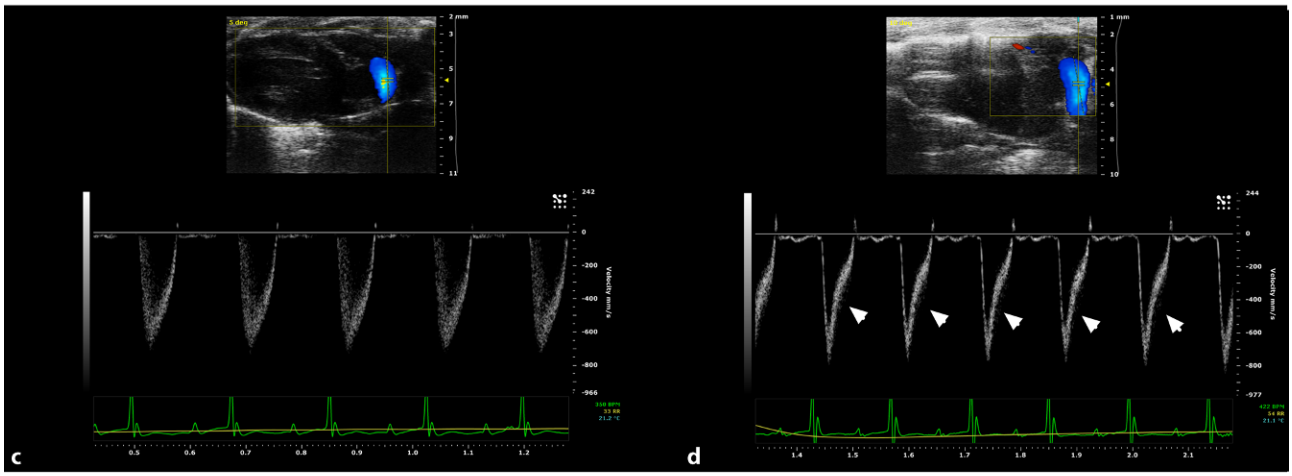


Fig. 1|FP 1-7





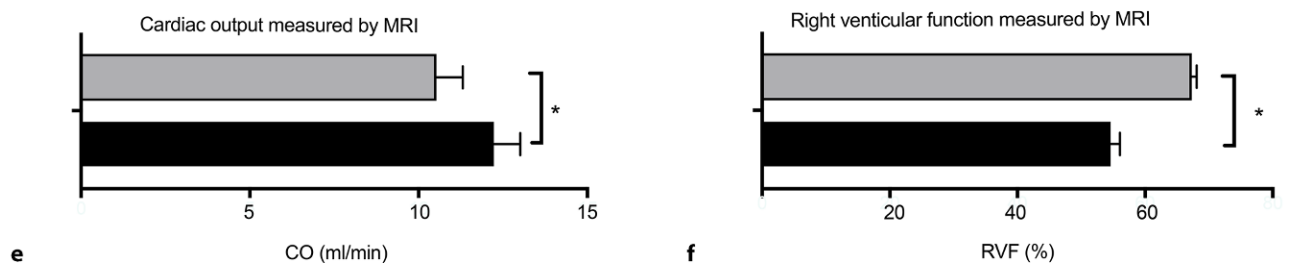


Fig. 2|FP 1-7

design-based stereology. Data were analyzed using Student's t-test or Mann-Whitney test and are reported as mean±S.E.M.

Results: Absolute volume of the LV myocardium and most organelles in cardiomyocytes were similar between control and Atg5-/- mice. However, autophagy-deficient cardiomyocytes had slightly, but significantly increased relative volume of myofibrils and decreased relative mitochondrial volume. At baseline, Atg5-/- cardiomyocytes had markedly increased time-to-peak (31 ± 2 ms vs. 24 ± 1 ms, P < 0.02), time for 50% relaxation from peak of the cytosolic CaT (RT50: 268 ± 9 ms vs. 235 ± 9 ms, *n* = 38–43 cells; P < 0.004) and reduced cytosolic CaT amplitude (F/F0: 3.29 ± 0.21 vs. 2.53 ± 0.14; P < 0.009) as also nucleoplasmic CaT amplitude (F/F0: 1.86 ± 0.07 vs. 1.58 ± 0.05; P < 0.002). Isoprenaline administration expectedly increased CaT amplitude and reduced decay time of the CaT in cytosol as well as nucleus. In Atg5-/- cells, however, isoprenaline increased cytosolic CaT amplitude to a significantly higher level compared to Atg5+/+ cardiomyocytes (by 149% vs. 74% with respect to baseline, respectively; N = 13–16 cells). Additionally, RT50 was reduced to a greater extent than in Atg5+/+ cells (by 32% vs. 20% with respect to baseline, respectively). In contrast, these isoprenaline-induced changes were not detected in the nucleus. The SR Ca_{2+} load upon isoprenaline administration was comparable between groups.

Conclusions: Autophagy-deficient ventricular cardiomyocytes show early alterations of subcellular Ca_{2+} homeostasis and potentiated cytosolic and nuclear Ca_{2+} cycling upon acute beta-adrenergic activation by isoprenaline. Our results suggest that intact autophagy has a protective role in the intracellular Ca2+ handling under normal conditions and during beta-adrenergic stress.

FP 1-9

Influence of lycorine and bufalin on cardiac fibrosis in domestic female pigs

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Background: Myocardial fibrosis is a progressive cardiac disease caused by excessive proliferation of fibroblasts. As a consequence, collagen production increases, leading to stiffness in the affected tissue, which impairs myocardial function.

In vitro screening of a compound library for specific anti-fibrotic effects on primary fibroblasts identified bufalin (BUF) and lycorine (LYC) as promising substances. In subsequent experiments, both BUF and LYC showed beneficial outcome on cardiac fibrosis in mice and rats.

Originally isolated from Chinese toad venom, BUF has a positive inotrope effect on the heart. LYC is a plant alkaloid inhibiting biosynthesis of ascorbic acid. This inhibition leads to a decrease of collagen synthesis.

Methods: Based on these observed results in rodents, different dosages of BUF (up to 0.5 mg/kg) and LYC (up to 5 mg/kg) were initially tested in healthy pigs to detect eventual toxicity. For efficacy evaluation, the animals underwent MI (myocardial infarction) by occlusion of the left anterior descending coronary artery and were randomised in 4 groups: BUF (0.1 mg/kg), LYC (0.2 mg/kg), SAL (placebo) and control (CO; no treatment after MI). The treatment started 7 days after MI, every other day for 2 months. Because of adverse effects, dosing was reduced after 14 days to 0.05 mg bufalin/kg and 0.1 mg lycorine/kg. After 2 months, magnetic resonance imaging (MRI) was performed and tissue samples were collected in RNAlater. Expression levels of MMP-9 (matrix metallopeptidase 9), COL1A1 (collagen type 1 alpha chain) and miR-29a (micro-RNA 29a) were analysed in the acute MI region and the remote zone (lateral wall). RNA was isolated from tissue using column-based extraction, then transcribed into cDNA, followed by qPCR. The geometric mean of Act-B and GAPDH was used for normalisation.

Results: Doses of BUF and LYC that had reduced cardiac fibrosis in mice and were well tolerated resulted in severe toxic effects in pigs. Thus, the doses had to be adjusted for long-term treatment post MI. Evaluation with MRI data showed no significant difference in scar size in the LYC group (14.4 ± 4.2%) and BUF (12.7 ± 1.8%) compared to CO (15.8 ± 2.5%) and SAL group (14.6 ± 2.4%).

MMP-9 is crucial for the degradation of the extracellular matrix. COL1A1 is a component of the extracellular matrix in connective tissue of skin, tendon and bone, amongst others. miR-29a regulates cell differentiation and possesses antifibrotic effects in the myocardium. let-7a was used as normalisation for miR-29a.

COL1A1 was upregulated in the remote region of the CO group compared to the remote region of SAL (4.2-fold) and LYC group (3-fold). By comparing acute MI region and remote region, miR-29a was upregulated in both regions in the BUF group compared to CO group (7.3-fold in the acute MI region and 8.9-fold in the remote region).

However, no significant differences between treatment groups were found for expression levels of MMP-9, COL1A1 and miR-29a.

Conclusions: Treatments with BUF and LYC showed decrease of cardiac fibrosis in murine models, however these advantageous results could not be confirmed in pigs. Severe adverse effects were dose-limiting, and applied doses were insufficient to reduce cardiac fibrosis. The investigated molecular markers failed to show specific mechanisms for an impact on fibrosis.

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FP 1-10

Lipid metabolism of neutrophils influences priming and effector function in ACS patients

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Background: Presence of primed neutrophils in the circulation of hyperlipidemic patients correlates positively with levels of density lipoprotein (LDL). Priming of neutrophils raises their propensity to undergo NETosis, a controlled cell death program leading to expulsion of chromatin in form of net-like structures. These neutrophil extracellular traps (NETs) constitute important risk factors for acute coronary syndrome (ACS) due to their pro-thrombotic and pro-inflammatory properties. An atherosclerotic environment and the inflammatory state of hyperlipidemia are predestined to give rise to a variety of substances acting synergistically or antagonistically on neutrophil activation.

Pro-protein convertase subtilisin/kexin 9 (PCSK9) is a regulator of LDL receptor expression and has gained attention specifically in the treatment of hyperlipidemia.

We aimed to investigate mechanisms of neutrophil priming in relation to important cardiovascular risk factors and lipid metabolism focusing on the LDL receptor and its interaction with PCSK9.

Methods: We enrolled ACS patients 72 hours after STEMI or NSTEMI at high cardiovascular risk, determined by presence of at least two of the following risk factors: dyslipidemia, hypertension, diabetes, obesity, or active smoking. In addition, we recruited a cohort of healthy controls. Neutrophils were stimulated with phorbol-12-myristate-13-acetate (PMA) or left untreated and analyzed in flow cytometry for production of reactive oxygen species (ROS), activation markers, and presence of receptors being able to interact with LDL, i.e. LDL receptor and lectin-like oxidized LDL receptor-1 (LOX-1). Concomitantly, neutrophils were isolated and stimulated to assess degree of ex vivo NET formation using ionomycin and PCSK9.

Results: An average of 79% of neutrophils were LDL receptor positive. Interestingly, the LDL receptor negative population produced significantly more ROS. In accordance with this finding, stimulation with PMA decreased the percentage of neutrophils expressing LDL receptor to 57% providing further evidence for a mechanistic link. In contrast, the reversed effect was observed for LOX-1. Ex vivo quantification of NET formation revealed an inhibitory effect of PCSK9 when added prior to stimulation with the NET inducer ionomycin in ACS patients. However, this was not observed in healthy controls where PCSK9 enhanced NETosis leading to a significant difference in relative NET quantification between both cohorts.

Conclusions: Lipid metabolism and treatment of hyperlipidemia by PCSK9 inhibition might be of importance for innate immune mechanisms and function.

Featured Poster Session 2

FP 2-1

Effects of acute exercise on miRNA expression in coronary artery disease patients

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Background: Micro ribonucleic acids (miRNAs) are small non-coding RNA molecules that control gene expression by translational inhibition in health and disease. Exercise has been shown to affect expression of several miRNAs in healthy subjects, but this has not yet been studied in patients with coronary artery disease (CAD). Therefore, we set out to assess miRNA expression in response to acute all-out exercise in both healthy subjects and patients with CAD of both sexes.

Methods: In this study, 20 CAD patients (10 males; 10 female) performed an all-out cycle ergometry. Total RNA was extracted from blood drawn before and 5 min after exercise. Each plasma sample was analyzed by quantitative reverse transcription polymerase chain reaction for a set of 187 target miRNAs that are known to be associated with endothelial function/dysfunction, cardiovascular, myocardial infarction and sudden cardiac death.

Results: In response to all-out exercise, 57 miRNAs changed their expression levels (all $p<0.05$). These miRNAs are known to interact with HIF-1 (oxygen homeostasis); AMPK (cellular energy homeostasis); PI3K-Akt (regulation of cell cycle, metabolism, angiogenesis); and FoxO (glucose metabolism, oxidative stress). Also, 14 of these miRNA were differently expressed in men and women ($p<0.05$). In relation to performance data, we could show that only miR-423-5p revealed a significant positive correlation with exercise capacity ($R=0.561$, $p=0.01$). Using multi variance analysis 9 miRNAs (let-7e-5p; miR-1; miR-19b-1-5p; miR-103a-3p; miR-148b-3p; miR-181b-5p; miR-188-5p; miR-423-5p; miR-874–3p) showed significantly different response to exercise between genders.

Conclusions: We described for the first time, that miRNA expression changes after all-out exercise in coronary artery disease patients. Affected were miRNAs that are associated among others with glucose metabolism, oxidative stress, and angiogenesis. Future studies may wish to assess whether disease specific miRNA expression in response to exercise might serve as marker for patient outcome.

FP 2-2

Cangrelor in resuscitated patients with myocardial infarction

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Background: Dual antiplatelet therapy is a mainstay of treatment in patients with myocardial infarction complicated with cardiogenic shock, resuscitation and receiving therapeutic hypothermia. According to guidelines, potent oral P2Y12 inhibitors as prasugrel or ticagrelor should be used over clopidogrel in this special population. As patients in therapeutic hypothermia are also administered opioid analgesics, this results in a consecutive gastroparesis, which slows down absorption of P2Y12 inhibitors.

Aim: To compare the antiplatelet effect of intravenous cangrelor as compared to oral P2Y12 inhibitors administered via gastric line in patients with myocardial infarction receiving therapeutic hypothermia.

Methods: This was a prospective comparison of two matched patient cohorts: all patients had acute myocardial infarction, were resuscitated, and received PCI and therapeutic hypothermia. The CANGRELOR cohort in 22 patients received cangrelor for at least 24 h. The ORAL P2Y12 inhibitor cohort (matched to age, gender and weight) in 17 patients received oral P2Y12 inhibitors (NCT02914795). All patients were loaded with 150–300 mg intravenous aspirin and 100 mg Aspirin once daily via gastric line from day 1. Platelet function testing was performed by light transmittance aggregometry (LTA) and moni-

tored for 4 days. Aspirin reactivity was monitored by inducing platelet aggregation with 2 µg/mL collagen and 0.5 mmol/L arachidonic acid (AA) respectively. P2Y12 inhibition was recorded by stimulation with 10 µmol/L adenosine diphosphate (ADP). To quantify the overall platelet response 40 µmol/L thrombin receptor-activated peptide (TRAP-6) was used.

Results: P2Y12-inhibition was 2–3 fold stronger in CANGRELOR treated patients compared to ORAL P2Y12 inhibitors (ADP [% Aggregation] 15 ± 8 vs. 26 ± 15 respectively; $p = 0.013$); ADP [AUC] 45 ± 62 vs. 131 ± 129 respectively; $p = 0.002$) at day 1. This difference vanished for AUC as well as %-aggregation within the following days as more patients were switched to oral P2Y12 inhibitors in the cangrelor group, too (8/22 on day 2, 12/21 on day 3 and 14/20 on day 3).

Aspirin effect was not different between the two groups 112.6 ± 140.8 vs. 151.1 ± 145.2 on day 1 but revealed significant higher collagen AUC values (less inhibitory effect) on day 3 (240.8 ± 89.3 and 202.1 ± 118.7) and 4 (272.8 ± 146.9 and 246.4 ± 98.2) in both groups.

We did not observe significant differences between both groups with respect to major bleedings, number of blood transfusions or drop in Hb over time.

Overall 5 patients died within the observation period of 4 days (2 cangrelor, 3 oral P2Y12).

Conclusions: Cangrelor inhibited platelet more effectively than oral P2Y12 inhibitors.

FP 2-3

Invasive vs echocardiographic systolic pulmonary artery pressure for risk assessment in TAVI patients

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Background: Pulmonary hypertension (PH) is independently associated with short- and long-term outcome in patients undergoing transcatheter aortic valve implantation (TAVI). However, little is known about the difference of systolic pulmonary artery pressure (sPAP) assessed by echocardiography (sPAPe) vs. right-heart catheterization (sPAPi).

Methods: We assessed sPAP measured invasively or by echocardiography in terms of (1) correlation of sPAPe with sPAPi, (2) incidence of PH according to both methods, and (3) influence on long-term outcome in patients undergoing TAVI.

Results: Out of 520 consecutive patients from our monocentric TAVI registry, a total of 212 patients (41%) with sufficient tricuspid regurgitation signal to evaluate sPAPe from echocardiography and complete right-heart catheterization were included into the study (age 82 ± 6 years, 68% female). sPAPe correlated only moderately with sPAPi ($\rho = 0.515$, $p < 0.001$). Echocardiography overestimated sPAP in most cases (sPAPe-sPAPi: median difference +3.6 mmHg; IQR –6.3.13.1 mmHg). PH was present in 80.2% according to sPAPe (tricuspid regurgitation velocity ≥ 3.4 m/s) and in 66.5% of patients according to mean invasive PAP (≥ 25 mmHg). 28.7% of patients were reclassified due to invasive measurements. In bivariate analysis, increased sPAPe was associated with 2-year mortality, while sPAPi was not ($p = 0.029$ vs. $p = 0.083$, respectively). When matched for age, gender, and left-ventricular function, sPAPe remained a significant predictor (Cox regression $p = 0.043$, HR 1.197, 95% CI 1.005–1.425 for 10 mmHg increase).

Conclusions: PH is present in the majority of TAVI patients. sPAPe correlated only moderately with sPAPi and overestimated the prevalence of PH. Still, sPAP estimated by echocardiography significantly predicted long-term outcome after TAVI in our cohort while invasively measured sPAP did not. We hypothesize that one reason for poorer prognostic performance of sPAPi might be specific preparations prior to right heart catheterization such as reduced fluid intake that alter loading conditions.

FP 2-4

Riociguat for the treatment of transthyretin cardiac amyloidosis—Data from a national named patient use program in Austria

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Background: Transthyretin cardiac amyloidosis (TTR CA) is a rare disease and represents the prototype of a restrictive cardiomyopathy. A vast majority of affected patients present with advanced heart failure and face significant morbidity and mortality. However, an effective therapy is still lacking and a diagnosis of CA precludes patients from participation in standard heart failure clinical trials.

The soluble guanylate cyclase—stimulator riociguat, already approved for the treatment of pre-capillary pulmonary hypertension, has also been shown to have favorable hemodynamic effects in heart failure.

We aimed to test the safety and efficacy of riociguat in a case-series of patients with TTR CA.

Methods: TTR CA was diagnosed either by histological assessment of endomyocardial biopsy samples with Congo red staining and subsequent immunohistochemical typing or non-invasively in accordance with current recommendations.

Parameters of interest were change in invasively measured hemodynamics, exercise capacity, quality of life as well as safety and tolerability.

Results: Between August 2014 and June 2017, 11 patients with wild-type TTR CA and 2 patients with mutations of the TTR gene (His108Arg) were included into our study. 2 patients discontinued with the study and the remaining 11 patients completed all procedures.

Median age of the study population was 75.0 years (IQR: 69.0–83.0) and 9 (81.8%) were male. The majority of the patients were in New York Heart Association (NYHA) class ≥III ($n = 6$, 54.6%), and NT-proBNP values were markedly elevated with a median of 2923 pg/mL (IQR: 1773–7912). Median 6-MWD was 370 m (IQR: 330–526).

Cardiac output improved significantly from 4.3 L/min (IQR: 3.8–5.1) to 4.5 L/min (IQR: 4.2–5.1) ($p = 0.022$, Fig. 1 a) whereas diastolic pressure gradient decreased (baseline: 0.0 mmHg, IQR: –2.0–3.0; follow-up: –1.0 mmHg, IQR: –3.0–1.0; $p = 0.049$).

6-MWD increased from 370 m (IQR: 330–526) at baseline to 400 m (IQR: 350–570) at follow-up ($p = 0.045$) Correspondingly,

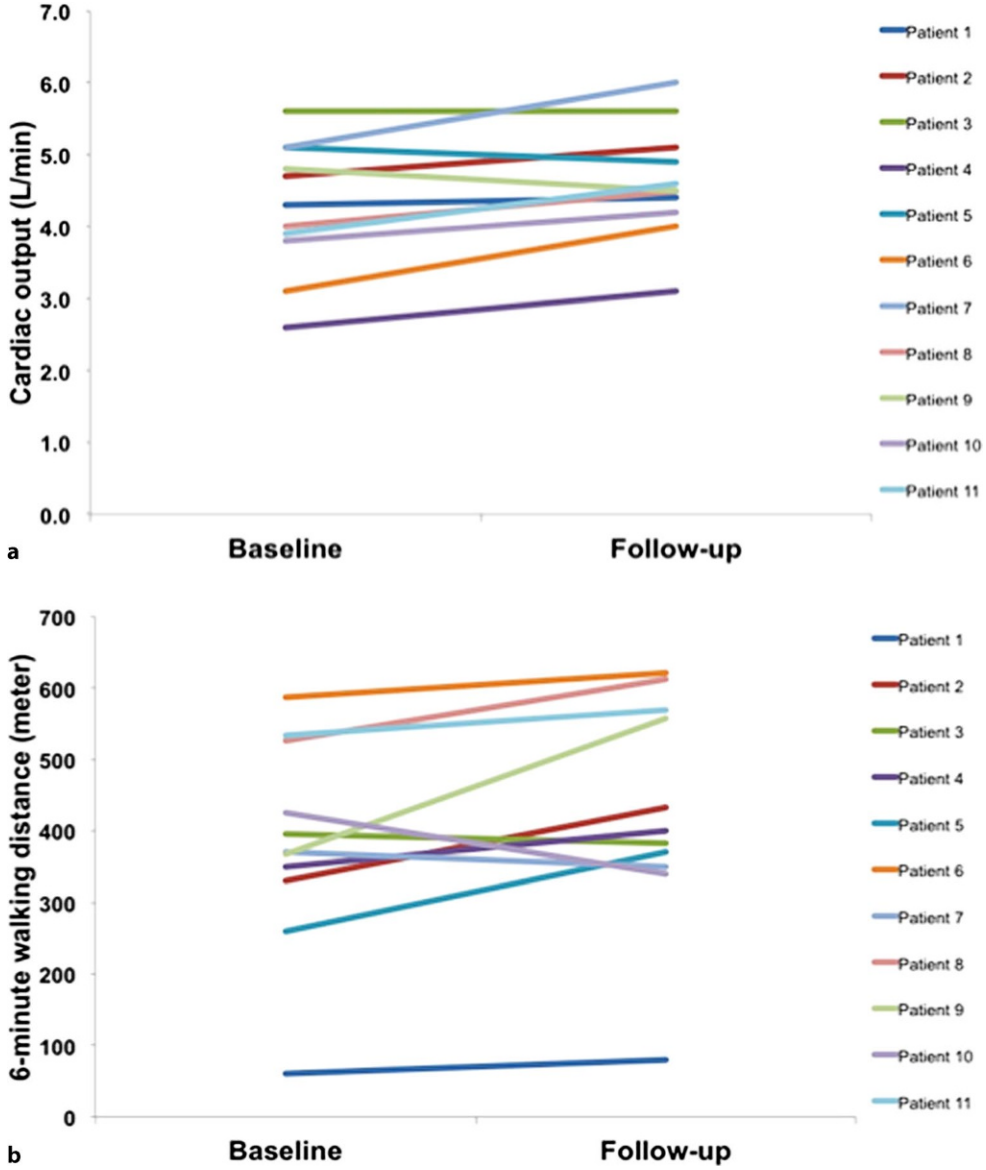

Fig. 1 | FP2-4

NYHA class improved significantly (baseline: NYHA class ≥III: $n=6$, 54.6%; follow-up: $n=0$, 0.0%; $p=0.031$). However, NT-proBNP did not change from baseline 2923 pg/mL (IQR: 1773–7912) to follow-up: 2584 pg/mL (IQR: 1804–7255) ($p=0.929$). Overall health status improved significantly from 50% (IQR: 40.0–50.0) at baseline to 60% (IQR: 50.0–75.0) at follow-up ($p=0.021$).

Conclusions: The present case series of TTR CA patients suggests beneficial effects of riociguat administration in this patient population. However, further studies of stronger design are warranted to explore the therapeutic potential of riociguat in TTR CA.

FP 2-5

Cardiac magnetic resonance T1 mapping in cardiac amyloidosis

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Background: In cardiac amyloidosis (CA) extracellular deposition of amyloid fibrils within the myocardium significantly expands the extracellular volume (ECV). Currently, several disease-modifying drugs with the potential to either stop disease

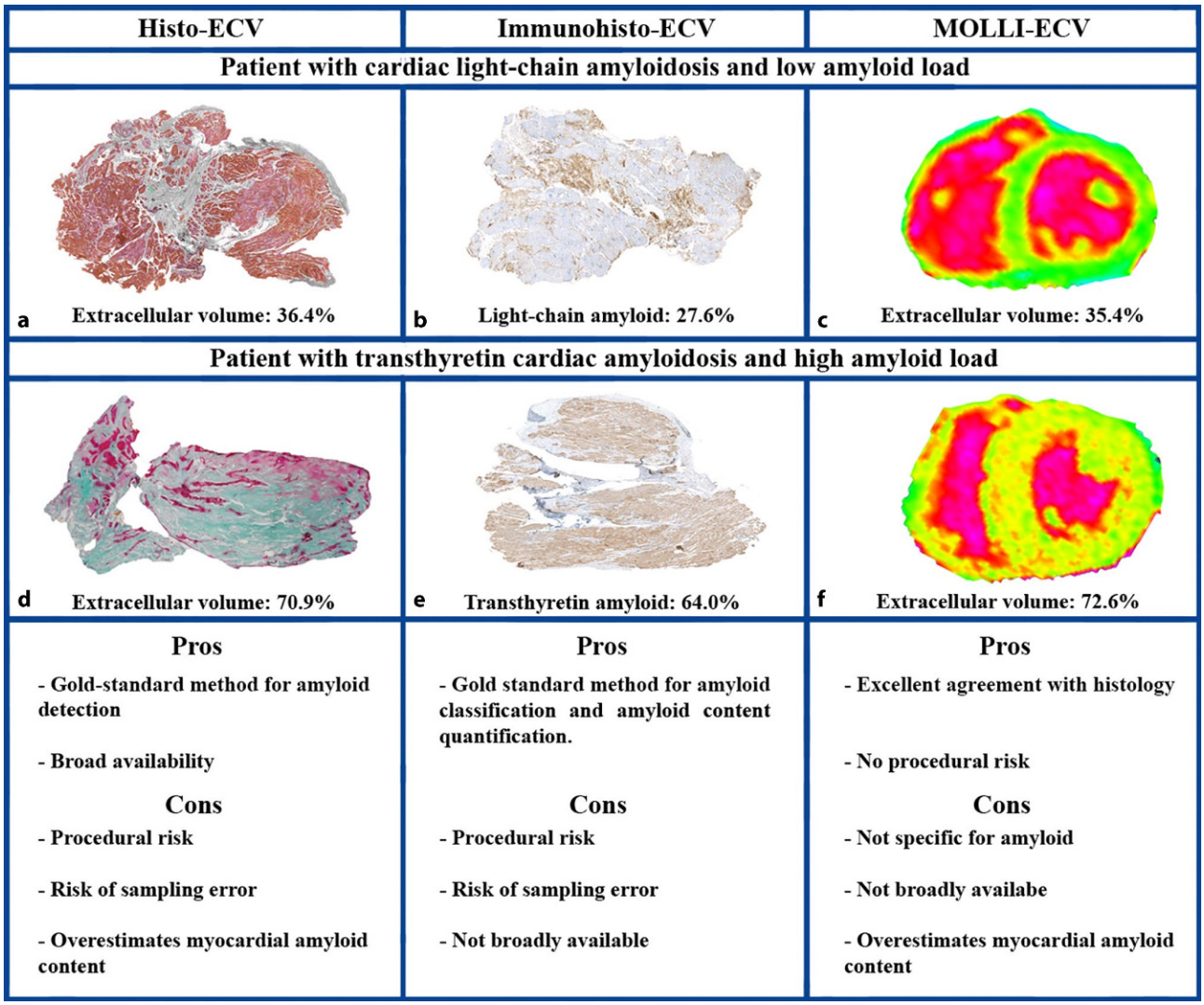

Fig. 1|FP 2-5 Panels **a** to **c** depict endomyocardial biopsy (EMB) specimens and a cardiac magnetic resonance (CMR) T1 map of a patient with light-chain (AL) cardiac amyloidosis (CA) and low amyloid load. Panels **d** to **f** show similar images, from a patient with transthyretin (TTR) CA and high amyloid load. For the quantification of extracellular volume (ECV) by histology (Histo-ECV) EMBs were stained with modified trichrome (cardiomyocytes stain red, ECV stains green/grey; Panels **a** and **d**). Panels **b** and **e** show immunohistochemical stains (Immunohisto-ECV) with AmY-kit amyloid antibodies (Martinsried, Germany; cardiomyocytes stain blue, amyloid stains brown). Corresponding T1 maps, using the modified Look-Locker inversion (MOLLI) recovery sequence are shown in panels **c** and **f**. Advantages and disadvantages of each method are are summarized in the bottom row

progression or reduce the amount of deposited amyloid are tested and a reliable biomarker is needed. The gold standard is histological quantification of amyloid in endomyocardial biopsies (EMBs). Cardiac magnetic resonance (CMR) T1 mapping is increasingly used for the quantification of ECV in CA. However, the method has not been validated against histology in CA. We aimed to validate ECV by CMR against histology and relate it with clinical and hemodynamic parameters, and outcome.

Methods: Consecutive patients with CA underwent EMB and T1 mapping using the modified Look-Locker inversion recovery (MOLLI) sequence. EMBs were stained with modified trichrome and specific amyloid antibodies for histological assessment (Histo-ECV and Immunohisto-ECV). In addition, clinical, invasive hemodynamic, and outcome data were collected.

Results: 26 patients, 9 with transthyretin and 17 with light-chain CA, were studied. MOLLI-ECV was highly correlated with Histo-ECV ($r=0.613$, $p=0.001$) and Immunohisto-ECV ($r=0.525$, $p=0.006$). By Bland-Altman analysis excellent agreement was found between MOLLI-ECV and Histo-ECV (mean difference 2.4%), while MOLLI-ECV systematically overestimated Immunohisto-ECV (mean difference -13.7%).

During a median follow-up of 123 days, 14 (53.9%) study participants reached the combined endpoint of cardiac hospitalization or cardiac death. MOLLI-ECV remained significantly associated with event-free survival, ($p=0.005$) even after adjustment for N-terminal prohormone brain natriuretic peptide and troponin t. In addition, MOLLI-ECV was significantly correlated with markers of disease severity: NT-proBNP ($r=0.460$, $p=0.018$), mean pulmonary arterial pressure ($r=0.522$, $p=0.009$), and pulmonary artery wedge pressure ($r=0.559$, $p=0.005$).

Conclusions: CMR T1 mapping allows quantification of ECV. Actual myocardial amyloid content is overestimated by

MOLLI-ECV, as it also reflects other components of the extracellular space such as collagen. Fig. 1 shows the advantages and disadvantages of each ECV quantification method. Furthermore, MOLLI-ECV is an independent predictor of adverse outcome in CA, even after adjustment for clinically established predictors.

Therefore, ECV by CMR T1 mapping is useful to monitor disease progression as well as response to treatment, and might serve as a tool for risk-stratification in patients with CA.

FP 2-6

Laktatclearance: unabhängiger Prädiktor der Mortalität kritisch kranker Patienten an der Intensivstation

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Grundlagen: Untersuchung der prognostischen Relevanz der Laktatclearance innerhalb der ersten 24 Stunden (LC24) in einem heterogenen, kritisch kranken Patientenkollektiv an einer Intensivstation (ICU).

Methodik: 1863 Patienten (67 ± 14 Jahre), zwischen 2004 und 2009 an einer Intensivstation aufgenommen, wurde untersucht. Einschlusskriterium war eine Laktatkonzentration über 2,3 mmol/L bei Aufnahme. Ein Langzeitfollow-up wurde zwischen Mai und November 2013 durchgeführt.

Die Patienten wurden wegen Pneumonie ($n = 287$), Pulmonalembolie ($n = 161$), akutem Koronarsyndrom ($n = 453$), Sepsis ($n = 396$) und dekompensierter Herzinsuffizienz ($n = 317$) an der ICU aufgenommen. Assoziationen von LC24 mit Kurzzeit- (intra-hospital) und Langzeitmortalität wurden mittels Cox Regressionsanalyse untersucht. Mittels Youden-Index wurde ein optimaler Cut-off berechnet.

Ergebnisse: Patienten mit reduzierter LC24 wiesen erhöhte renale und hepatale laborchemische Parameter (ALAT: $p < 0{,}001$; ASAT: $p < 0{,}001$; Kreatinin: $p < 0{,}001$) als Zeichen eines Multiorganversagen auf und waren klinisch kränker (SAPS2 61 ± 23 versus 46 ± 18; $p < 0{,}001$ und APACHE2 29 ± 10 versus 23 ± 9; $p < 0{,}001$). Patienten mit einer LC24 unter 0 % wiesen unabhängig von der Aufnahmediagnose eine deutliche Übersterblichkeit gegenüber jenen mit einer LC24 ≥ 50 % auf. Der optimale statistische Cut-off lag bei 24 %, war mit einer Übersterblichkeit auch nach Korrektur für APACHE2 (HR 1,56; 95 %CI 1,28–1,91; $p < 0{,}001$), SAPS2 (HR 1,47; 95 %CI 1,20–1,80; $p < 0{,}001$) und ein integratives Modell mit mehreren Parametern von Multiorganversagen (HR 2,36; 95 %CI 1,99–2,80; $p < 0{,}001$) assoziiert.

Weiters wurden 336 Patienten anhand ihres APACHE2 Scores in einer Fall-Kontroll-Analyse gepaart: Auch in der gepaarten Analyse blieb eine LC24 < 24 % mit einer erhöhten intra-hospitalen Mortalität (Differenz 24 %; 95 %CI 17–32 %; $p < 0{,}0001$) assoziiert.

Schlussfolgerungen: Reduzierte Laktat-Clearance (LC24) ist in kritisch kranken Patienten an einer ICU mit einer Übersterblichkeit verbunden. Sowohl für die Kurzzeit- als auch die Langzeitmortalität ist die LC24 ist ein robuster Prädiktor, auch nach Korrektur für klinisch relevante Störvariablen.

FP 2-7

Physical exercise induces coronary artery collateral growth and affects cardiovascular biomarkers: A biomarker sub-analysis of the EXCITE trial

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Background: Coronary artery disease (CAD) represents a major burden for patients and healthcare systems worldwide. The EXCITE trial revealed that 4 weeks of exercise training in clinically stable patients with CAD has beneficial effects on coronary collateral flow compared to an optimal medical therapy (OMT) only control group. In this current sub-analysis, we sought to determine if exercise training affects levels of cardiovascular biomarkers (i. e. soluble suppression of tumorigenicity, sST2; growth-differentiation factor-15, GDF-15; soluble urokinase plasminogen activator receptor, suPAR; and insulin-like growth factor binding protein-2, IGF-BP2).

Methods: 60 patients with significant but stable CAD (fractional flow reserve ≤0.75) were randomly assigned to either high-intensity exercise training (group A, 20 patients) or moderate-intensity exercise (group B, 20 patients) for 4 weeks or to a control group (group C, 20 patients). The primary endpoint of this prospective, open-label study was the change of the coronary collateral flow index (CFI) after 4 weeks. We here analyzed levels of 4 novel cardiovascular biomarkers (i. e. sST2, GDF-15, suPAR and IGF-BP2) by ELISA.

Results: After 4 weeks, baseline CFI increased by 39% in group A (from 0.14 ± 0.07 at beginning to 0.19 ± 0.09 at 4 weeks; $p = 0.001$) compared to 41% in group B (from 0.14 ± 0.06 to 0.20 ± 0.09, $p = 0.001$) whereas CFI in the control group remained unchanged (0.7%, from 0.14 ± 0.09 to 0.15 ± 0.08). High-intensity exercise did not lead to a greater CFI than moderate intensity exercise. After 4 weeks of training, exercise capacity, peak VO2 and ischaemic threshold showed a significant increase in both group A and B compared with group C. sST2 increased both in group A and C (+11% and +23%, $p = 0.005$ and 0.047, respectively) but not in group B (moderate exercise). IGF-BP2 levels increased significantly in group A + 24%, $p = 0.02$) but not in the other two groups. No differences were detected for GDF-15 and suPAR.

Conclusions: A significant improvement in CFI was found in response to moderate- and high-intensity exercise. In addition to the results found in the EXCITE trial, we found that high-intensity training increased IGF-BP2 and sST2 levels. Elevated IGFBP-2 levels have been shown to be protective against the

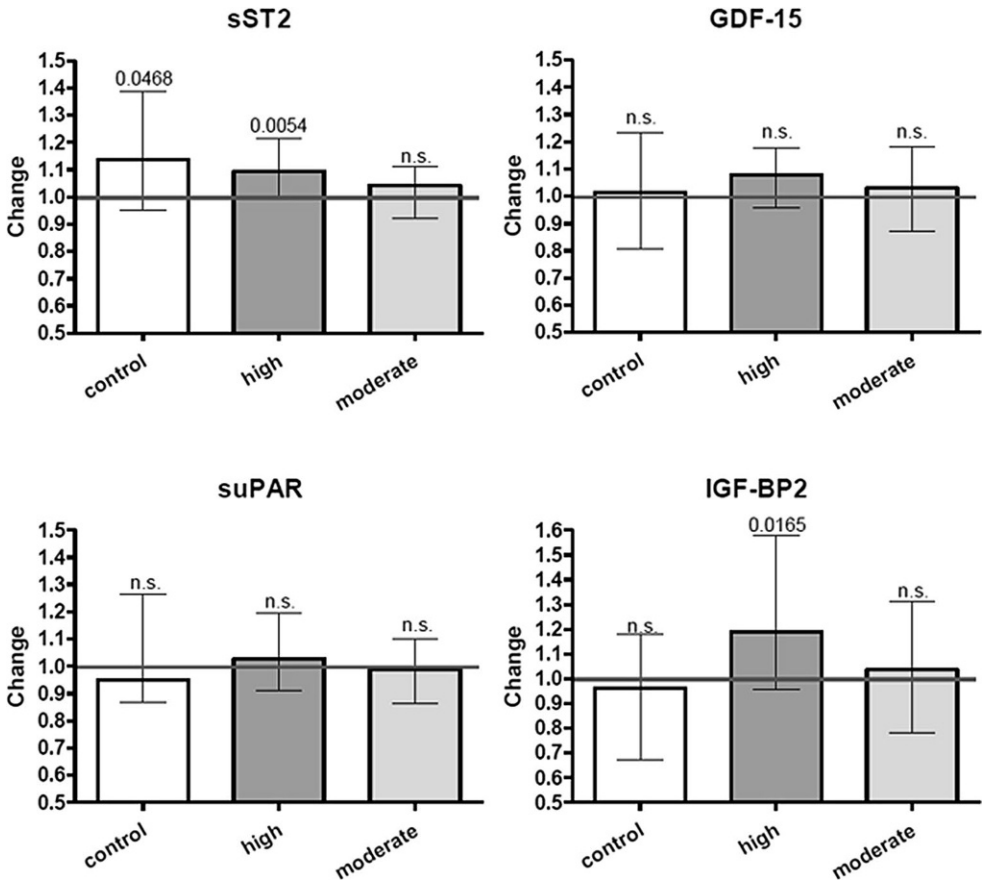

Fig. 1 | FP 2-7

development of diabetes as IGFBP-2 inhibits adipogenesis and can modulate insulin sensitivity. In obese patients levels of IGFBP-2 are decreased and low IGFBP-2 levels are associated with the development of diabetes.

A divergent response was found for sT2, as it was elevated both after high-intensity training and also in controls but not after moderate-intensity training.

FP 2-8

The Q222R deoxyribonuclease 1 single nucleotide polymorphism independently predicts mortality in patients with coronary artery disease after ST-elevation myocardial infarction

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Background: Neutrophils are able to release their nuclear content into extracellular space by formation of neutrophil extracellular traps (NETs). NETs neutralize pathogens, but have also been implicated in autoimmune and thrombotic diseases, including ST-elevation myocardial infarction (STEMI). Deoxyribonuclease (DNase) 1 degrades NETs. DNase 1 Q222R single nucleotide polymorphism (SNP), which impairs DNase 1 function, was associated with an increased incidence of MI. In STEMI, impaired DNase 1 activity correlates with increased NET burden and infarct size. In a mouse model of coronary artery ligation, DNase 1 treatment decreased infarct size, indicating a therapeutic role. We hypothesized that DNase 1 is crucial to counteract dysregulated NET formation in coronary artery disease (CAD). The Q222R SNP in the DNase 1 gene, resulting in dysfunction of the enzyme, might thereby induce chronic NET burden, influencing long-term outcome.

Methods: We enrolled CAD patients with a history of STEMI treated at the Vienna general hospital which received primary percutaneous coronary intervention between 2006 and 2016 ($n=711$). Genotyping using allelic discrimination was performed to identify DNase 1 Q222R SNP (rs1053874). Mortality data was obtained from the national registry of death. Causes of death were classified according to ICD-10. By multivariable Cox regression, we assessed the influence of DNase 1 SNP on all-cause and cardiovascular mortality, adjusting for the following established cardiovascular risk factors: hyperlipidemia, arterial hypertension, diabetes mellitus, ever smoker, age, male sex, body mass index (BMI) and renal function as measured by serum creatinine concentration at admission. Levels of citrullinated histone H3 (citH3) at the culprit lesion site (CLS) during STEMI were measured using ELISA.

Results: Homozygous mutation of the DNase 1 SNP was present in 64 (9.0%) patients; 304 (42.8%) and 343 (48.2%) were heterozygous and homozygous for the wild-type allele, respectively. Patients with a homozygous mutation had higher levels of citH3 at the CLS (661 [interquartile range, IQR 323; 1287] vs. 383 [197; 1033], $p=0.016$). Median survival was 60.0 [IQR 30.3; 91.5] months. A total of 133 (18.7%) patients deceased; 78 (11.0%) died of cardiovascular causes. Homozygous mutation of DNase 1 was independently associated with all-cause mortality (hazard ratio 2.09, 95% CI 1.24–3.51, $p=0.006$) and cardiovascular mortality (hazard ratio 2.6, 95% CI 1.04–4.09, $p=0.037$).

Conclusions: We report a negative influence of the Q222R DNase 1 SNP on survival after STEMI. Our findings argue for a

deleterious role of NETs not only in acute STEMI, but also in stable CAD.

FP 2-9

Long-term Outcome in cardiomyopathies according to etiology: Survival is best in inflammatory CMP and worst in cardiac amyloidosis

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Background: Early studies have shown that etiology of underlying cardiomyopathy (CMP) predicts prognosis in heart failure. However, diagnostic work-up and goal-directed therapy have improved substantially over time. We were interested if advancements in diagnosis and therapy have changed the impact of various etiologies on prognosis.

Methods: In this single-centre registry 2029 consecutive patients treated for heart failure according to prevailing guidelines between 2000 and 2016 were analysed. Underlying CMPs were classified into eight groups: idiopathic (25.9%), ischemic (24%), hypertensive (16.4%), inflammatory (15.0%), various (5.5%), toxic (4.5%), cardiac amyloidosis (4.4%), and valvular (2.9%). Patients were followed for a median of 80 (IQR 34–134) months. Primary endpoint was death of any cause. Kaplan-Meier estimator was used to calculate 5-year survival. A multivariate cox regression analysis was performed to compare survival between groups.

Results: Five year overall survival in the whole cohort was 81.9% (inflammatory 91.9%, various 90.4%, idiopathic 85.3%, hypertensive 81.1%, valvular 80.8%, toxic 77.7%, ischemic 76.3%, cardiac amyloidosis 48.4%).

In multivariate analysis adjusted for age, gender, LV-EF, and NYHA class, individuals with cardiac amyloidosis were 6.5 time (95% CI 3.0–14.0; $p<0.01$) more likely to die of any reason than were individuals with inflammatory CMP. In this model, mortality was also higher in ischemic (HR 3.0, 95% CI 1.8–5.2; $p<0.01$), valvular (HR 2.5, 95% CI 1.2–5.4; $p=0.02$) and toxic CMP (HR 2.4; 95% CI 1.3–4.4; $p<0.01$).

Conclusions: Comparing long-term outcome according to CMP etiology survival is worst in patients with cardiac amyloidosis and best in patients with inflammatory CMP. From this perspective, thorough etiologic evaluation and targeted therapy is mandatory in the management of patients with heart failure.

FP 2-10

Tissue tracking by cardiovascular magnetic resonance imaging is associated with outcome in heart failure with preserved ejection fraction

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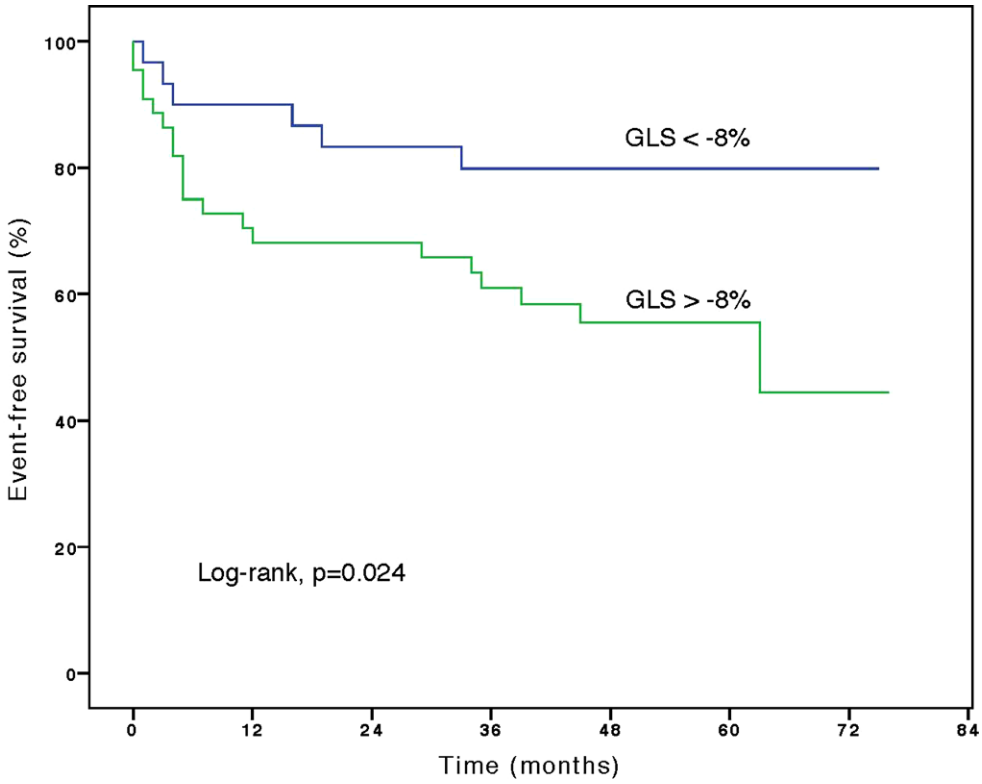

Fig. 1 | FP 2-10

Background: Heart failure with preserved ejection fraction (HFpEF) accounts for nearly one half of all heart failure patients and is associated with high morbidity and mortality rates. Echocardiography-based studies have demonstrated that strain analyses can detect impaired systolic function despite preserved left ventricular ejection fraction (LVEF) in these patients. Global longitudinal strain (GLS) by echo has been reported to be of prognostic relevance in the TOPCAT trial. Recently, strain analysis using tissue tracking (TT) by cardiovascular magnetic resonance imaging (CMR) has been reported to detect early changes in systolic function. However, the prognostic relevance of TT-CMR has not been studied so far. In addition, CMR is the gold standard for assessment of both left and right ventricular volumes and ejection fractions (LVEDV, RVEDV, RVEF). Also, CMR allows non-invasive quantification of extracellular volume (CMR-ECV) by T1-mapping.

We aimed to investigate 1) the association between CMR-ECV and GLS by TT-CMR, and 2) the prognostic relevance of TT-CMR in HFpEF patients.

Methods: Consecutive patients with confirmed diagnosis of HFpEF underwent CMR including T1-mapping using a Modified Look-Locker Inversion Recovery (MOLLI) sequence. We used dedicated software (cvi42, Circle Cardiovascular Imaging Inc.) for strain analysis. The correlation between CMR-ECV and strain was investigated. Patients were prospectively followed in a 6-month interval and a composite of cardiovascular hospitalization and death was used as primary endpoint. The prognostic value of TT-CMR was tested by Kaplan-Meier estimates and Cox-regression analysis. The study was registered on clinicaltrials.gov (NCT03405987).

Results: A total of 74 HFpEF patients (71.0 ± 8.9 years old, 71.6% female) were analyzed. LVEF was 63.2 ± 10.7%, LVEDV was 125.0 ± 37.0 ml, and CMR-ECV was 30.6 ± 4.1% on average. GLS by TT-CMR was –6.9 ± 4.6% and was significantly correlated with both LVEF and RVEF (r = –0.524, $p < 0.001$, and r = –0.511, $p < 0.001$, respectively) as well as NT-proBNP levels (r = 0.355, $p = 0.002$) and CMR-ECV (r = 0.239, $p = 0.046$).

26 (35.1%) events were recorded during a follow-up of 40.5 ± 23.8 months. 44 patients (59.5%) had a GLS > –8% which was associated with a decreased event-free survival (log-rank, $p = 0.024$). By multivariable Cox-regression analysis, a GLS > –8% remained independently associated with outcome (HR 3.108 [1.085–8.903], $p = 0.035$), even when corrected for established risk factors including age, NT-proBNP, and RVEF.

Conclusions: In patients with HFpEF, GLS by TT-CMR is correlated with extracellular matrix expansion, and reduced strain rates are significantly associated with cardiovascular events.

Featured Poster Session 3

FP 3-1

Analyse der Assoziation von Luftverschmutzung und der Inzidenz von Akutem Koronarsyndrom und Myokardinfarkt in einer großen Kohorte im Großraum Graz, Steiermark

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Grundlagen: Luftverschmutzung gefährdet die öffentliche Gesundheit, nicht nur in Entwicklungsländern in Afrika oder Süd-Ost Asien, sondern auch in großen mitteleuropäischen Städten. Kardiovaskuläre Erkrankungen wie Akutes Koronarsyndrom (ACS) oder Myokardinfarkt (MI) wurden in der Literatur mit erhöhten Konzentrationen von Schadstoffen in der Atemluft in Zusammenhang gebracht. Das Phänomen der Inversionswetterlage begünstigt die Bindung von Schadstoffen in tieferen Luftschichten und beschreibt einen Zustand, bei dem die bodennahe Luft kälter ist als höhere Luftschichten. Risikofaktoren für die Inversionswetterlage sind ein hoher geographischer Breitengrad und Gebirge, welche vorwiegend in den kalten Wintermonaten auftritt, wobei dies mit dem vermehrten Verbrennen von fossilen Energieträgern zusammenfällt. Die Inversionswetterlage verhindert die vertikale Bewegung von tieferen Luftschichten und erhöht die Konzentration von Feinstaubpartikel (PM2.5 und PM10) und gasförmigen Schadstoffen wie Kohlenmonoxid (CO), Stickoxide (NO und NO_2) und Schwefeldioxid (SO_2).

Methodik: Wir führten eine retrospektive Analyse der Inzidenz von ACS und den Untergruppen in der Zeitspanne von 2007–2015 im Großraum Graz und der näheren Umgebung durch. Insgesamt wurden 18.075 Fälle erfasst, welche an der Abteilung für Kardiologie der Universitätsklinik für Innere Medizin Graz und der Abteilung für Kardiologie des Krankenhauses Graz-Südwest angiographiert wurden. Wir verglichen die Inzidenz von ACS und den Untergruppen mit Tagesdurchschnitten von Konzentrationen von NO_2, NO, CO, SO_2, PM2.5 and PM10. Das Vorliegen einer Inversionswetterlage wurde mit einem binären Verfahren erhoben, wobei Tage mit negativen Temperaturdifferenzen zwischen zwei Messstationen unterschiedlicher Höhe im Grazer Becken als Tage mit Inversionswetterlage klassifiziert wurden.

Ergebnisse: Wir beobachteten statistisch signifikante Korrelationen zwischen Konzentrationen von NO_2, NO, CO, SO_2, PM2.5 und PM10 mit der Inzidenz von ACS insgesamt (NO_2: r = 0,171, NO: r = 0,113, CO: r = 0,129, SO2: r = 0,08, PM10: r = 0,096, PM2,5: 0,08; Signifikanzniveau $p < 0,001$) und MI (NO_2: r = 0,145, NO: r = 0,098, CO: r = 0,114, SO_2: r = 0,065, PM10: r = 0,076, PM2.5: 0,065; Signifikanzniveau $p < 0,001$). Tage mit Inversionswetterlage zeigten eine statistisch signifikante Assoziation mit erhöhten Raten von MI (M = 4,55, SD = 2,428), verglichen mit Tagen ohne dem Vorliegen einer Inversionswetterlage (M = 4,18, SD = 2,30); t(2125) = –2,297, $p = 0,002$. Der Luftschadstoff Ozon (O_3) zeigte eine statistisch signifikante negative Korrelation mit ACS (r = –0,072, $p < 0,001$) und MI (r = –0,07, $p < 0,001$) und des Weiteren statistisch signifikante negative Korrelationen ($p < 0,001$) mit den Konzentrationen von NO_2, NO, SO_2, CO, PM10 und PM2.5 (respektive r = –0,675, r = –0,647, r = –0,692, r = –0,376, r = –0,445 und r = –0,474). In der graphischen Darstellung zeigte sich folglich ein beinahe inverser Verlauf der Konzentrationen von Ozon und den anderen Luftschadstoffen.

Schlussfolgerungen: Tägliche Schwankungen der Konzentrationen der Schadstoffe NO_2, NO, CO, SO_2, PM2.5 und PM10 in Graz zeigten positive statistisch signifikante Korrelationen mit der Inzidenz von ACS und MI über den Beobachtungszeitraum. Die Inversionswetterlage war statistisch signifikant mit erhöhter Inzidenz von MI assoziiert. Interessanterweise zeigte Ozon eine negative Korrelation mit ACS und MI, wobei dies in erster Linie durch ein Bias erklärbar ist.

FP 3-2

Ein Screening-Programm für Gefäßaltermessung und arterielle Hypertonie in Österreich

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Grundlagen: Der Anteil an Personen mit nicht ausreichend kontrolliertem Blutdruck in Österreich ist weitgehend unbekannt. Das Ziel unserer Querschnittsstudie war es daher ein Screening für arterielle Hypertonie unter Zuhilfenahme der neuen Konzepte bezüglich arterieller Gefäßsteifigkeit und vorzeitiger Gefäßalterung durchzuführen.

Methodik und Ergebnisse: Wir erhoben den Blutdruck am Oberarm und die aortale Pulswellengeschwindigkeit (PWV) der Studienteilnehmer mit einem Messgerät zur Pulswellenanalyse (agedio) in 45 öffentlichen Apotheken sowie bei zwei Gesundheitsveranstaltungen in Oberösterreich. Die PWV wurde unter Verwendung eines invasiv validierten Algorithmus (ARCsolver) aus Alter, Blutdruck und Kurvenform ermittelt. Vorzeitige Gefäßalterung wurde definiert als ein Wert über der 90. Perzentile, wobei die entsprechenden Perzentilen in einer früheren Bevölkerungsstudie erhoben worden waren. In einer Subgruppe wurde zusätzlich eine 24-Stunden-Blutdruckmessung durchgeführt, um den Hypertoniestatus der Teilnehmer zu verifizieren.

Insgesamt nahmen 10.973 Personen an der Studie teil (Durchschnittsalter 61,2 Jahre, 20–94 Jahre), davon 67,6 % Frauen. Der mittlere Blutdruck lag bei 133/83 mmHg. 38,1 % der Teilnehmer hatten einen erhöhten Blutdruck (> 140/90 mmHg). Eine arterielle Hypertonie war bei 37,3 % der Teilnehmer vorbekannt, 32,4 % nahmen zum Untersuchungszeitpunkt Antihypertensiva ein. Von 3980 Personen mit bekannter Hypertonie hatten 57,3 % einen erhöhten Blutdruck, in der Gruppe der Teilnehmer ohne bekannte Hypertonie war bei 29,5 % der Blutdruck erhöht.

19,9 % der Teilnehmer hatten eine aortale Pulswellengeschwindigkeit unter der 50. Perzentile, 42,8 % zwischen 50. und 90. Perzentile und 37,3 % über der 90. Perzentile (vorzeitige Gefäßalterung). Bei Teilnehmern mit vorzeitiger Gefäßalterung war der Blutdruck bei der Messung in der Apotheke in 82,6 % der Fälle erhöht.

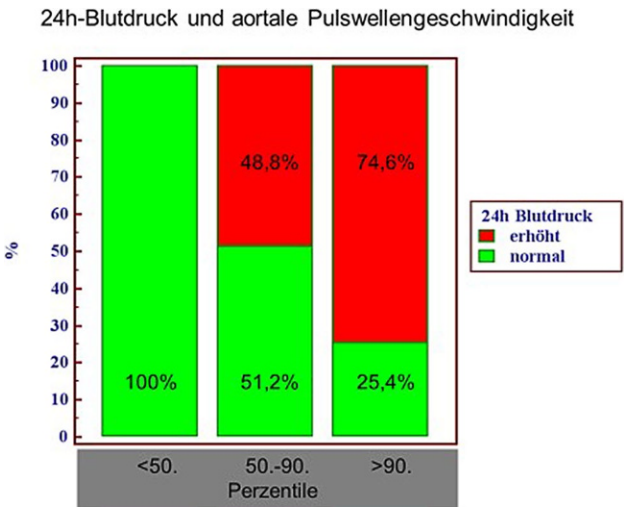

Fig. 1 | FP 3-2

Von den Studienteilnehmern mit 24-Stunden-Blutdruckmessung waren 74,6 % derer mit „vorzeitiger Gefäßalterung", hypertensiv (Gesamtdurchschnitt der Messungen > 135/85 mmHg).

Schlussfolgerungen: Das Bewusstsein der oberösterreichischen Bevölkerung bezüglich Hypertonie und die Blutdruckkontrollraten erwiesen sich als suboptimal. Dennoch gelang es uns eine große Zahl von Kunden in Apotheken für die Teilnahme an unserer Studie zu motivieren, indem wir die Blutdruckmessung mit der Messung des Gefäßalters kombinierten.

FP 3-3

Papillary muscle dyssynchrony mediated functional mitral regurgitation: mechanistic insights and modulation by cardiac resynchronization

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Background: Mechanistic features of functional mitral regurgitation (FMR) include papillary muscle displacement due to left ventricular remodeling. Intraventricular conduction delay might further augment this condition by introducing interpapillary muscle dyssynchrony. We aimed to define this mechanism as a major contributing factor to FMR and proof reversibility of FMR by interpapillary muscle resynchronization.

Methods: We enrolled 269 chronic HFrEF patients with conduction delay and comprehensively assessed dyssynchrony by a set of complementary multidimensional echocardiographic techniques covering the entire spectrum of cardiac dyssynchrony.

Results: Patients with severe FMR had markedly increased interpapillary longitudinal dyssynchrony (160 ms [IQR120-200]) compared to patients with moderate (70 ms [IQR40-110]) or no/mild FMR (60 ms[30–100];$P < 0.001$) (Fig. 1 a). Increased interpapillary muscle dyssynchrony strongly correlated with regurgitant volume ($r = 0.50$, $P < 0.001$) and vena contracta width ($r = 0.49$, $P < 0.001$) (Fig. 1B). Restoration of longitudinal papillary muscle synchronicity by cardiac resynchronization therapy (CRT) strongly correlated to FMR regression (Fig. 2 a) reflected by reduction in regurgitant volume ($r = 0.46$, $P < 0.001$) and vena contracta width ($r = 0.58$, $P < 0.001$). Vice versa, improvement of FMR severity was associated with improved interpapillary radial ($P = 0.006$) and longitudinal ($P < 0.001$) dyssynchrony (Fig. 2 a). Improvement of dyssynchrony-mediated FMR conveyed a better prognosis compared to FMR non-improvers during 8-year long-term follow-up (Fig. 2 b) even after comprehensive adjustment by a bootstrap-selected confounder model (adj. HR of 0.41;95%CI 0.18–0.91; $P = 0.028$).

Conclusions: Intraventricular dyssynchrony introduces dysbalanced contraction by papillary muscle bearing walls that contributes adversely to FMR. CRT can effectively restore the interpapillary balance thereby reestablishing a less tented leaflet configuration resulting in clinically meaningful reduction of FMR. Finally, restoration of papillary muscle synchronicity in dyssynchrony-mediated FMR translates to a significant prognostic improvement.

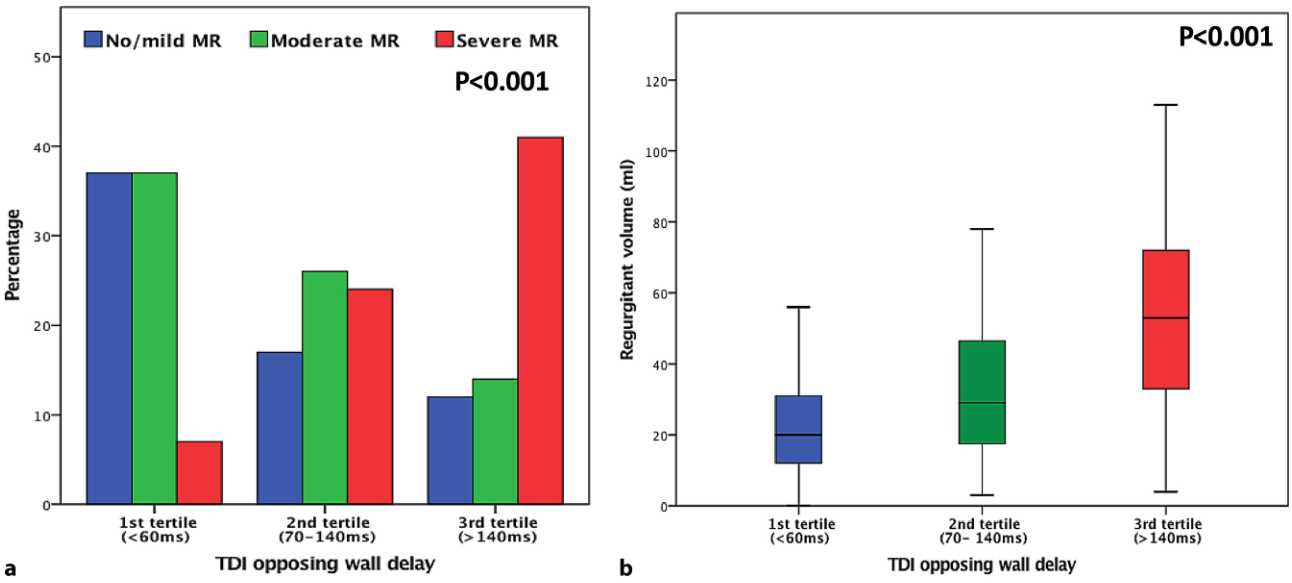

Fig. 1|FP 3-3

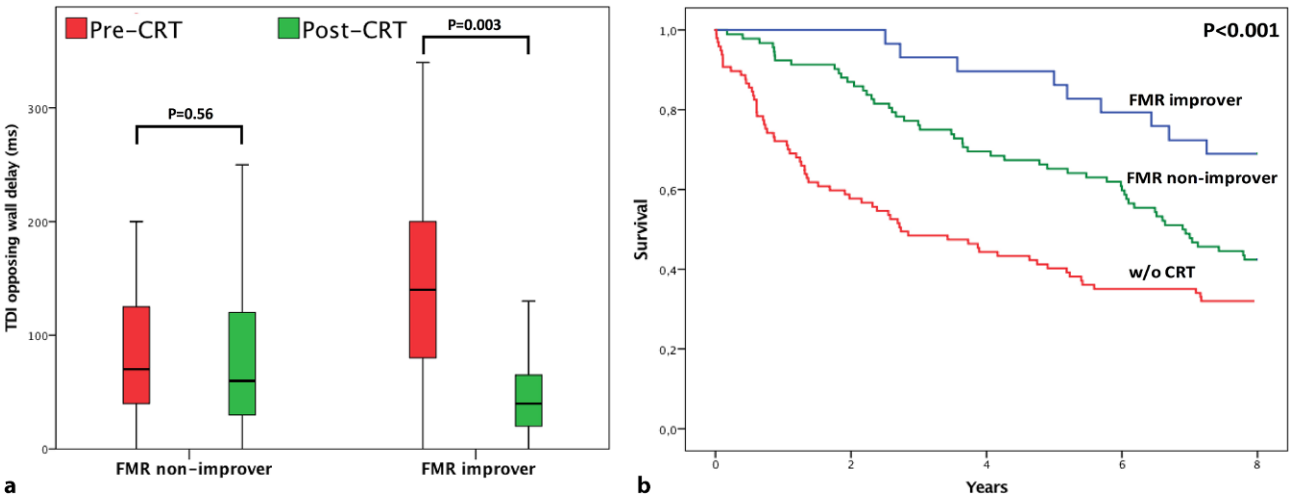

Fig. 2|FP 3-3

FP 3-4

Evolution of secondary mitral regurgitation

H. T. Arfsten, P. Bartko, N. Pavo, A. Pérez-Serradilla, S. Neuhold, R. Wurm, I. Lang, G. Strunk, J. Dal-Bianco, R. Levine, M. Hülsmann, G. Goliasch

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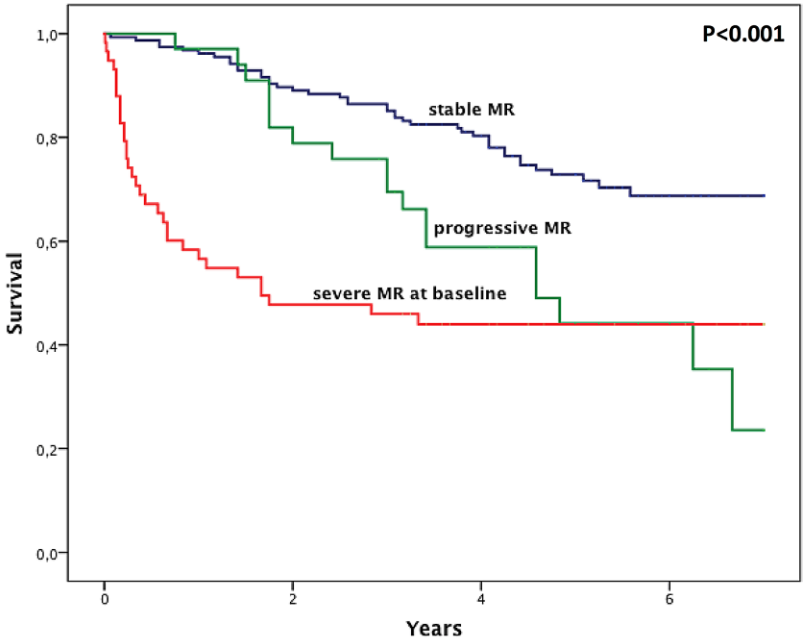
Background: Secondary mitral regurgitation (MR) drives adverse remodeling towards late heart failure stages. Little is known about the evolution of MR under guideline-directed therapy and its relation to cardiac remodeling and outcome. We therefore aimed to assess incidence, impact and predictors of progressive secondary mitral regurgitation in patients under guideline-directed therapy.

Methods and Results: We prospectively enrolled 249 patients with chronic heart failure and reduced ejection fraction receiving guideline-directed therapy in this long-term observational study. Of patients with non-severe MR at baseline 81% remained stable whereas 19% had progressive MR. Those patients were more symptomatic ($P < 0.001$), had higher neurohumoral activation (encompassing various neurohumoral pathways in heart failure, all $P < 0.05$), larger left atrial size ($P = 0.004$) and more tricuspid regurgitation ($P = 0.02$). During a median follow up of 61 months (IQR 50–72), 61 patients died. Progression of MR conveyed an increased risk of mortality—univariately (HR 2.33; 95%CI 1.34–4.08; $P = 0.003$), that persisted after multivariate adjustment using a bootstrap-selected confounder model (adj.HR 2.48; 95%CI 1.40–4.39; $P = 0.002$). In contrast, regression of MR was not associated with a beneficiary effect on outcome (crude HR 0.84; 95% CI 0.30–2.30; $P = 0.73$).

Conclusions: Every fifth patient with chronic heart failure suffers from MR progression. This entity is associated with a more than two-fold increased risk of death even after careful multivariable adjustment. Symptomatic status, left atrial size, tricuspid regurgitation and neurohumoral pathways help to



Stable MR	157	138	108	34
Progressive MR	34	27	16	6
Severe MR at baseline	58	27	19	9

Fig. 1 | FP 3-4

identify patients at risk for progressive secondary MR in an early disease process and open the possibility for closer follow-up and timely intervention.

FP 3-5

The Role of Neurohumoral Biomarkers to Predict Progression of Functional Mitral Regurgitation

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Background: Functional mitral regurgitation (FMR) drives adverse cardiac remodeling in patients with heart failure with reduced ejection fraction (HFrEF). Furthermore, MR is well known to have a strong dynamic component over time progressing in severity and contributing to a transition towards late heart failure stages. Early identification of patients at risk for FMR progression remains challenging. We therefore sought to assess a broad spectrum of neurohumoral biomarkers in patients with HFrEF and to explore their ability to predict progression of FMR.

Methods: 249 HFrEF patients were enrolled. Biomarkers encompassing key neurohumoral pathways in heart failure (i. e. NT-proBNP, MR-proANP, MR-proADM, CT-proET1, copeptin) were sampled at baseline. FMR progression was defined as advance of ≥one grade in severity with transition to ≥moderate during 3 years of follow-up.

Results: Of 191 patients with non-severe MR at baseline 18% showed progressive MR within three years after study enrollment. Among patients with severe MR ($n=58$), we observed a regression of MR in 22%. Progression of MR was associated with higher levels of MR- proADM (OR 1.71, 95%CI 1.21–2.40;P = 0.002), MR-proANP (OR1.48, 95%CI 1.07–2.04;P = 0.017), Copeptin (OR1.41, 95%CI 1.03–1.93;P = 0.03) and CT-proET1 (OR1.52, 95%CI 1.08–2.14; P = 0.01) compared to non-progressing patients, reflecting an association of key neurohumoral-pathways with FMR progression. Importantly, NT-proBNP as the reference biomarker in HFrEF did not predict FMR progression (P = 0.52). Interestingly, the presented neurohumoral markers were not associated with FMR regression (all P > 0.5). Morphological and functional features of patients with subsequent FMR progression were larger left atrial size at baseline (OR 1.70, 95%CI 1.16–2.50;P = 0.006) and more often concomitant tricuspid regurgitation (OR 2.24, 95%CI 1.46–3.42;P < 0.001). No differences in medical and device therapies between patients with subsequent progressive MR and those with stable MR could be found.

Conclusions: Increased plasma levels of neurohumoral cardiac biomarkers are predictors of FMR progression suggesting a potential role to guide clinical workup and follow up in patients with HFrEF. Identifying those patients at significant risk early opens the intriguing possibility to alter the clinical course, either by an early switch to newer heart failure treatment regimens or allocation to low-risk, trans-catheter mitral valve repair techniques in an attempt, to not only reduce symptoms—but also to disrupt the vicious cycle of progressive MR. Importantly, NT-proBNP is not useful to predict progressive MR in the present analysis. The exact mechanism behind this finding might be related to a relative unloading of the LV in the presence of MR- leading to a volume shift directed towards the left atrium. Complementary, MR-proANP, primarily produced in the atrium, increases based on a progressive loading burden by FMR thereby being a better predictor of progression.

FP 3-6

Syncope—The underestimated threat in severe aortic stenosis

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Background: The cardinal symptoms of aortic stenosis (AS) indicating a need for intervention are angina, symptoms of heart failure, and syncope. Nevertheless, it remains unknown whether the presence of these more advanced symptoms conveys an increased risk after surgical aortic valve replacement (SAVR). Since decision-making in severe AS requires a comprehensive pre-operative evaluation of the risk-to-benefit ratio, the aim of this study was to assess whether certain pre-operative symptoms are associated with outcome after SAVR.

Methods and Results: We prospectively enrolled 625 patients with isolated severe AS undergoing elective SAVR in this long-term observational study. Patients experiencing syncope had significantly smaller LV diameters (P = 0.02), LA diameters (P = 0.043), RA diameters (P = 0.001) and RV diameters (P = 0.04) and a smaller AV area (P = 0.048) compared to patients without syncope. During a follow-up period of 10 years, 195 patients died. Kaplan Meier plots demonstrated that patients experiencing syncope had a significantly worse long-term survival compared with those who suffered from exertional dyspnea ≥ NYHA functional class II or exertional angina CCS class ≥ II or reduced LV function (P = 0.004 for comparison between syncope and other primary indications for SAVR, Fig. 1).

Syncope conveyed an increased risk of mortality after SAVR, that persisted after multivariate adjustment for our bootstrap selected confounder model (i.e. EuroSCORE, diabetes, concomitant coronary artery bypass graft (CABG), mean AV gradient) with an adjusted HR of 2.27 (95%CI 1.04–4.95, P = 0.04) for one-year short-term mortality and an adjusted HR of 2.11 (95%CI 1.39–3.21, P < 0.001) for 10-year long-term mortality. In contrast, preoperative NYHA functional class≥II, angina CCS class≥II, or reduced LV function were not significantly associated with outcome.

Conclusions: Syncope represents an underestimated threat in AS patients, associated with poor prognosis after SAVR. Importantly, other primary indications for SAVR, i. e. heart failure symptoms, angina and decreased LV function, had significantly better post-operative outcome than syncope. Patients experiencing syncope displayed a specific pathophysiologic phenotype characterized by a smaller aortic valve area and smaller cardiac cavities.

FP 3-7

Von Willebrand Factor Multimer Ratio for subclassification of low-flow, low-gradient aortic stenosis

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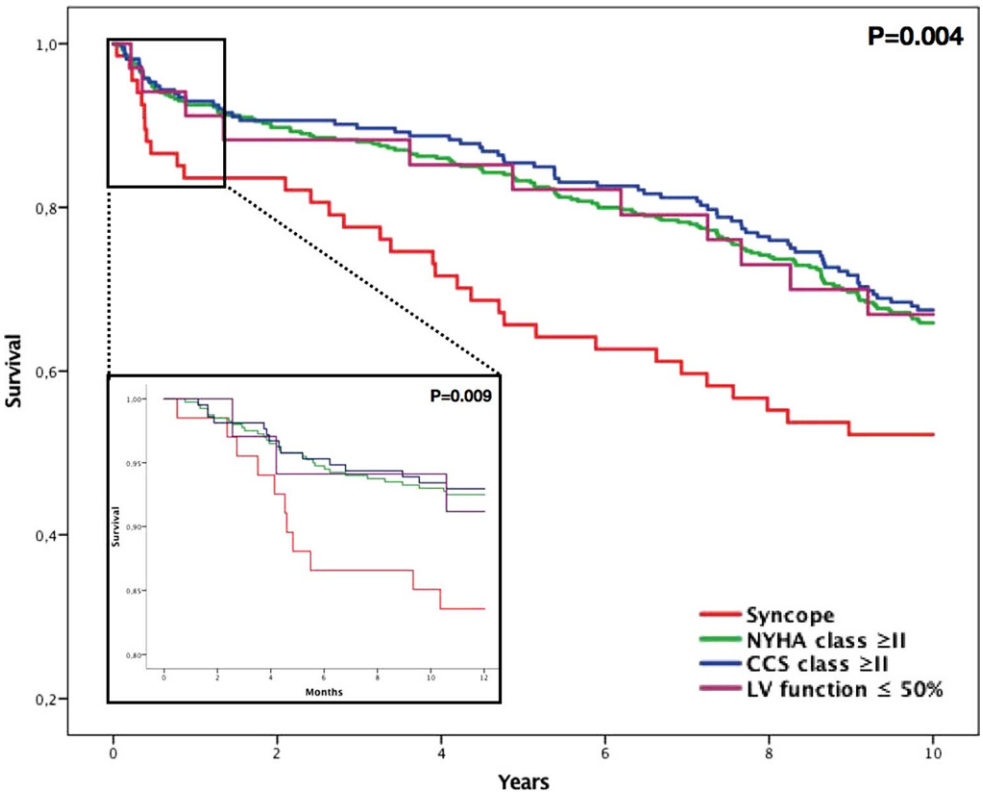

Fig. 1 | FP 3-6

Background: Subclassification of low-flow, low-gradient (LF/LG) aortic stenosis (AS) into a true-severe (TS) and a pseudo-severe (PS) subform bases on dobutamine stress echocardiography (DSE) and multi-detector computed tomography (MDCT). Uncertainty about stenosis severity frequently persists even after these imaging modalities. Therefore, there is a need for a biomarker-based discrimination to expand the diagnostic portfolio. Unfortunately, valueable parameters have not been identified so far.

Sheer-stress induced degradation of high-molecular-weight (HMW) von Willebrand factor (VWF) multimers is a frequent phenomenon at the site of AS, thus, it might represent a valueable biomarker. The present study analysed the value of HMW VWF multimer ratio for LF/LG AS subcategorization.

Methods: Sixty consecutive patients with diagnosis of LF/LG AS (defined by a peak aortic jet velocity <4 m/s + a mean transvalvular pressure gradient <40 mmHg + an AVA <1 cm^2 + a stroke volume index of <35 ml/m^2 + left ventricular ejection fraction <50%) were prospectively recruited and subclassified using DSE and/or MDCT. HMW VWF multimers of all patients were analysed using a densitometric quantification of Western Blot bands and HMW VWF multimer ratio was calculated.

Results: Patients were subclassified into TS LF/LG AS ($n=36$) and PS LF/LG AS ($n=24$) using DSE in 44 patients and MDCT in 16 patients. Patients with PS LF/LG AS showed a mean HMW VWF multimer ratio of 1.07 ± 0.09 while in patients with TS LF/LG AS the mean ratio was 0.82 ± 0.28 ($p<0.001$). HMW VWF ratio presented a ROC-AUC of 0.780 (95%CI: 0.667–0.894; $p<0.001$) with a calculated sensitivity of 0.47 (95%CI: 0.30–0.65) and a specificity of 1.00 (95% CI: 0.86–1.00) at the optimal cut-off <0.91 for diagnosis of the TS subform.

Conclusions: The present study introduces HMW VWF multimer ratio as a novel biomarker for LF/LG AS subclassification. HMW VWF multimer ratio identifies patients with a TS pattern without the use of other imaging modalities, and, therefore, may be integrated in an early stage of the diagnostic work-up of patients with LF/LG AS.

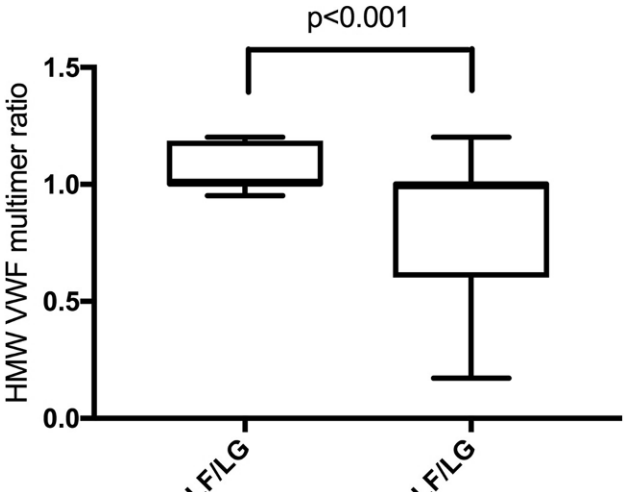

Fig. 1|FP 3-7

Comparison of baseline data of patients with true-severe and pseudo-severe LF/LG AS.

	True-severe LF/LG AS	Pseudo-severe LF/LG AS	p-value
Baseline patient characteristics	**(n=36)**	**(n=24)**	
Age (mean years ± SD)	81 ± 10	79 ± 7	0.088
Male Gender (%)	29/36 (80.6%)	18/24 (75%)	0.751
BMI (mean kg/m^2± SD)	26 ± 4	30 ± 6	<0.001
Baseline echocardiographic data			
Indexed stroke volume (mean ml/m^2 ± SD)	28 ± 4	31 ± 5	0.450
Mean aortic gradient (mean mmHg ± SD)	29 ± 6	25 ± 6	0.002
AVA (mean cm^2± SD)	0.73 ± 0.10	0.84 ± 0.13	<0.001
Baseline laboratory characteristics			
Hemoglobin (mean g/dL ± SD)	13.7 ± 2.3	12.7 ± 1.6	0.018
Platelet count (mean G/L ± SD)	205 ± 37	207 ± 68	0.773
proBNP (mean pg/mL ± SD)	10951 ± 10990	7873 ± 13756	0.039
HMW VWF multimer ratio (mean ± SD)	0.82 ± 0.28	1.07 ± 0.09	<0.001

Abbreviations: AVA: aortic valve area, BMI: body mass index, HMW: high-molecular-weight, proBNP: pro brain natriuretic peptide, SD: standard deviation, VWF: von Willebrand Factor

Fig. 2|FP 3-7

FP 3-8

Advantages of single- and multi-chamber cardioverter defibrillators in reducing inappropriate therapies in 1471 patients

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Background: Inappropriate implantable cardioverter-defibrillator (ICD) therapy is associated with adverse outcome and previous studies indicated that patients with a cardiac resynchronization therapy-defibrillator (CRT-D) might have lower risk for inappropriate therapy than patients with a single or dual chamber ICD (VVI or DDD).

Methods: ICD recipients from 2000–2015 were included in this retrospective analysis. Outcome parameters were occurrence of inappropriate and successful antitachycardia pacing (ATP) and shock therapy.

Results: A total of 1471 patients were analyzed: 629 (42.8%) patients with a VVI-ICD, 486 (33.0%) with a DDD-ICD and 356 (24.2%) with a CRT-D. The mean follow-up was 2.1 ± 1.5, 2.2 ± 1.6 and 1.8 ± 1.4 years in the VVI, DDD and CRT-D group, respectively. Negative binomial regression revealed that CRT-D patients had 82% lower risk of inappropriate ATP (Rate Ratio (RR) = 0.18, $p=0.007$) and 72% lower risk of inappropriate shock therapy (RR = 0.28, $p=0.012$) compared to VVI-ICD patients. Successful ATP occurred 68% less frequent (RR = 0.32,

$p = 0.043$) in CRT-D patients than in VVI-ICD recipients. No significant difference was observed in the incidence of successful shock therapy (RR = 0.63, $p = 0.224$) between the two groups (Fig. 1 | FP 3-8). A non-significant difference of 47% in inappropriate ATP (RR = 0.53, $p = 0.288$) and 54% in inappropriate shock therapy (RR = 0.46, 95%, $p = 0.128$) was observed comparing CRT-D with DDD. Successful ATP occurred 72% less frequent (RR = 0.28, $p = 0.018$) in CRT-D recipients. No significant difference was observed in incidence of successful shock therapy (RR = 0.36, $p = 0.125$) between CRT-D and DDD (Fig. 1). Kaplan-Meier analysis showed a significant difference in time to first inappropriate ATP and shock therapy: CRT-D patients had the lowest cumulative probability of first occurrence of inappropriate ATP ($p = 0.012$, Fig. 2 | FP 3-8a) and inappropriate shock therapy ($p < 0.001$, Fig. 2 | FP 3-8b).

Conclusions: CRT-D patients had the lowest incidence of inappropriate ATP and shock therapy while ATP therapies were less successful compared to VVI and DDD patients. Successful shock therapies were independent from device type and were lowest in CRT-D patients

FP 3-9

Klinische Ergebnisse nach epi-/endokardialer Ablation bei ARVC

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Grundlagen: Die arrhythmogene rechtsventrikuläre Cardiomyopathie (ARVC) ist eine progrediente Herzmuskelerkrankung, die echokardiographisch durch einen morphologisch und funktionell pathologischen rechten Ventrikel (RV) und klinisch durch rezidivierende ventrikuläre Tachycardien (VT), Herzinsuffizienz und plötzlichen Herztod (SCD) charakterisiert ist. Ihre Rolle beim SCD von Athleten und jungen Erwachsenen ist bedeutsam. Die Diagnose wird multimodal anhand umfangreicher Task Force Kriterien gestellt. Ziel des Registers ist eine retrospektive Analyse von klinischen Endpunkten vor Ablation und beim Follow-Up (FU) im Jahr 2018.

Methodik: In den Jahren 2012 bis 2017 wurden 12 Patienten mit bestätigter ARVC einer elektrophysiologischen Untersuchung (EPU) unterzogen. Erfasst wurden demographische, krankheitsspezifische, echokardiographische und Ablations-

Events and rate ratios (RR) of inappropriate and successful therapy, results of negative binomial regression analysis.

	VVI n = (629)	DDD n = (486)	CRT-D n = (356)	CRT-D vs DDD		CRT-D vs VVI	
	Patients with inappropriate and successful therapy n (%)			RR (95% CI)	p-value	RR (95% CI)	p-value
Inappropriate ATP	64 (10.2)	44 (9.1)	15 (4.2)	0.53 (0.17-1.71)	0.288	0.18 (0.05-0.62)	0.007
Inappropriate Shock	64 (10.2)	44 (9.1)	9 (2.5)	0.46 (0.17-1.25)	0.128	0.28 (0.10-0.76)	0.012
Successful ATP	144 (22.9)	123 (25.3)	38 (10.7)	0.28 (0.10-0.80)	0.018	0.32 (0.11-0.96)	0.043
Successful Shock	117 (18.6)	85 (17.5)	36 (10.1)	0.36 (0.10-1.32)	0.125	0.63 (0.30-1.33)	0.224

Fig. 1 | FP 3-8

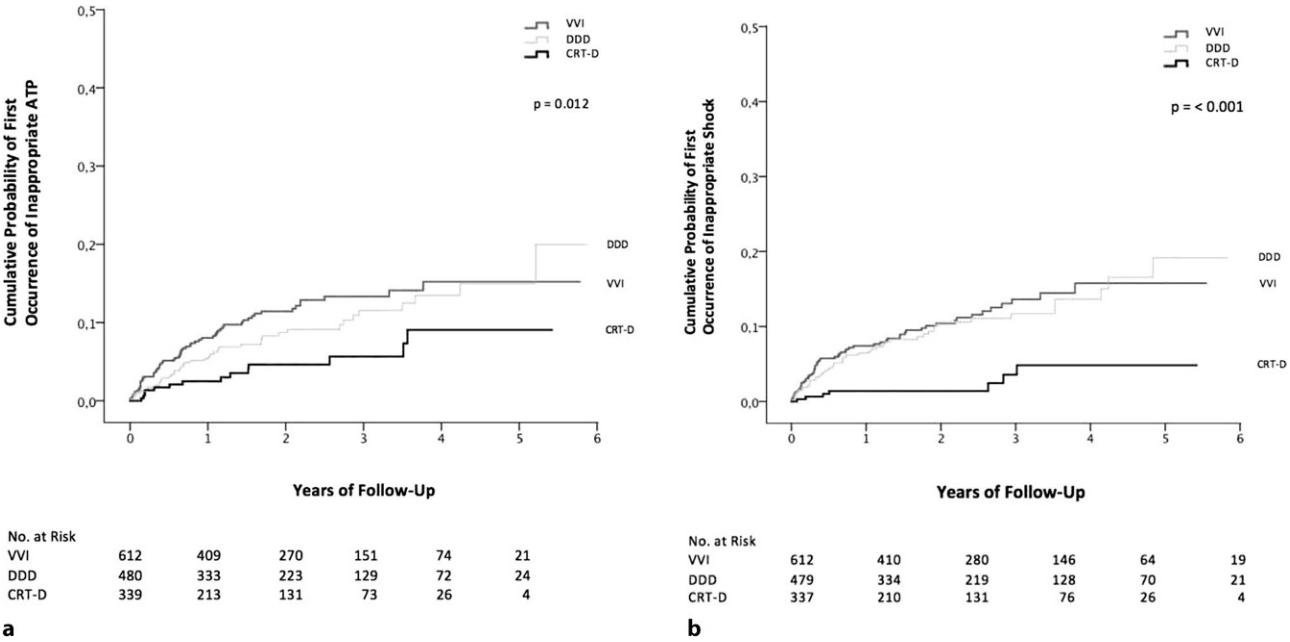

Fig. 2 | FP 3-8

bezogene Daten sowie Therapien durch implantierte Defibrillatoren (ICD). Das FU der Patienten erfolgte über Deviceabfragen, telefonische Kontaktaufnahme oder Krankenhausaufenthalte.

Ergebnisse: 12 konsekutive Patienten (58 % männlich, Alter 46,1 ± 13 Jahre) mit ARVC und implantiertem ICD wurden in die Analyse inkludiert. Relevante Begleiterkrankungen lagen nur bei 1 Patientin mit stattgehabter Myokarditis und weiterhin hochgradig eingeschränkter LVEF vor. Alle Patienten hatten rezidivierende, symptomatische VTs, 27 % rhythmogene Synkopen und 50 % teils repetitive ICD-Schocks in der Anamnese. Zwischen Einschränkung bzw. Dyskinesie des RV im Echo und dem kardialen MRT bestand eine gute Korrelation. Negative T-Wellen über die Brustwandableitung V2 hinaus fand sich im Unterschied zu weiteren EKG-Kriterien bei allen Patienten. ARVC-bezogene Details finden sich in Fig. 1. Im Rahmen der EPUs (Dauer 274 ± 33 min, Narkose) konnte bei 58,3 % endo- bzw. 90,9 % epikardiale Narben detektiert und mit Hochfrequenzenergie ablatiert werden. Punktiert wurde femoral-venös sowie subxiphoidal-epikardial. Substrat-, Voltage- und Pace-Mapping, sowie Ablation von späten und stark fraktionierten Potentialen bildeten die Grundlage der EPU. Alle klinischen VTs wiesen eine LSB-Morphologie und superiore Achse auf. Eine VT-Induktion gelang vor bzw. nach Ablation bei 75 % bzw. 0 % der Patienten. 2 Komplikationen traten auf: 1 × Hämoperikard (Pigtail-Anlage, konservativ), 1 Verschluss eines kleines RCA-Seitenastes. Das FU betrug 30,7 ± 15,6 Monate, wo sich 83,3 % der Patienten als asymptomatisch (VTs, ICD-Schocks, Rehospitalisierung, Lebensqualität) beschrieben. 1 Patientin mit nur endokardialer Ablation erlitt 21 Monate nach Erstpro-

	n	n (%)	mean	SD	min	max
Zn Synkope	3	25%				
Zn Reanimation	0	0%				
ICD implantiert	12	100%				
RV Einschränkung	10	83%				
LV Einschränkung	1	8%				
Rechtskardiales MRT pathologisch	10	83%				
EKG: monotope VES	4	33%				
EKG: Epsilon Wellen	6	50%				
EKG: T-Wellen-Negativierung >V2	12	100%				
Zugang endokardial	11	92%				
Zugang epikardial	11	92%				
Pathologische Voltage endokardial	7	58%				
Pathologische Voltage epikardial	10	91%				
Ablation endokardial	7	58%				
Ablation epikardial	10	91%				
Tachykardie Zykluslänge (ms)			391	92	240	544
Prozedurdauer (min)			274	33	215	315
Maximale Energieabgabe (Watt)			39	4	35	50
VT Induzierbarkeit prä	9	75%				
Nicht-Induzierbarkeit post	12	100%				
Komplikationen	2	17%				

Fig. 1 | FP 3-9

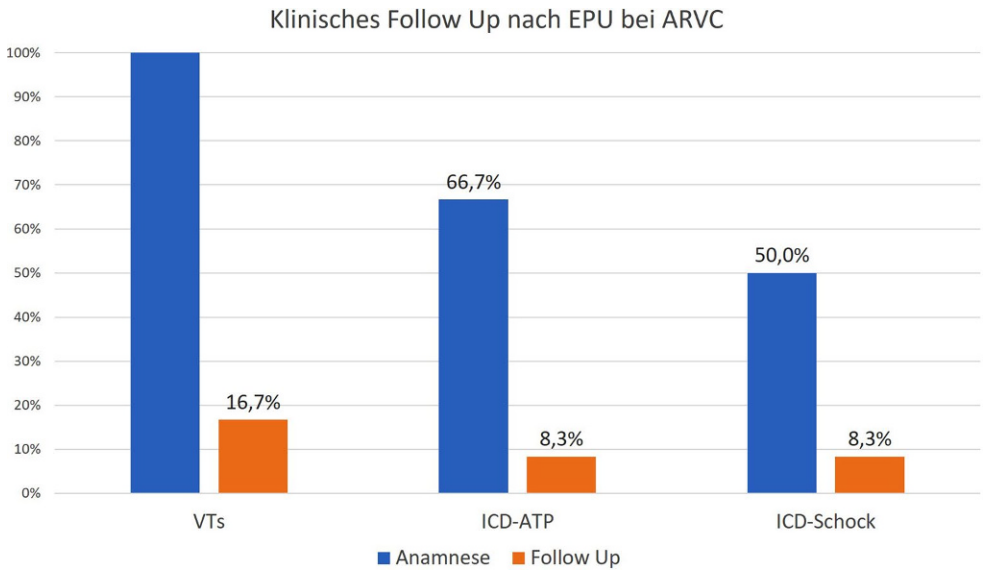

Fig. 2 | FP 3-9

zedur einen VT-Sturm mit repetitiven ICD-Schocks, 1 Patientin oligosymptomatische, nichtanhaltende VTs.

Schlussfolgerungen: Die kombinierte endo-/epikardiale Ablation an Patienten mit symptomatischer ARVC (repetitive VTs, ICD-Schocks) stellt bei erfahrenem EP-Team eine gut durchführbare Therapieoption mit moderatem Komplikationsrisiko und wesentlicher Besserung der Klinik des Patienten durch Reduktion von VTs und ICD-Schocks dar.

FP 3-10

Temporal trends and procedural characteristics of catheter ablation in Austria: Reports from the Austrian Catheter Ablation Registry

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Background: Catheter ablation is an established treatment option for cardiac arrhythmias. Over the past years, ablation outcomes have improved and indications have increased, especially with regard to atrial fibrillation (AF) and ventricular tachycardia (VT) ablation. At the same time, the number of patients eligible for catheter ablation have increased significantly.

Methods: Analysis of the Austrian ablation registry of the working group of arrhythmias of the Austrian Society of Cardiology to report number, indications, procedural characteristics, and outcomes of ablations performed in Austria 2012–2016. The data of all ablation centers was collected via yearly retrospective questionnaire. In addition, centers were invited to enter procedural characteristics in a centralized database.

Results: In 2016, data were collected from all 19 centers performing ablation in Austria. A total of 3342 ablations were performed (median 149 [range 15–455] procedures per center). 14/19 (74%) of all centers performed a total of 1209 AF ablations (median 80 [range 9–220]). Only 9/14 (64%) of all centers performing AF ablation performed >50 AF ablations, a cutoff generally suggested by international guidelines. 12/19 (63%) of all centers performed 145 VT ablations [median 8 (range 1–47)] in patients with structural heart disease. Only 5/12 (42%) of all centers performing VT ablation performed >10 VT ablations.

The median Austrian ablation center performed 43 AF ablation procedures and 2 VT ablation procedures in 2016. Overall, the 19 centers had a capacity of 51 ablation days/week [median 2.5 (range 0.5–5). Only 4 centers had ablation capacity 5 days/week. A median of 2 (range 1–4) trained electrophysiologists and 1 (range 0–3) EP fellows worked per center.

In a representative subset of 9 centers more detailed procedural data of 1679 ablations (41% female patients; 50% of all ablations in 2016) was collected via a centralized database. 199 (12%) of all referrals came from outside the center's state. The most frequent ablation indication was AF (35%), followed by AVNRT (23%) and atrial flutter (14%). The overall rate of re-ablations was 11%. Radiofrequency energy is used most frequently (86%), followed by cryoenergy (8%), and other (6%). A 3D mapping system was used in 59% of ablations. The procedural endpoint was reached in 91%, and the overall rate of major and minor complications was 3.6%. Most common major complications was pericardial effusion requiring drainage (0.9%).

Between 2012 and 2017, total number of EP studies (2845 vs. 3601), total number of ablations (2671 vs. 3342), AF ablations (880 vs. 1209), and VT ablations (100 vs. 145) increased significantly (all $p<0.05$). Over the past 10 years, whereas the number of ablation centers in Austria did not increase (2.3 vs 2.2 ablation centers/Mio 2007 vs 2016; $p=$ ns), the number of total ablations (182 vs. 384 ablations/Mio 2007 vs. 2016; $p<0.01$) and of AF ablations performed (29 vs. 139 ablations/Mio 2007 vs. 2016; $p<0.01$) increased significantly

Conclusions: AF is the most common catheter ablation indication in Austria, followed by AVNRT and atrial flutter. Success rates, procedural characteristics, and complication rates are similar to international registries and major studies. While ablation numbers in Austria are constantly increasing, the number of ablation centers is not.

POSTERSITZUNG 1 – Akutes Koronarsyndrom

1-1

De-Ritis ratio predicts long-term mortality in patient with acute myocardial infraction

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Background: Despite decreasing rates of acute myocardial infarction (AMI) within the western society, the identification of patients at risk for fatal cardiac adverse events after the acute phase of AMI is still a challenging field in clinical practice. While, recent data revealed that liver-transaminases such as aspartate aminotransferase (AST) or alanine transaminase (ALT) are potential predictors for patient survival after AMI, the impact of AST/ALT (De-Ritis) ratio on patient outcome has not been investigated so far. Therefore, we aimed to elucidate the prognostic potential of the De-Ritis ratio on the patient outcome after AMI from a long-term perspective.

Methods: A total of 1355 patients presenting with AMI admitted between 12/1996 and 01/2010 to the Medical University of Vienna were included within a clinical registry. Blood samples were taken at time of hospital-admission. The De-Ritis ratio was calculated as the ratio of AST and ALT using (Cobas C System, Roche Diagnostics, Switzerland). Patients were followed prospectively until the primary study endpoint (= cardiovascular mortality) was reached. Cox regression hazard analysis was used to assess the impact of the De-Ritis ratio on long-term

mortality. The multivariate model was adjusted for potential confounders.

Results: In 1355 enrolled individuals (median age: 63 years [IQR: 43–81]; 58.7% male gender) median the De-Ritis ratio was 1.5 (IQR: 1.0–2.6). After a median follow-up time of 8.6 years, corresponding to 11.499 patient years, a total of 554 (40.9%) individuals died. We found that AST (crude HR of 1.20 per one standard deviation (1-SD) [95%CI: 1.10–1.32; $p<0.001$]) and De-Ritis ratio (crude HR of 1.46 per 1-SD [95%CI: 1.28–1.66; $p<0.001$]) were significantly associated with long-term survival while we observed no effect of ALT (crude HR per 1-SD of 0.99 [95%CI: 0.88–1.13, $p=0.946$]). However, while the prognostic potential of AST was lost after adjustment for confounders in the multivariate model, De-Ritis remained independently associated with long-term mortality with an adjusted HR of 1.36 per 1-SD (95%CI: 1.12–1.66; $p=0.002$). With regard to receiver operating characteristics (ROC) the discriminatory power for De-Ritis was better with an area under the curve (AUC) of 0.642 than both AST (AUC: 0.537) and ALT (AUC: 0.463).

Conclusions: De-Ritis ratio proved to be a strong and independent predictor for mortality after AMI from a long-term perspective. As a routinely available marker in clinical practice, it can be easily used to identify patients at risk for fatal cardiovascular events and contribute to proper secondary prevention after AMI.

1-2

Impact of ST-segment elevation pattern in patients with TakoTsubo syndrome

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Background: The clinical significance of ST-segment elevation pattern in patients with TakoTsubo syndrome is unknown. However, in patients with anterior STEMI, both the convex and the straight type ST-segment elevation are associated with worse left ventricular function and a higher rate of cardiovascular complications. We sought to investigate the implications of ST-segment elevation pattern in TakoTsubo syndrome.

Methods: The present single-center study included 85 patients diagnosed with TakoTsubo syndrome between 2006 and 2017. The study population was divided into three groups based on the pattern of ST-segment elevation on 12-channel ECG at admission: Group A (concave type, $n=38$), group B (straight type, $n=5$) and group C (convex type, $n=9$), respectively. Patients with no ST-segment elevation ($n=33$) were excluded from the further analysis. Baseline characteristics, cardiac biomarkers, LVEF and in-hospital complications were compared among the groups.

Results: Baseline characteristics were largely comparable, except for a higher prevalence of chronic renal failure and no history of hypertension in the straight type ST-segment elevation group. The number of in-hospital cardiovascular complications was significantly higher in the straight type group ($p<0.001$) and patients with convex type ST-segment elevation were hospitalized for a significantly longer time than patients from the other two groups ($p<0.001$). Logistic regression analysis demonstrated that patients with straight type ST-elevation were at a higher risk of cardiovascular complications (OR: 33.750, 95% CI: 3.445 to 330.608; $p=0.003$), while concave type ST-elevation was associated with a lower risk (OR: 0.068, 95% CI: 0.007 to 0.674; $p=0.022$). Presence of convex ST-segment elevation had no effect on cardiovascular complications (OR: 1.219, 95% CI: 0.120 to12.397; $p=0.867$). Furthermore, there were no statistically significant differences in left ventricular ejection fraction or level of cardiac biomarkers between the groups.

Conclusions: The present study indicates that ST-segment elevation pattern in patients with TakoTsubo syndrome has an impact on in-hospital cardiovascular complications and length of hospital stay. In order to use ST-segment pattern at admission ECG as a tool for risk stratification in patients with TakoTsubo syndrome, additional studies with larger sample sizes are needed to validate the findings of the study.

1-3

Long-term mortality in TakoTsubo patients treated with different antiaggregation therapy

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Background: TakoTsubo syndrome (TTS) is an acute and usually reversible heart failure syndrome, which initially presents similarly as an acute coronary syndrome (ACS). Although, the underlying pathophysiology of TTS is different to myocardial infarction patients are occasionally discharged on antiplatelet therapy due to the lack of clear recommendations.

Aim: The aim of this study was to investigate if antiplatelet therapy improves the outcome of patients with TakoTsubo syndrome after discharge compared to no such strategy.

Methods: Data from 117 consecutive TTC patients, who were admitted to our department between 2006 and 2016, were analyzed. Patients on oral anticoagulation were excluded. The study population was stratified into patients on no antiplatelet therapy, patients on aspirin only life-long and patients on dual antiplatelet therapy for 12 months (DAPT) followed by ASA monotherapy, respectively. The different secondary prevention strategies were based on the discretion of the treating cardiologist. Differences in patient characteristics, as well as all-cause and cardiovascular long-term mortality, were investigated. Multivariable regression analysis was performed to adjust for confounders.

Results: In total 99 patients were included into the study (no antiplatelet therapy, $n=11$; aspirin only, $n=44$; DAPT, N = 44). Mean follow-up time of all patients was 5.9 years. There were no differences in patient's characteristics between the three groups. Neither the long-term cardiovascular or all-cause mortality was significantly different in the crude (cardiovascular mortality $\chi^2(2)=0.835$, $p=0.659$; all cause mortality $\chi^2(2)=0.387$, $p=0.824$, respectively) and multivariable regression analysis (long-term cardiovascular mortality HR = 0.611; CI = 0.209–1.788, $p=0.368$; long-term all-cause mortality HR = 0.811; CI = 0.449–1.464, $p=0.488$, respectively).

Conclusions: Despite some limitations, the study was neither randomized nor blinded, single center and retrospect in design, the data obtained show that long-term antiplatelet treatment in patients after an index TTS has no impact on hard clinical outcome and has therefore no indication.

Variables	Total (N=99)	No antiplatelet therapy (N=11)	Aspirin only (N=44)	Dual antiplatelet therapy (N=44)	p-value
Age, yrs (mean +/- SD)	67,8 (±12,28)	65,2 (±15,88)	67,7 (±10,0)	68,6 (13,48)	0,722
Female (%)	81,8	63,6	77,3	90,9	0,064
Hypertension (%)	62,2	45,5	62,8	65,9	0,455
Hyperlipidemia (%)	27,8	27,3	25,6	30,2	0,890
Diabetes mellitus (%)	19,2	9,1	18,2	22,7	0,575
• on diet	5,2	0	7,0	4,7	0,639
• on oral antidiabetics	10,3	9,1	7,0	14,0	0,565
• on insulin	2,1	0	2,3	2,3	0,880
History of MI (%)	6,2	9,1	4,7	7,0	0,827
History of PCI (%)	5,2	0	2,3	9,3	0,245
Family history of CAD (%)	5,4	18,2	2,4	5,0	0,117
History of stroke (%)	7,3	0	9,5	7,0	0,554
COPD (%)	21,6	27,3	20,9	20,9	0,891
PAOD (%)	4,1	0	7,0	2,3	0,425
Atrial fibrillation (%)	2,0	0	2,3	2,3	0,879
Renal insufficiency (%)	8,2	9,1	9,3	7,0	0,921
Psychiatric disease (%)	13,7	27,3	16,7	7,1	0,169
Neurological disease (%)	16,7	18,2	20,9	11,9	0,531
Cancer (%)	4,0	9,1	2,3	4,5	0,575
Trigger (%)					
• Emotional	12,2	18,2	15,6	6,5	0,294
• Physical	39,2	27,3	50,0	32,3	0,321
• Both	5,4	9,1	6,3	3,2	0,586
EF; % (mean, ±SD)	50,3 (±14,39)	48,4 (±16,99)	47,5 (±13,72)	53,7 (±14,13)	0,137

Fig. 1|1-3 Baseline characteristics of 99 TakoTsubo patients and groups based on the antiplatelet therapy on discharge. *SD* – Standard deviation, *MI* – myocardial infarction, *PCI* – percutaneous coronary intervention, *CAD* – coronary artery disease, *COPD* – chronic obstructive pulmonary disease, *PADD* – peripheral arterial occlusive disease, *EF* – ejection fraction

1-4

The presence of non-significant coronary artery atheromas vs. completely normal coronary arteries as demonstrated by CAG in patients with Tako-Tsubo syndrome has no impact on clinical outcome

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Background: With respect to the Mayo Clinic diagnostic criteria, patients with Tako-Tsubo cardiomyopathy (TTC) demonstrate either completely normal coronary arteries or present with non-significant luminal narrowing of less than 50% in epicardial coronary arteries as confirmed by coronary angiography (CAG).

Aim: The aim of this study was to investigate potential differences in in-hospital and long-term all-cause and cardiovascular mortality in TTC patients with/without nonsignificant atheromas (luminal narrowing ≤ 50%) at diagnostic CAG.

Methods: Data from 117 consecutive TTC patients, who were admitted to our department between 2006 and 2016, were analyzed. The study population was stratified into patients presenting with completely normal diagnostic CAG or with one or more non-significant luminal narrowings. Differences in patient characteristics, levographic findings, discharge medication, as well as in in-hospital and long-term all-cause and cardiovascular mortality were investigated. Multivariable regression analysis was performed to adjust for confounders.

Results: Patients presenting with non-significant stenoses were older, had a more frequent history of percutaneous coronary intervention and the TTC event has been more often preceded by emotional or physical trigger. However, there were no differences in patient characteristics, including the risk factors hypertension, hyperlipidemia and diabetes mellitus or concerning laboratory values, ejection fraction, anatomical type of TTC or discharge medication, respectively (Fig. 1). The mean follow-up time of all patients was 5.7 years. We could demonstrate only a numerical but non-statistically significant difference between groups with higher in-hospital (3.6% vs. 8.3%) and long-term all-cause mortality (29.2% vs. 37.7%) but lower rates for long-term cardiovascular mortality (7.1% vs. 4.9%) for patients with wall irregularities as compared to patients with normal coronary arteries at diagnostic CAG. This difference remained non-significant by unadjusted (in-hospital mortality HR = 1.831; CI = 0.335–10.000, $p = 0.485$; long-term all-cause mortality HR = 1.316; CI = 0.695–2.493, $p = 0.400$, long-term cardiovascular mortality HR = 0.711; CI = 0.159–3.180, $p = 0.655$, respectively) or by multivariable regression analysis adjusted for confounders (in-hospital mortality HR = 1.184; CI = 0.205–6.858, $p = 0.850$; all-cause long-term mortality HR = 0.960; CI = 0.477–1.934, $p = 0.909$, long-term cardiovascular mortality HR = 0.425; CI = 0.087–2.085, $p = 0.292$, respectively) (Fig. 2).

Conclusions: The presence of non-significant coronary artery disease had no effect on short- and long-term mortality rates in patients presenting with TTC despite a higher cardiovascular risk profile. Future investigations should include high solution imaging methods like OCT or IVUS for TTC patients with normal looking arteries and might deliver further information about underlying vessel pathologies and clinical outcome.

Variables	Total (N=117)	Normal CAG (N=56)	Non-significant stenosis (N=61)	p-value
Age, yrs (mean +/- SD)	79,7 (±12,49)	66,6 (±13,57)	72,5 (±10,75)	**0,009**
Female (%)	81,2	78,6	83,6	0,486
Hypertension (%)	63,5	61,8	65,0	0,723
Hyperlipidemia (%)	30,4	32,7	28,3	0,609
Diabetes mellitus (%)	19,7	14,3	24,6	0,161
• on diet	6,0	3,6	8,2	0,292
• on oral antidiabetics	10,3	5,4	14,8	0,094
• on insulin	0,9	1,8	0	0,295
History of MI (%)	5,3	1,9	8,3	0,122
History of PCI (%)	4,4	0	8,3	**0,030**
Family history of CAD (%)	6,3	7,7	5,1	0,573
History of stroke (%)	7,4	8,5	8,0	0,468
COPD (%)	21,1	27,8	15,0	0,095
PAOD (%)	7,9	3,7	11,7	0,115
Atrial fibrillation (%)	13,9	12,7	15,0	0,725
Renal insufficiency (%)	9,6	5,6	13,3	0,160
Psychiatric disease (%)	10,7	17,0	5,1	0,042
Neurological disease (%)	12,4	13,2	11,7	0,804
Cancer (%)	6,0	5,4	6,6	0,785
Hospitalized for another reason (%)	24,8	27,3	22,4	0,550
Trigger (%)				
• Emotional	7,7	10,7	4,9	0,249
• Physical	34,2	28,6	39,3	0,220
• Both	2,6	5,4	0	0,067
• None	35,0	50,0	21,3	**0,001**
Smoking (%)	29,9	33,9	26,2	0,364
Alcohol addiction (%)	7,9	7,4	8,3	0,855
In-hospital complications (%)				
• Cardiovascular	12,8	10,7	14,8	0,514
• Non-cardiovascular	8,5	10,7	6,6	0,422
• Both	6,0	5,4	6,6	0,785
Cardiac decompensation (%)	17,0	13,0	20,7	0,276
EF; % (mean, ±SD)	49,3 (±13,45)	51,1 (±14,26)	47,7 (±12,52)	0,195
Ventricle dysfunction (%)				
• apical	34,2	28,6	39,3	0,220
• midventricular	7,7	10,7	4,9	0,240
• apical-midventricular	45,3	50,0	41,0	0,328
• basal	3,4	1,8	4,9	0,352
Beta blockers (%)	62,7	58,5	66,7	0,376
ACE-i (%)	44,5	43,4	45,6	0,815
Diuretics (%)	35,5	28,3	42,1	0,130
Sartans (%)	12,7	11,3	14,0	0,670
Calcium channel blockers (%)	7,3	5,7	8,8	0,530
P2Y12 inhibitors (%)	41,8	37,7	45,6	0,403
Acetylsalicyl acid (%)	80,9	77,4	84,2	0,361
CK, U/L (mean, ±SD)	368,2 (±589,48)	424,0 (±670,74)	317,1 (±504,32)	0,505
CK-MB, U/L (mean, ±SD)	52,5 (±37,3)	48,2 (±36,36)	56,2 (±38,45)	0,450
Troponin I, ng/mL (mean, ±SD)	4,3 (±6,85)	4,6 (±7,90)	3,9 (±,68)	0,988
NT-pro-BNP, pg/mL(mean, ±SD)	6927,6 (±12307,94)	5257,2 (±6789,01)	9112,3 (±17075,13)	0,427

Fig. 1|1-4 Baseline characteristics, discharge medication and laboratory values of 117 TakoTsubo patients and groups based on the stenosis of coronary arteries.
SD – Standard deviation, *MI* – myocardial infarction, *PCI* – percutaneous coronary intervention, *CAD* – coronary artery disease, *EF* – ejection fraction, *ACE-I* – angiotensin-converting-enzyme inhibitor, *CK* – creatine kinase, *CK/MB* – Creatine kinase-MB, *NT-pro-BNP* – N-terminal pro brain natriuretiv peptide, *SD* – Standart deviation

1-5

Using Manchester Triage plus nurses' standard procedure in emergency departments may identify patients at risk earlier

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Background: Using Manchester Triage System (MTS) is standard procedure in Emergency Departments (ED) worldwide [1]. Misjudgments in MTS are well known [2]. Patients with acute coronary syndrome (ACS) presenting with atypical clinical symptoms may have waiting periods up to 120 minutes to first medical contact (FMC). Notably, current guidelines of the European Society of Cardiology (ESC) postulate an ECG within 10 minutes after FMC and a door-in to door-out time ≤30 minutes in non PCI-centers for patients with ACS [3]. Optimizing clinical management addressing patients at risk with atypical clinical presentation in ED is deemed necessary.

Methods: Recognizing that a noteworthy number of patients with cardiac diagnoses had delayed FMC applying standard MTS, we adopted medical proceedings in our ED. We combined MTS with nurses' standard procedure (NSP) for all ED patients in MTS-categories 3–5 including ECG recording and blood draws for predefined lab analyses immediately after triage. We denominated our proceedings MTS-2.0 (Fig. 1). Prior to adopting MTS-2.0 and six month subsequently, we measured time intervals of ED patients with respect to duration of treatment periods such as administration, triage, NSP or time to FMC (Fig. 2). It was our intention to demonstrate, whether

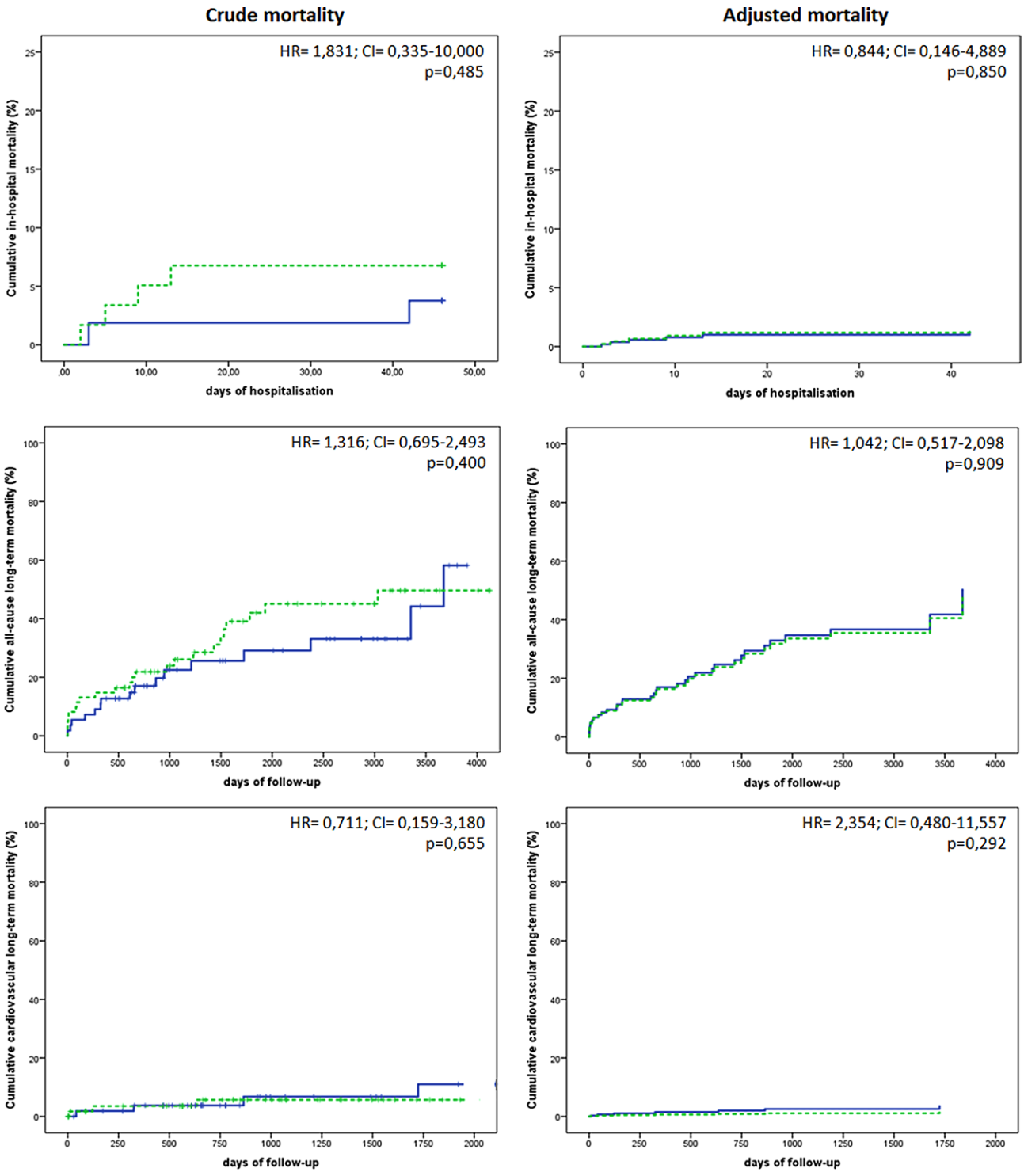

Fig. 2|1-4

an ECG recording as soon as possible could identify patients at risk earlier.

Results: Screening 198 patients before and 250 after initiating MTS-2.0 patients with ACS were addressed primarily. There was no problem to manage patients with ACS and typical clinical presentation according to ESC-guidelines after they were assigned to MTS-category 1. This was not the case, if patients with ACS had atypical clinical symptoms. Using MTS-2.0 all ED patients in MTS-categories 3–5 received ECG recording within 25 minutes after administration (T1→T4). If these patients had suspicious ECG they were assigned immediately to MTS-category 1 (Fig. 2, red arrow). A case series of patients in MTS categories 3–5 showed that diagnosis of ACS was made up to 74 minutes earlier with MTS-2.0 than with routine MTS. Nevertheless we did not attain door-in to door-out time according ESC-guidelines for these patients in our non PCI-center.

Conclusions: MTS-2.0 ascertains ECG for all patients in our ED within at least 25 minutes after administration. Early ECG

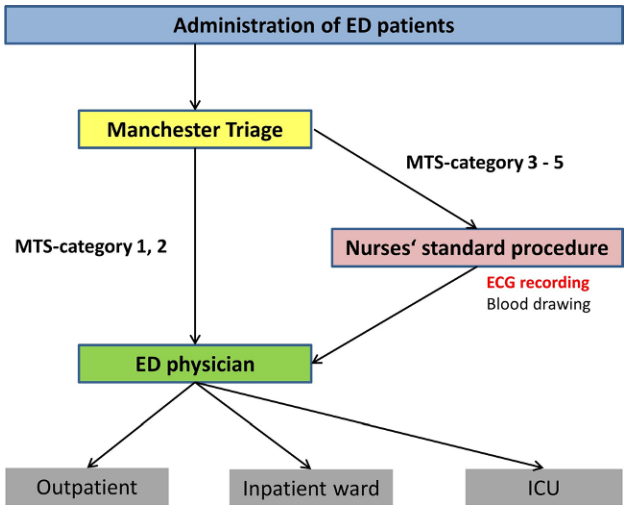

Fig. 1|1-5

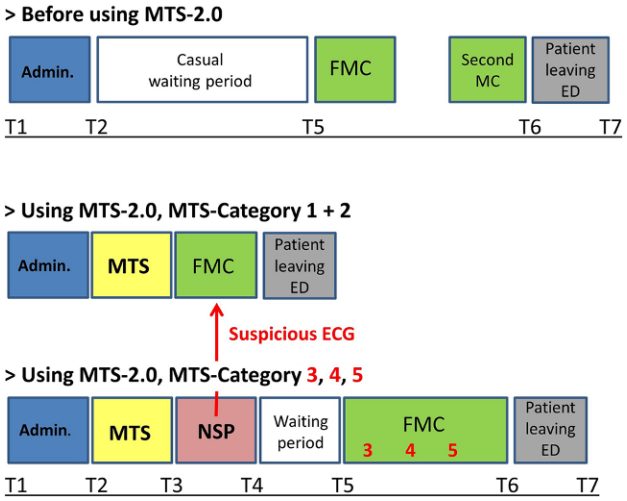

Fig. 2|1-5

is crucial to identify patients at risk with atypical clinical presentation who might receive delayed medical treatment when standard MTS is applied. MTS-2.0 may increase the quality of patients' medical care in ED. Prospective studies are necessary to proof our concept.

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1-6

Prevalence, predictors, and prognosis of premature discontinuation or switch of oral antiplatelet therapy after acute coronary syndrome: ATLANTIS—SWITCH substudy

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Background: Non-adherence to medication regimen after acute coronary syndrome (ACS) leads to increased morbidity and mortality and generates additional cost to the healthcare system. In particular, cessation of antiplatelet treatment after coronary interventions may lead to serious adverse events.

Aim: To investigate the prevalence and predictors of premature discontinuation or switch of antiplatelet therapy and its association with serious adverse events.

Methods: 571 consecutive ACS patients receiving ticagrelor ($n=258$, 45%) or prasugrel ($n=313$, 55%) undergoing percutaneous coronary intervention in the course of ACS were enrolled in the prospective, observational, multicenter ATLANTIS-SWITCH substudy. Predictors of premature discontinuation or switch of antiplatelet therapy and their association with major adverse cardiovascular events (MACE: composite endpoint of cardiovascular death, myocardial infarction, repeat revascularization, ischemic stroke) and TIMI bleeding events were evaluated during one year follow-up period.

Results: In the overall cohort, 36 (5.8%) patients prematurely stopped and 38 (6.7%) switched antiplatelet therapy (all were switched down: from ticagrelor/prasugrel to clopidogrel). Ticagrelor treated patients were significantly more likely to prematurely stop/switch therapy as compared to prasugrel treated patients (15.5% vs. 8.9%, $p=0.016$). Within a period of one year, patients were on average 16 days longer treated with prasugrel than with ticagrelor: the mean adherence time to ADP-blocker therapy was 342 days for prasugrel vs 326 days for ticagrelor (Log Rank $p=0.0346$) (Fig. 1). The mean time until stop or switch of ADP-blocker was 87 days for ticagrelor and 105 days for prasugrel treated patients ($p=0.502$). TIMI major bleeding was a significant driver of premature ticagrelor discontinuation or switch (bleeding occurred in 5% in those who stopped/switched vs 0.4% in those who did not stop/switch; $p<0.001$), whereas no major bleeding events leading to stop/switch of therapy occurred in the prasugrel group. In the majority of patients (42%), the ADP blocker therapy was stopped/switched due to the additional indication for oral anticoagulation. The majority of stop/switch actions (75%) were physicians driven decisions. Importantly, stop/switch of antiplatelet therapy was not associated with increased risk of MACE ($p=0.470$).

Conclusions: Major bleeding events were significant driver of therapy cessation or switch to clopidogrel in ticagrelor but not in prasugrel treated patients. Premature switch/stop of ADP blockers seems to be safe when mainly driven by physician's decision and clinical indication.

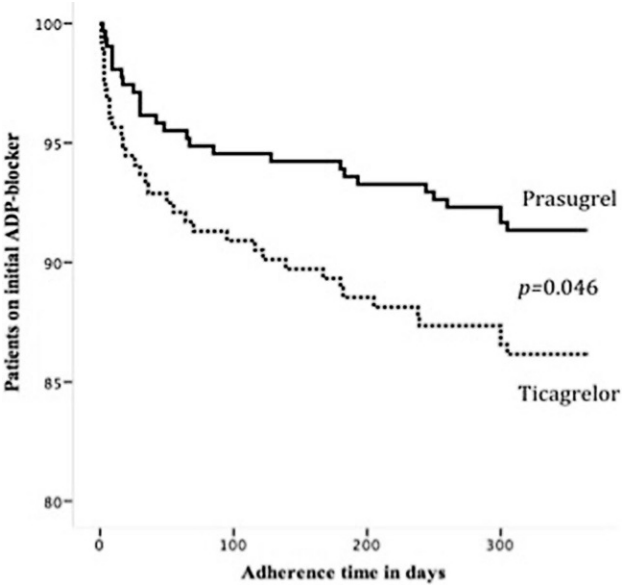

Fig. 1|1-6

1-7

Antithrombotische Therapie nach Myokardinfarkt und Indikation für eine orale Antikoagulation

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Grundlagen: Bei 3–8 % aller Patientinnen und Patienten, die eine perkutane koronare Intervention (PCI) im Rahmen eines akuten Koronarsyndroms (ACS) erhalten, und daraufhin eine duale Plättchenhemmung benötigen, ist zusätzlich eine dauerhafte Antikoagulation indiziert. Die sogenannte antithrombotische Triple-Therapie, bestehend aus einem oralen Antikoagulans, Acetylsalicylsäure und einem P2Y12-Rezeptorantagonisten, ist mit einem hohen Risiko für Blutungen besetzt. Die Anzahl der hierfür möglichen Therapieschemata ist groß, jedoch das Vorgehen nicht mit großen prospektiven randomisierten kontrollierten multizentrischen Studien belegt.

Methodik: Ziel dieser Arbeit war die Erstellung einer Standortanalyse bezüglich der Therapieempfehlungen der Jahre 2005 bis 2013 für dieses Patientenkollektiv an der Inneren Medizin III (Kardiologie) des Universitätsklinikums Innsbruck. Die Auswertungen basieren auf Daten der 3774 Innsbrucker Patienten des „Akut-PTCA Registers“ der Österreichischen Kardiologischen Gesellschaft (ÖKG) der Jahre 2005 bis 2013.

Ergebnisse: Bei 7,4 % ($n=258$) der Patienten stellte sich die Indikation zur Antikoagulation (AK). Von diesen Patienten bekamen 43,2 % ($n=120$) eine AK-Therapie. Triple-Therapie war die hierfür am häufigsten empfohlene Kombination (32,9 %), gefolgt von dualer Therapie mit ASS plus AK (6,2 %), P2Y12-Rezeptorantagonist plus AK (3,9 %) und AK-Monotherapie (3,5 %). Den restlichen 56,8 % ($n=158$) wurde eine DAPT empfohlen. Es ließ sich weder eine sichere Korrelation zwischen den Risikoprofilen für Schlaganfälle und Blutungen bezüglich der Dauer der initialen Triple-Therapie, noch für Empfehlungen weniger intensiver Schemata (DAPT, duale Therapie oder AK-Monotherapie) feststellen. Patienten, die eine AK-Therapie erhielten, waren durchschnittlich 9 Jahre älter und wiesen ein breiteres Risikoprofil auf.

Schlussfolgerungen: Es besteht eine Diskrepanz zwischen Indikation für Antikoagulation und tatsächlicher Therapieempfehlung bei Patienten nach ACS und PCI. Es bedarf klarer evidenzbasierter risikoadaptierter Therapiealgorithmen für dieses Patientenkollektiv, welches ein Zwölftel aller ACS-Patienten darstellt.

1-8

Long-term prognosis of patients developing de-novo atrial fibrillation after acute myocardial infraction

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Background: With a prevalence ranging from 2% to 21%, the development of atrial fibrillation (AF) in the acute phase of acute myocardial Infarction (AMI) is a well-known and common condition in clinical practice. While the prognosis of patients presenting with de-novo AF (dnAF) has been controversially discussed, it seems intuitive that affected individuals have an increased risk for both thromboembolic events and mortality. However, profound data on long-term mortality of this highly vulnerable patient population are not available in current literature. Moreover, the 2017 ESC Guidelines on the management of ST-segment elevation myocardial infarction underlined a strong need to elucidate treatment strategies for this high-risk patient population. Therefore, we aimed to investigate the impact of dnAF on the patient outcome from a long-term perspective.

Methods: A total of 1372 patients presenting with AMI between 12/1996 and 01/2010, treated at the Medical University of Vienna, were enrolled within a clinical registry and screened for the development of dnAF. After discharge participants were followed prospectively until the primary study endpoint (=cardiovascular mortality) was reached. Cox regression hazard analysis was used to assess the impact of dnAF on long-term mortality. The multivariate model was adjusted for potential confounders.

Results: Out of 1372 enrolled individuals (median age: 57 years [IQR: 42–80]; 58.8% male gender), 90 (6.5%) presented with a pre-existing AF (peAF) and 149 (10.9%) developed dnAF during the acute phase of AMI. After a median follow-up time of 8.6 years, corresponding to 11.617 patient years, a total of 418 (30.5%; including 25 patients [5.9%] with fatal cerebrovascular event) individuals died due to cardiovascular causes, with 16 individuals in the peAF subgroup (17.8%; including 1 patient [6.3%] with fatal cerebrovascular event) and 93 (62.4%; including 9 patients [9.6%] with fatal cerebrovascular event) in the dnAF subgroup, respectively. We found that dnAF was significantly associated with long-term cardiovascular mortality with an adjusted HR of 1.67 (95%CI: 1.29–2.16; $p<0.001$). Both, dual anti-platelet therapy (DAPT; $p=856$) and vitamin-K antagonist therapy (VKA; $p=0.346$) alone were not associated with a survival benefit in individuals presenting with dnAF. Of utmost interest, while patients with dnAF were less likely to receive a triple therapy at the time of discharge (dnAF: 37.6% vs. peAF:

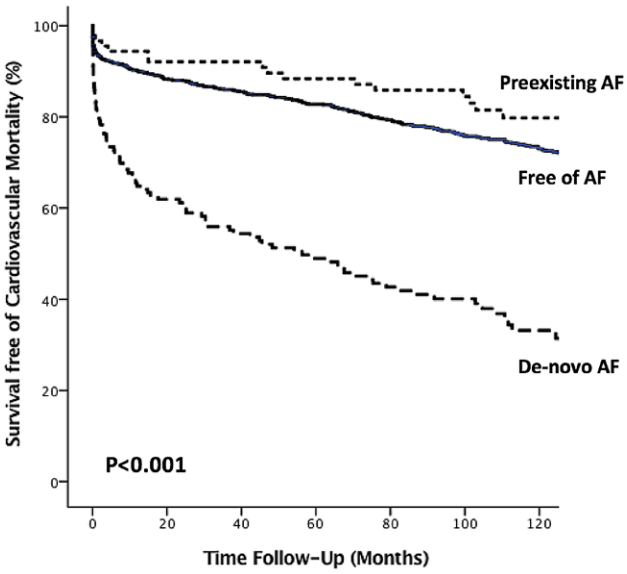

Fig. 1|1-8

65.6%; $p<0.001$), it showed a strong and inverse association with mortality in dnAF, with an adj. HR of 0.86 (95%CI: 0.45–0.92; $p=0.012$).

Conclusions: dnAF was independently associated with a poor patient prognosis with an increased long-term risk for cardiovascular mortality by 67%. These data prompt prospective studies focusing on a comprehensive and intensified management of this high-risk patient population.

1-9

Copeptin plasma level in type 1 and type 2 myocardial infarctions

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Background: During the last years, distinguishing between type 1 (T1MI) and type 2 myocardial infarction (T2MI) by use of biomarkers became a matter of clinical interest. This study aimed to investigate whether copeptin plasma levels can help to differentiate between T1MI and T2MI.

Methods: In a retrospective analysis, 959 unselected consecutive patients with chest discomfort and suspicion of acute MI were evaluated. Patients diagnosed with ST-elevation MI were excluded from the analysis. The remaining patients were classified into T1MI, T2MI, and no-MI, using clinical assessment and coronary angiography. Copeptin concentrations were measured using Thermo Scientific BRAHMS Copeptin ultrasensitive Kryptor assay and compared between both MI subtypes. Furthermore, univariable and multivariable regression analyses for significant confounders were performed.

Results: After exclusion of 848 patients (747 no MI and 102 STEMI), 111 (11.6%) subjects with NSTE-ACS were included in the analysis. Of those, 62 (55.9%) were classified by clinical means as T1MI and 49 (44.1%) as T2MI. The Mann-Whitney-U test revealed a significant difference in copeptin plasma concentrations between T1MI and T2MI patients (7.95 pmol/l [IQR 13.53] vs 20.45 pmol/l [IQR 85.74]; $p=0.002$) (Fig. 1). Univariable logistic regression model for copeptin as a predictor for T2MI was statistically significant (OR 1.007 [95% CI 1.001–1.013]; $p=0.023$). After adjustment for the significant confounder (heart rate) elevated copeptin levels remained signifi-

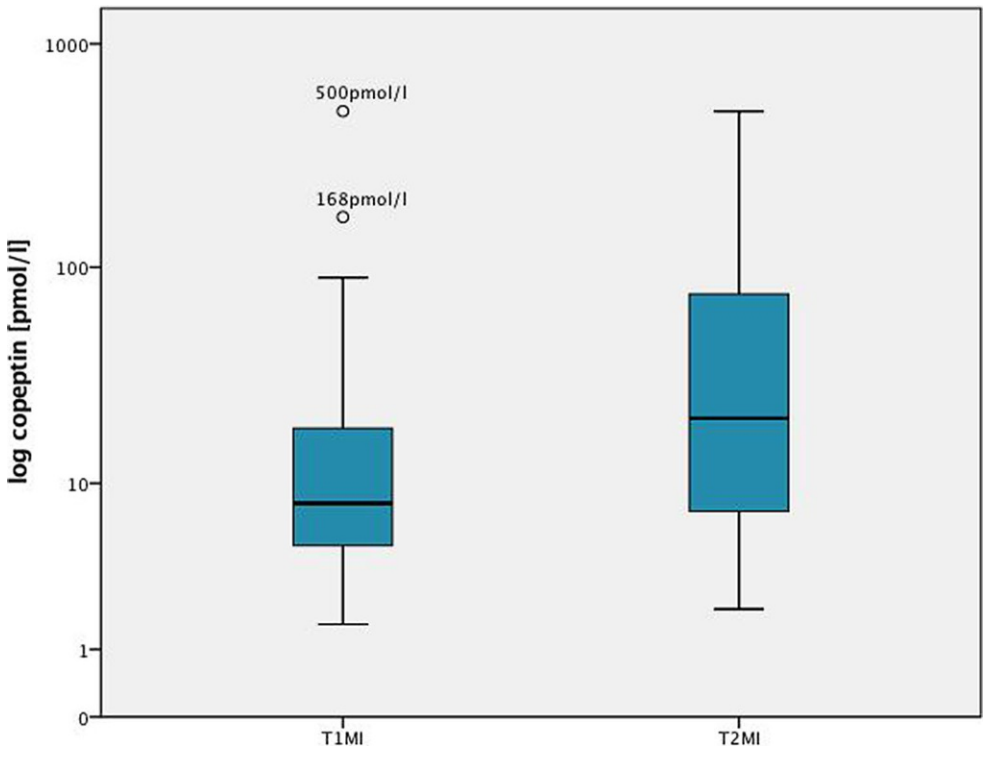

Fig. 1|1-9

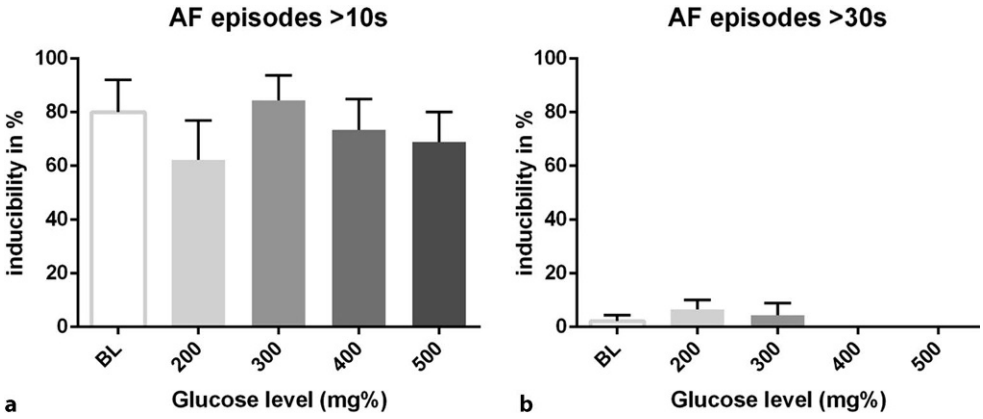

Fig. 1|2-1 Mean incidence of AF after atrial burst pacing with increase in blood glucose levels (episodes >10 s in panel A, episodes >30 s in panel B, error bars indicate SEM)

cantly associated with the diagnosis of T2MI (OR 1.017 [95% CI 1.004–1.029]; $p=0.008$).

Conclusions: Compared to T1MI patients copeptin levels were significantly higher in patients with T2MI. This association persisted after correction for significant confounders. A more pronounced elevation of copeptin levels might help in differentiating between patients with T1MI and T2MI in combination with clinical judgement.

POSTERSITZUNG 2 – Basic Science 1

2-1

Acute hyperglycaemia does not promote atrial fibrillation—an in vivo study in healthy pigs

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Background: Development and progression of atrial fibrillation (AF) is driven by comorbidities such as arterial hypertension and diabetes mellitus. While oxidative stress, apoptosis and fibrosis have been proposed as drivers of AF progression in animal models of chronic hyperglycaemia, acute glycosylation of CaMKII has been attributed to increased susceptibility to arrhythmias in rodents. We aimed to study the proarrhythmogenic effect of hyperglycaemia per se to investigate, whether this mechanism plays an important role in AF development during hyperglycaemia.

Methods: Nine healthy, anesthetized pigs (54 ± 6 kg) were instrumented with a quadripolar stimulation catheter in both atria, a decapolar catheter in the coronary sinus and a 256 electrode multielectrode array on the left atrial epicardium. Measurements included peripheral arterial blood sampling, left and right atrial effective refractory periods (AERP), left atrial inducibility of AF and left atrial epicardial conduction velocities (CV) and were repeated at baseline (BL1), increasing steps of blood glucose (200 to 500 mg% in steps of 100 mg%) and repeated after normalisation of blood glucose levels (BL2). Glucose levels were elevated by means of glucose infusion, serum electrolytes were kept constant during measurements by means of sodium and potassium infusion. AF was defined as the onset of irregular atrial electrograms with an average cycle length shorter than 150 ms for more than 10 s.

Results: There were no significant differences in AERP, CV or AF inducibility between BL1 and BL2. Heart rate remained constant regardless of blood glucose levels (BL: 103 ± 18 bpm, 500 mg%: 103 ± 18 bpm, r = 0.02, $p=0.346$). Mean left AERP (BL: 143 (127, 160) ms, 500 mg%: 157 (137, 185) ms, r = 0.97, $p=0.003$) as well as right AERP (BL: 163 (142, 193) ms, 500 mg%: 188 (177, 204) ms, r = 0.97, $p=0.003$) increased with higher glucose levels. CV increased with glucose levels (1.25 (1.04, 1.67) m/s at BL vs. 1.53 (1.22, 2.15) m/s at 500 mg%, r = 0.85, $p=0.034$). Rate of AF inducibility remained constant throughout the whole protocol (AF episodes >10 s: mean inducibility of 80% at BL vs. 69% at 500 mg%, $p=0.318$, Fig. 1).

Conclusions: Our data imply that hyperglycemia per se does not promote AF. The proposed mechanism of glycosylation of CaMKII does not seem to influence atrial arrhythmogenicity in a large animal model with balanced electrolytes.

2-2

Acute hyperglycaemia increases left and right atrial effective refractory periods

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Background: Development and progression of atrial fibrillation (AF) is driven by comorbidities such as arterial hypertension and diabetes mellitus. Acute glycosylation of CaMKII has been attributed to increased susceptibility to arrhythmias in acute hyperglycaemia. Until now, proarrhythmic effects of hyperglycaemia have only been demonstrated in rodents. We hypothesized, that this effect might be explained by electrolyte shifts rather than a specific proarrhythmic effect of glucose.

In the present study, we aimed to study the effect of hyperglycaemia per se on bi-atrial electrophysiology.

Methods: Nine healthy, anesthetized pigs (54 ± 6 kg) were instrumented with a quadripolar stimulation catheter in both atria and a decapolar catheter in the coronary sinus as a reference catheter. Measurements included peripheral arterial blood sampling, left and right atrial effective refractory periods (AERP, S1S2 protocol with S1 = 500, 400, 350, 300, 250 und 200 ms, data displayed as mean AERP) and were repeated at baseline (BL1), increasing steps of blood glucose (200 to 500 mg% in steps of 100 mg%) and repeated after normalisation of blood glucose

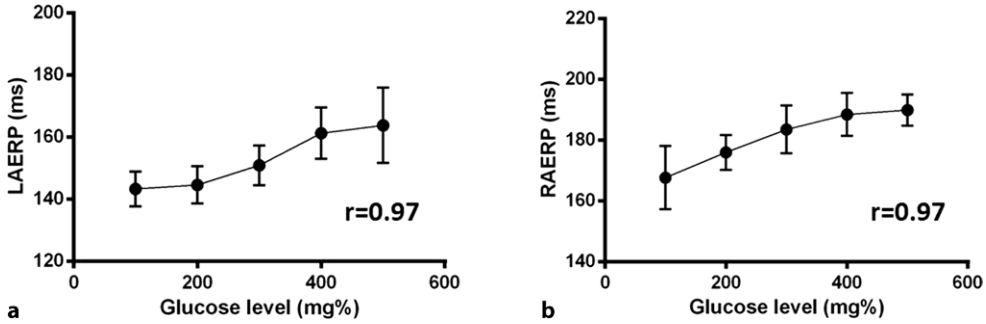

Fig. 1|2-2 a+b: Left and right atrial effective refractory periods increased with higher glucose levels (Pearson's correlation, both $p = 0.003$, error bars indicate SEM)

levels (BL2). Glucose levels were elevated by means of glucose infusion, serum electrolytes were kept constant (K: 3.5 mmol/L, Na: 135 mmol/L) during measurements by means of sodium and potassium infusion.

Results: There were no significant differences in AERP between BL1 and BL2. Spontaneous heart rate remained constant regardless of blood glucose levels (BL: 103 ± 18 bpm, 500 mg%: 103 ± 18 bpm, r = 0.02, $p = 0.346$). Left AERP (BL: median 143 (IQR: 127, 160) ms, 500 mg%: 157(137, 185) ms, r = 0.97, $p = 0.003$, Fig. 1 a) as well as right AERP (BL: 163 (142, 193) ms, 500 mg%: 188 (177, 204) ms, r = 0.97, $p = 0.003$, Fig. 1 b) increased with higher glucose levels.

Although electrolytes were substituted, exact balance throughout the complete protocol was not achieved. Serum potassium (BL: 3.5 ± 0.15 mmol/L, 500 mg%: 3.84 ± 0.43; r = 0.92) was over substituted, while sodium decreased with increasing glucose (BL: 140 (139.5, 141.5) mmol/L, 500 mg%: 132 (129, 136.5) mmol/L, r = –0.99). Serum calcium and chloride levels remained unchanged.

Conclusions: Our data show that atrial refractory periods increase with increasing glucose levels. This indicates that a potential proarrhythmic effect of acute hyperglycaemia is not mediated via shortening of refractory periods.

2-3

Increase of endothelial von Willebrand Factor secretion upon supra-physiologic shear stress mimicking severe aortic stenosis

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Background: Severe aortic stenosis (AS) is accompanied by an acquired von Willebrand Syndrome (AVWS) due to shear-stress induced degradation of high-molecular weight (HMW) von Willebrand Factor (VWF) multimers. The prevalence of an AVWS in severe AS is up to 80%, however, it remains unclear why some patients do not develop AVWS. We hypothesized that this subgroup compensates the loss of VWF with a shear-stress induced increase of endothelial VWF secretion. Therefore, in this proof-of-concept study, we exposed "MyEnd" endothelial cells to supra-physiologic shear-stress and analyzed VWF secretion.

Methods: "MyEnd" endothelial cells were seeded on a dish (10 cm^2) and exposed to physiologic and supra-physiologic (2 RPS, 1 h, >100 dynes/cm^2, mimicking shear flow in severe AS) shear flow using a dynamic shear rheometer. Endothelial VWF release was evaluated by measuring the concentration in the supernatant by ELISA and determining immunofluorescent signal of Weibel Palade bodies by immunofluorescence staining against VWF.

Results: After exposure of supra-physiologic but not physiologic shear flow we measured markedly increased (+26%) levels of VWF in the cell supernatant. Higher levels of extracellular VWF were accompanied by a reduced immunofluorescent signal in Weibel Palade bodies (Fig. 1). This finding indicates that elevated extracellular VWF derives from endothelial Weibel Palade bodies upon supra-physiologic shear stress.

Conclusions: Supra-physiologic shear stress mimicking severe AS leads to an compensatory increase of VWF secretion from endothelial Weibel Palade bodies. This mechanism might potentially contribute to avoid AVWS in patients with severe AS.

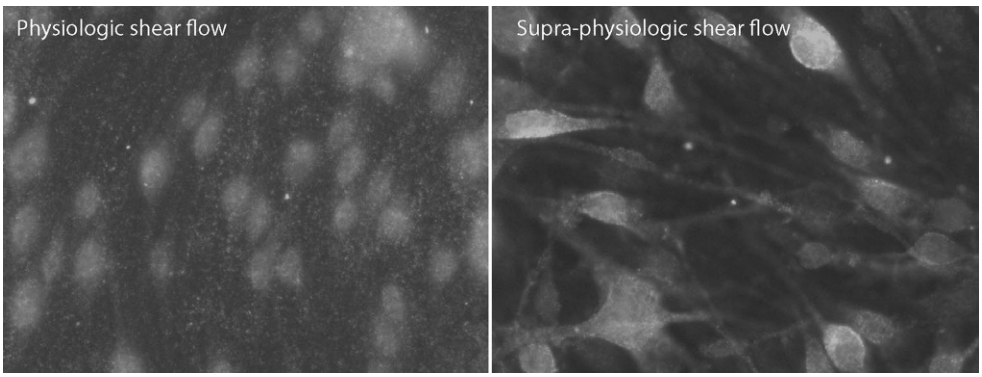

Fig. 1|2-3

2-4

The association of cardiovascular risk factors and circulating pro-coagulatory extracellular vesicles in patients with stable coronary artery disease

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Background: During activation, stimulation and apoptosis cells release extracellular vesicles (EV). They cargo different RNAs and proteins, wherefore we understand them as a communication tool between cells and accredit them high biomarker potential. The aim of this study was to investigate whether the presence cardiovascular risk factors influences circulating EVs in patients with stable coronary artery disease.

Methods: Patients were enrolled one year after PCI and had no ischemic or bleeding complications since then. Collection of platelet free plasma from citrate blood was performed at baseline and 10, 30 and 180 days later. Up to 30% of all vesicles have high pro-coagulatory potential due to the expression of negatively charged phosphatidylserine (PS) on their surface. We particularly studies EVs expressing PS and distinctive markers of their cellular origin; monocyte- (CD14+), platelet- (CD41+), endothelial- (CD54+/CD31+/CD146+/CD41-) and erythrocyte-

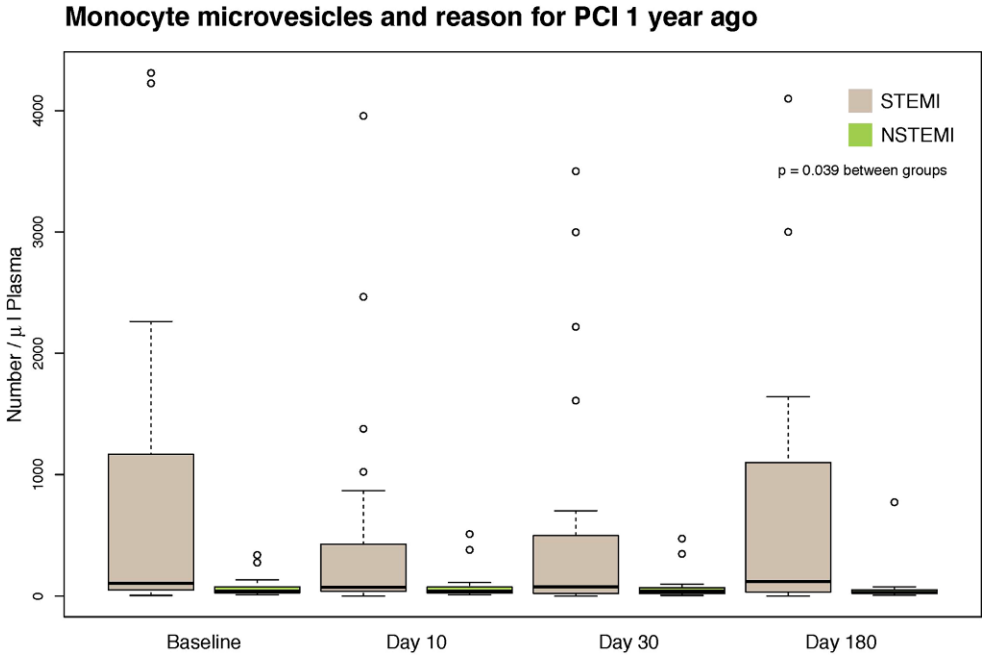

Fig. 1|2-4

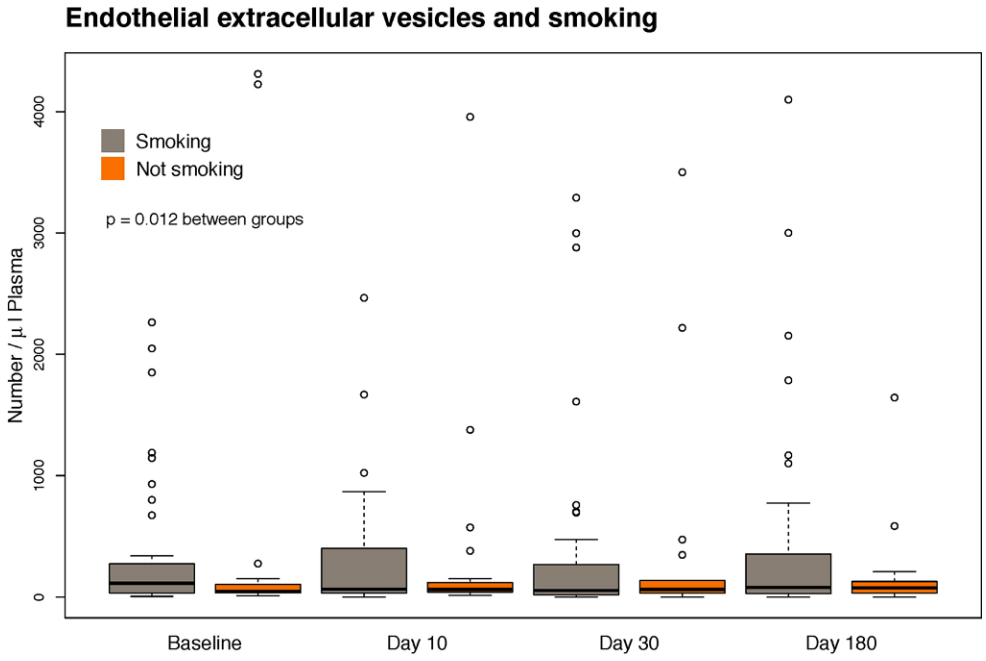

Fig. 2|2-4

derived (CD235a+) EVs. All measurements were performed using a high-sensitive flow cytometer (Cytoflex S, Beckman Coulter) and fluorescence triggering with AnnexinV-Cy5 (targets PS). Detection gates and an upper size limit were set using isotype control antibodies and 1000 nm Silica beads, respectively. EVs are reported as count/µl of pure plasma.

Results: We analyzed 62 patients (75% male, 62.6 ± 10.9 years) of whom 71.4% received PCI due to ACS. We identified significant higher amounts of platelet EVs in men ($p = 0.01$) and reduced numbers of endothelial EVs in smokers ($p = 0.012$). There was a significant association of the number of monocyte EVs with respect to the index event leading to PCI ($p = 0.024$ for the whole study population). If solely comparing patients with STEMI and NSTEMI (index event one year before this study), the latter had significantly reduced monocyte and endothelial EV levels ($p = 0.039$ and $p = 0.032$, respectively). While there was no correlation of any EV sub-population with BMI, eGFR, triglycerides, total-, LDL- or HDL cholesterol or the diagnosis of hypercholesterolemia (all $p > 0.05$, respectively), patients treated with high-power statins had lower monocyte EV levels ($p = 0.01$).

Conclusions: Established cardiovascular risk factors, the index event leading to PCI, as well as contemporary lipid-lowering therapy have impact on the expression of different populations of EVs in plasma. Endothelial cells and monocytes are involved in the pathophysiology of arteriosclerotic plaques; our findings reveal that the number of released EVs differs depending on the presence of distinctive risk factors or high-power statins. This suggests a relationship with respect to the underlying pathophysiology of arteriosclerosis. Furthermore, monocyte EVs very well distinguish between patients with NSTEMI or STEMI even up to 18 months after presentation. Future studies investigating the cargo of the studied vesicles will provide further insights and may point at specific biomarkers to assess different states of disease.

2-5

Pro-coagulatory plasma extracellular vesicles and their association with platelet function, platelet indices and micro RNAs associated with platelet function

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Background: Up to 30% of all extracellular vesicles (EV) have high pro-coagulatory activity (200-fold higher compared to platelets); partly due to the expression of negatively charged phosphatidylserine (PS) on their surface. Most EVs are released by platelets and are actively involved in thrombus formation. In-vitro and small human studies reported influence of antiplatelet drugs on the expression of EVs. The aim of this study was to investigate 1) the influence of dual anti platelet therapy (DAPT) on EVs and 2) potential correlations with platelet function.

Methods: Patients with no ischemic or bleeding events during DAPT were enrolled one year after PCI. Collection of platelet free plasma from citrate blood was performed at baseline (scheduled at the last day of P2Y12 inhibitor intake) and 10, 30 and 180 days later. We particularly studies EVs expressing PS; monocyte- (CD14+), platelet- (CD41+). endothelial- (CD54+/CD31+/CD146+/CD41-) and erythrocyte-derived (CD235a+) EVs. Measurements were performed using a high-sensitive flow cytometer (Cytoflex S, Beckman Coulter) and fluorescence-triggering with AnnexinV-Cy5 (targets PS). Detection gates and an upper size limit were set using isotype control antibodies and 1000 nm Silica beads, respectively. Platelet function was assessed using multiple electrode aggregometry (MEA; Multi-

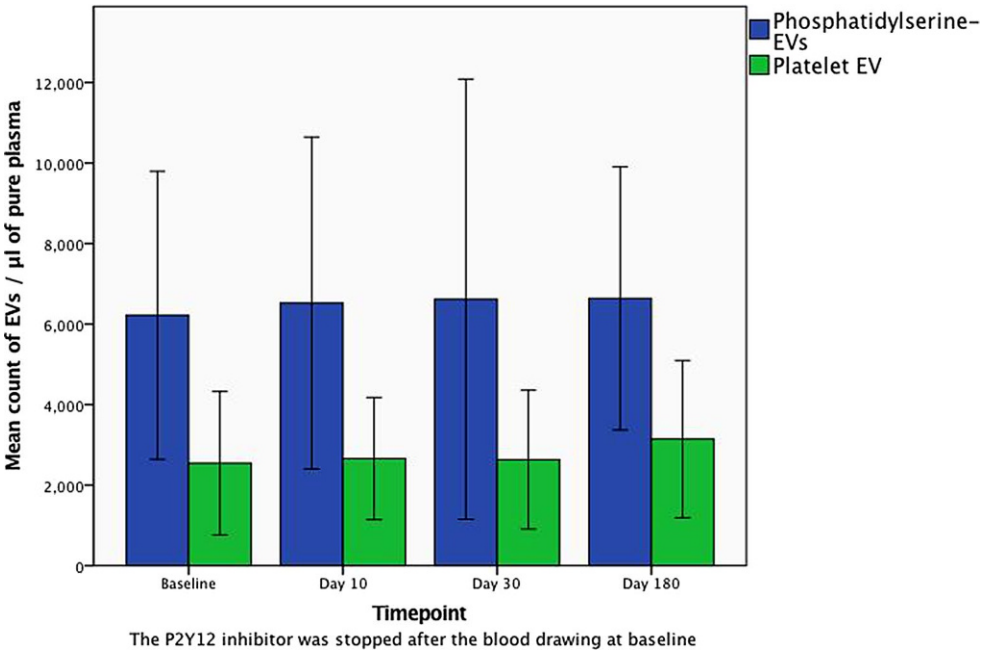

Fig. 1|2-5

plate ADP assay, Roche Diagnostics) and microRNAs (miRNA) were detected using the miRNeasy kit.

Results: We analyzed 216 samples (62 patients, 75% male, 62.6 ± 10.9 years, 71.4% stenting due to ACS). While platelet function (MEA) increased significantly after P2Y12-inhibitor cessation ($p < 0.001$), there were no differences with respect to any EV population (all $p > 0.05$). Correlation of EVs with platelet function and indices (MEA, platelet distribution width (PDW), mean platelet volume (MPV), reticulated platelets, fibrinogen) revealed no significant associations, with the following exceptions; monocyte EVs with PDW (r = –0.232; $p = 0.005$), platelets (r = 0.187. $p = 0.023$) and fibrinogen (r = 0.177; $p = 0.033$); platelet EVs and platelets (r = 0.232; $p = 0.004$). Additionally, we investigated the association of the EV populations with miRNAs associated with platelet function (miRNA-223, –21, –150, –126). Only the total amount of PS-expressing EVs was significantly correlated with miRNA-126 (r = –0.202, $p = 0.019$) (Fig. 1).

Conclusions: In contrast to previous findings performed in vitro or from healthy volunteers, our results do not support any use of the studied EV populations for monitoring platelet function or DAPT in patients with CAD. Our results suggest a close relationship between platelets, their EVs and monocyte EVs. Indeed, monocyte and platelet EVs are actively involved in thrombus formation as shown by previous in vitro investigations. However, the discrepant findings might result from the different clinical situation, as all samples were drawn in vivo in a clinically stable condition. Despite their involvement in thrombus formation, they are not useful for the investigation of function.

2-6

Vorhofflimmern – Unterschiedliches Remodeling in linken und rechten Vorhöfen

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Grundlagen: Vorhofflimmern (VHF) zählt zu den am häufigsten vorkommenden Herzrhythmusstörungen und ist durch strukturelles und elektrisches Remodeling im Vorhofgewebe charakterisiert, wobei neben den Pulmonalvenen die beiden Herzohren (RAA, right atrial appendage und LAA, left atrial appendage) als weitere Ausgangsorte für ektope Schläge identifiziert worden sind. In vorliegender Studie werden Ionenströme im LAA und RAA untersucht, welche die Entstehung ektoper Schläge mitverursachen können. Dazu zählen der Schrittmacherstrom If, der an der diastolischen Depolarisation beteiligt ist, sowie der Einwärtsgleichrichterstrom IK1, der für das stabile Ruhemembranpotential verantwortlich ist. Ein unausgewogenes Verhältnis dieser beiden Ströme zueinander kann die Arrhythmogenese begünstigen. Besonderes Augenmerk liegt auf dem Vergleich der Expression und der Funktionalität dieser beiden Ionenkanäle im Sinusrhythmus (SR) und VHF sowie dem Verhältnis der beiden Ströme zueinander.

Methodik: Für die elektrophysiologische Experimente (Patch-Clamp) wurden einzelne Zellen aus linken und rechten Herzohren von Patienten (SR und VHF) isoliert. Für die molekularbiologischen Untersuchungen hingegen wurden die Gewebestücke verwendet.

Ergebnisse: Diese Studie zeigt, dass der in SR-Patienten beobachtete Unterschied in der Ionenkanalexpression zwischen RAA und LAA in Geweben von VHF-Patienten weitgehend verschwindet. Die HCN mRNAs (codieren If-Kanäle) und Kir2.3 mRNAs (codieren IK1-Kanäle) sind in SR-Patienten im RAA stärker exprimiert als im LAA. Dieser Unterschied ist jedoch im VHF-Gewebe nicht mehr nachweisbar. Ferner ist die Expression zweier HCN-Isoformen (HCN1 und HCN4) in VHF-Geweben stark reduziert, und deren Verhältnis zueinander verändert. Die sich daraus ergebende Verschiebung der If Aktivierungskurve zu negativeren Membranpotentialen lässt einen deutlichen Verlust der physiologischen Funktion erkennen. Der IK1 hingegen gewinnt im VHF an Bedeutung, sowohl Stromdichte als auch mRNA sind erhöht. Die Reduktion des If korreliert jedoch nicht mit der Zunahme des IK1.

Schlussfolgerungen: VHF führt zu einer Vereinheitlichung des Expressionsmusters zwischen den Herzohren und zu einem Funktionsverlust des Schrittmacherkanals. Eine derartige Reduktion der biologischen Heterogenität/Variabilität ist unter pathologischen Bedingungen häufig zu beobachten und ist oftmals mit einer beeinträchtigten Anpassungsfähigkeit des Organismus auf physiologische Herausforderungen verbunden.

2-7

Withaferin A attenuates inflammatory response and cardiovascular dysfunction induced by LPS

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Background: Prevalence of diabetes is steeply rising in developing countries. Along with hyperglycaemia, other diabetic complications including impaired cardiovascular function, elevated inflammatory cytokines (primarily derived from monocytes/macrophages) and higher susceptibility to develop infection are detrimental and require substantial clinical attention. Withaferin A, a steroidal lactone derived from Withania somnifera belonging to Solanaceae family, has recently been identified as a potent anti-diabetic agent with positive effects against weight gain. In the present study we aimed to evaluate the effects of withaferin A against LPS-induced inflammation (in cardiomyocytes and macrophages) in vitro, and cardiovascular dysfunction (aortic ring contractile function and survival) and sepsis in vivo.

Methods: Murine cardiomyocyte (HL-1) and macrophage (RAW 264.7) cell lines were used to study intracellular signalling. C57BL6 mice were used to clarify the effects of withaferin A on LPS-induced cytokine release, cardiac and vascular dysfunction, and survival.

Results: Withaferin A (1 μM) impaired LPS-induced p42/44 MAPK and p65 activation in both cell lines. Inhibition of STAT1/3/6 phosphorylation was observed only in macrophages. As a consequence, LPS-induced cytokine (TNFα, IL-4/6/10) production and iNOS expression became apparent in response to LPS. Myography data revealed protective effect of withaferin A (10 mg/kg, i. p.) against LPS-impaired endothelial relaxation and significantly improved survival rate (~40%) in septic mice.

Conclusions: Our data reveval therapeutic potential of withaferin A against LPS-induced cardiovascular damage, inflammation and mortality.

POSTERSITZUNG 3 – Diverse 1

3-1

Produktfehler und korrektive Maßnahmen bei ventrikulären Unterstützungssystemen – Analyse der 2005–2017 vom BfArM veröffentlichten Kundeninformationen

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Grundlagen: Vermarktung und Marktüberwachung von Medizinprodukten und In-vitro Diagnostika (IVD) werden in Europa durch europäische Direktiven (z. B. The European Directive 93/42/EEC, Directive 98/79/EC) geregelt. Bei Vorkommnissen und korrektiven Maßnahmen (Field Safety Corrective Action, FSCA) müssen die Hersteller diese den zuständigen nationalen Behörden (Competent Authority (CA); in Deutschland: Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) für Medizinprodukte und die meisten IVD, in Österreich: BASG) melden und die Kunden über Kundeninformationen (Field Safety Notice, FSN) informieren, die auch den Behörden zur Verfügung gestellt werden. Ziel der Studie war die Untersuchung von FSN bei FSCA zu ventrikulären Unterstützungssystemen, die von Anfang 2005 bis Ende 2017 auf der Homepage des BfArM veröffentlicht wurden, in Hinblick auf vorliegende Produktprobleme und damit einhergehende Risiken, Art der FSCA und Einhaltung der in der MEDDEV-Leitlinie für FSN niedergelegten Kriterien.

Methodik: Für die in die Studie eingeschlossenen Produkte erfolgte eine Analyse der vom BfArM 2005 bis Ende 2017 auf der Homepage (http://www.bfarm.de/DE/Medizinprodukte/riskinfo/kundeninfo/functions/kundeninfo-node.html) veröffentlichten FSCA und FSN.

Ergebnisse: Im Untersuchungszeitraum fanden sich 51 FSCA (davon 3 Folgeberichte) zu den in die Studie eingeschlossenen Produkten. Betroffen waren, soweit abgrenzbar, meist Antriebseinheiten/Pumpen/Kanülen (16), Steuereinheiten (15) und Kabel (13), seltener Batterien (6). Damit einhergehende Fehlerbilder waren meist Pumpenausfall/Verminderungen der Pumpenleistung, Alarmprobleme und Probleme in situ (z. B. Blutung, Serom). Soweit zum Zeitpunkt der FSN überhaupt bekannt, wurden als Ursache vor allem Softwarefehler, Produktions- und Teilefehler benannt. In 8 FSN wurde auf Todesfälle (z. T. auch bei Austausch der Kontrolleinheit) hingewiesen, „Adverse Events“ und „Störungen“ (ohne Angabe von Patientenschädigungen) fanden sich häufiger und in einzelnen FSN wurde auch explizit auf das Fehlen von Vorkommnissen/Patientenschädigungen bis zum Zeitpunkt der FSN hingewiesen. Häufigste korrektive Maßnahmen (Mehrfachnennung) waren eine FSN (51, obligat bei Rückruf) mit Handlungsanweisungen für Anwender/Patienten (40, davon 18 Anweisungen zur Patientenkontrolle), Austausch/Rückruf oder Modifikation durch Servicetechniker (34), Modifikation des Produktes (11) bzw. dessen Herstellung (2), Änderung von Gebrauchsunterlagen (9), Schulung von Anwendern/Patienten (9), Software-Upgrade (6) und Implantations-/Vertriebsstopp (6).

Schlussfolgerungen: FSCA zu ventrikulären Unterstützungssystemen stellen aufgrund ihres hohen Gefährdungspotentials und der betroffenen schwerkranken Patienten bei Vorliegen von Produktmängeln eine wichtige Produktgruppe dar. Im Vergleich zu anderen Gruppen von Medizinprodukten (IVD) fanden sich häufiger Todesfälle. Bedingt durch die hohe Komplexität der Fehlerbilder und der von Anwendern zu treffenden Maßnahmen waren FSN meist ausführlich. Zugrundeliegende Fehler und durchzuführende Maßnahmen unterschieden sich in Abhängigkeit von den betroffenen Produktteilen (z. B. Steuereinheit, Batterie, Kabel) und zeigen die Notwendigkeit einer Einzelanalyse dieser Produkte. Aufgrund der Bedeutung der FSN zur Verminderung vom Produkt ausgehender Risiken im Falle einer FSCA sollten trotz weitgehender Einhaltung der MEDDEV-Kriterien Form und Inhalt der FSN jedoch weiter verbessert werden.

3-2

Outcomes of in-hospital versus out-of-hospital cardiac arrest in a tertiary referral center

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Background: Despite timely resuscitation cardiac arrest is still associated with a poor prognosis. We sought to define predictors of good neurological outcome by comparing clinical characteristics and outcomes in patients suffering from in-hospital (IHCA) versus out-of-hospital cardiac arrest (OHCA).

Methods: We retrospectively collected data of consecutive patients after cardiopulmonary resuscitation (CPR) due to IHCA (non-monitored patients) and all consecutive patients after CPR due to OHCA transferred to our hospital between January 2015 and June 2017.

Results: A total number of 333 patients were analysed, 148 (44.4%) had IHCA, 185 (55.6%) OHCA. There was no difference in distribution of gender or age beween IHCA and OHCA. Ventricular fibrillation or ventricular tachycardia as the first documented rhythm was more common in patients with OHCA (62.7% vs. 23%, $p<0.01$). Survival to discharge with good neurological outcome (cerebral performance category (CPC) score 1 or 2 was 20.3% in IHCA versus 32.4% in OHCA ($p<0.01$). Survival with severe neurological deficits (CPC 3 or 4) was 0.7% in IHCA vs. 3.2% in OHCA ($p=0.14$, n. s.). Predictors of survival to discharge were presence of a shockable rhythm as first detected rhythm in IHCA and OHCA and bystander CPR in OHCA. Survival was worst when the initial rhythm was asystole—in IHCA (1.7%) as well as OHCA (6.5%).

Conclusions: Patients who suffer from OHCA and are admitted to the hospital have a better prognosis than patients with cardiac arrest as in-patients. The higher percentage of shockable rhythms in the OHCA group is the main predictor for better neurological outcomes and lower mortality.

3-3

Potential role of microRNAs for diagnosis and/or monitoring of arterial stiffness

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Background: Arterial stiffness occurs during the course of atherosclerosis and can be assessed by pulse wave velocity (PWV). Circulating microRNAs (miRNAs) recently emerged as potential biomarkers for vascular remodeling. We set out to study, if circulating miRNAs are related to arterial stiffness in healthy subjects and patients with coronary artery disease (CAD).

Methods: PWV was measured non-invasively by Mobil-o-Graph® in 20 healthy subjects (10 men, mean age 54 ± 12 years) and 20 CAD patients (10 men, mean age 58 ± 8 years). In addition, 187 miRNAs were selected based on their reported association with endothelial function/dysfunction or cardiac diseases, and analyzed by quantitative reverse transcription polymerase chain reaction.

Results: In absolute numbers PWV was lower in healthy subjects than in CAD patients (7.64 ± 1.40 m/s vs. 8.13 ± 1.31 m/s), however this difference was not statistically significant ($p = 0.260$). Of 187 miRNAs, 18 miRNAs showed significantly different expression levels between healthy subjects and CAD patients. Of these, 5 miRNAs (let-7a-5p, let-7c-5p, let-7 d-5p, let-7f-5p, miR-30b-5p) which are known to have pro-angiogenic effects correlated negatively (all $r \geq 0.355$; all $p \leq 0.025$) and one miRNA (miR-185-3p) correlated positively ($r = 0.316$; $p = 0.047$) with PWV.

Conclusions: PWV was below the cut off for existing end organ damage in both healthy subjects and CAD patients, which is in keeping with the rather well-controlled cardiovascular risk factor profile even in our CAD patients (data not shown). Nonetheless, significant correlations were found between low miRNA expression levels of the pro-angiogenic let-7 family members and increased PWV. Furthermore, the majority of the remaining miRNAs which correlated with PWV have known protein targets which interact with the endothelium. Larger studies are needed to show whether miRNAs can be used to diagnose and/or monitor arterial stiffness.

3-4

ECG manifestations in patients with active myocarditis and impaired LV-function

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Background: We sought to assess the type of ECG changes in active myocarditis with reduced ejection fraction. Several ECG abnormalities in myocarditis have been described in literature:

Concave ST-segment elevation without ST segment depression (except in leads aVR and v1), conduction delays such as AV-block or bundle branch block, PR-segment depression in multiple leads, or TP-Segment downsloping (Spodick sign).

Symptomatic supraventricular or ventricular arrhythmias can be the first manifestation of the disease.

Methods: We assessed the 12-lead ECGs of 73 patients (47 male, 26 female) with newly diagnosed symptomatic heart failure and confirmed myocarditis based on myocardial biopsy results. The mean ejection fraction in MR scans was 33%. A significant coronary artery disease was excluded.

Results: With one exception all patients with diagnosed myocarditis had abnormal ECGs upon admission or documented prior to admission.

The most common features were negative T-waves (20pts) and new left bundle branch block (19 pts), both mimicking acute coronary syndroms. Whereas only 2 patients revealed ST-segment elevation.

Conduction disturbances (Sick sinus syndrome 2 pts, AV block type I 10 pts, AV block type III 1 pt, RBBB 6pts, bifscicular block 3 pts) other than LBBB built the other main type of ECG changes in our analysis.

15 Patients developed supraventricular tachykardia, mainly persiting atrial fibrillation.

Of the 4 patients with sustained ventricular tachycardia, 2 patients required—successful—resuscitation.

Symptomatic PVCs (7 pts), non sustained VTs (4 pts) and sinustachykardia (9 pts) were other ECG-features.

One patient presented with TP-segment downslope.

Conclusions: Active myocarditis can go along with a wide range of ECG abnormalities.

Careful interpretation and profound knowledge of 12-lead surface ECG can provide useful hints in the diagnosis of myocarditis

3-5

Causal attribution in patients with Coronary Heart Disease

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Background: Patients' causal attributions to illness are an important factor in cardiac therapy planning, motivational speaking and adherence to therapy. Our study aims to identify causal attributions in patients with angiographically verified Coronary Artery Disease (CAD).

Methods: We analysed 966 answers of 397 patients (age: 64.6 ± 11.2, male: 79.6%) to the open ended item of the Brief Illness Perception Questionnaire (BIPQ) asking for the three most important causes of illness from the patients' perspective.

Results: A vast majority of the answers (86.3%) fell in 15 categories, which could be summarized in 3 main categories, 13.7% differed widely in content and were characterised as miscellaneous and excluded from further analysis.

1. Psycho-social factors: Stress, mentioned by 40.1% of the patients, emerged as the single most important attribution. In 16.6% of the patients CAD was attributed to emotionally challenging events, anxiety or depression, in 12.1% to work related issues.

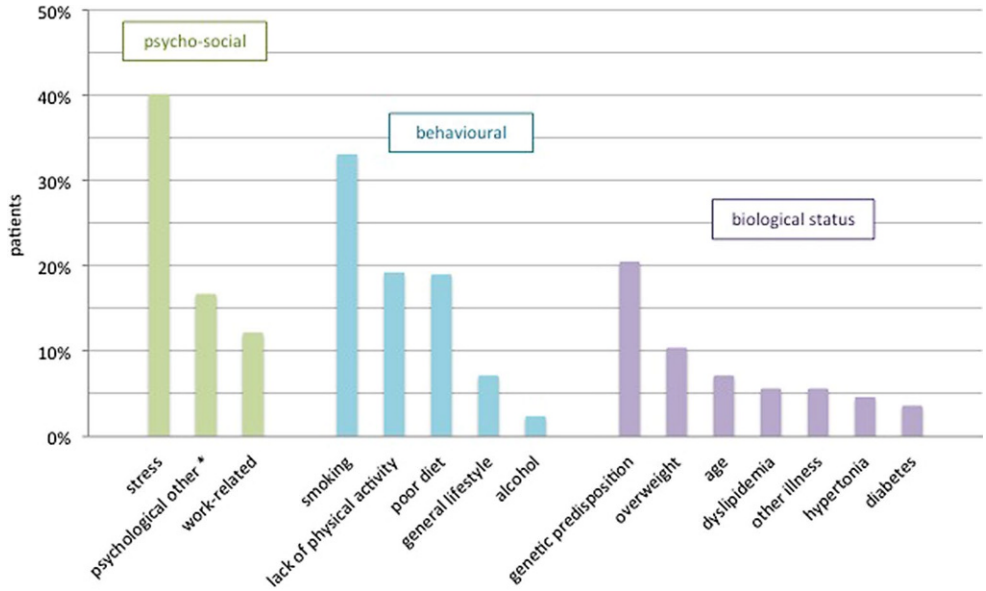

Fig. 1|3-5

2. Behavioural factors: Smoking (33%) was the most frequently reported behavioural factor, followed by lack of physical activity (19.1%), poor diet (18.9%), general lifestyle (7.1%) and alcohol consumption (2.3%).

3. Biological status: Patients referring to their biological status named genetic predisposition (20.4%), age (7.1%), overweight (10.3%), classic cardiovascular risk factors (dyslipidemia: 5.5%, hypertonia: 4.5% and diabetes: 3.5%) and other illnesses (5.5%) as cause of their CAD.

Only 54.2% of current smokers attributed their illness to nicotine abuse and only 53.2% of obese patients mentioned overweight, poor diet or lack of physical activity as a cause of disease.

Conclusions: Our results underscore the importance psychosocial factors in the anamnesis of CAD, especially the role of stress. Further research has to focus on the nature of stressors and on stress-vulnerability in CAD-patients. The finding that only about half of current smokers and obese patients refer to these risk factors in their causal attributions suggests a need for improvement in patient education.

3-6

Impact of marathon and ultra-marathon races on specific and unspecific cardiac biomarkers

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Background: Copeptin (Cop) and pregnancy plasma protein A (PAPP-A) are emerging but unspecific diagnostic cardiac markers, which are released very early during cardiac stress. The primary objective of this study was to investigate the differences in release of these markers in athletes after ultra-marathon and marathon in comparison to the specific sensitive cardiac troponin I (sc-TnI).

Methods: This was an observational, cross-over study including subjects performing an ultra-marathon (UM, 130 km) and marathon (M, 42.195 km) 6 months apart. Blood samples were taken before and immediately after the races. Cop and PAPP-A were measured, using the ultrasensitive KRYPTOR compact PLUS (B. R. A. H. M. S. GmbH, Thermo Scientific), sc-TnI was measured by use of Flex reagent cartridge (Dimension Vista 1500, SIEMENS).

Results: We included 15 experienced non-professional athletes (mean age 42.9 ± 8 years). When comparing baseline and post-race levels, we observed significant higher values for Cop after M (baseline median 3.8 [IQR, 2.9–7.3] pmol/L vs. post-race 26.3 [IQR, 16.3–39.0] pmol/L; $p < 0.001$) and UM (baseline median 4.1 [IQR, 2.4–5.6] pmol/L vs. post-race 9.8 [IQR, 6.6–39.4] pmol/L; $p < 0.001$), respectively. We also observed an increase after both races for sc-TnI (baseline median UM and M 0.015 [IQR 0.015–0.015] µg/L vs. post-race marathon 0.28 [IQR 0.015–0.049] µg/L and vs. post-race UM 0.56 [IQR 0.022–0.104] µg/L; $p = 0.003$ and $p = 0.001$). Regarding PAPP-A there was a significant elevation after the M (baseline median 7.3 [IQR, 6.4–9.0] mU/L vs. post-race 9.7 [IQR, 8.2–11.8] mU/L; $p = 0.001$), but not after the UM (baseline median 8.3 [IQR, 7.7–8.8] mU/L vs. post-race 9.0 [IQR, 8.0–9.8] mU/L; $p = 0.223$). When comparing post-race levels after UM and M we detected significant higher values for Copeptin after M compared to UM ($p = 0.039$) but no significance for PAPP-A ($p = 0.099$) and sc-TnI ($p = 0.089$).

Conclusions: In our study we concluded that the type of race has significant influence on unspecific and specific cardiac markers, with higher values after M compared to UM for Cop and PAPP-A, but vice versa elevated sc-TnI levels after UM. A potential explanation might be that M running reflects a higher physical stress for a shorter duration with an impact on unspecific markers, while the higher increase in sc-TnI in UM can be explained by a temporary change of the permeability of myocardial membranes based on several hours of exhaustive activity.

POSTERSITZUNG 4 – Herzinsuffizienz 1

4-1

24-Stunden Blutdruckmessung, steady-state und pulsatile Hämodynamik bei Patienten nach Herztransplantation

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Grundlagen: Die kardiale Denervierung, unvermeidlich nach einer Herztransplantation (HTX), resultiert in einem Anstieg der Ruheherzfrequenz (HF) und beeinflusst auch die Blutdruck (BD)-Regulation, insbesondere die zirkadiane Rhythmik des Blutdruckes. In früheren Studien zeigte sich eine höhere Prävalenz der nächtlichen „Non-Dipper" nach HTX. Bis dato fehlen jedoch genaue Analysen von BD, steady state (Schlagvolumen (SV), Herzminutenvolumen (HMV), peripherer Widerstand (TPR)) und pulsatiler (zentraler BD, antegrade und reflektierte Pulswellen) Hämodynamik in diesem Patientenkollektiv. Ziel dieser Studie war es, mittels 24-Messung von BD und Hämodynamik bei herztransplantierten Patienten mit einer Kontrollgruppe aus Patienten mit arterieller Hypertonie zu vergleichen.

Methodik: Insgesamt wurden 25 Patienten nach einer HTX mit einer Kontrollgruppe, gematcht nach Alter, Geschlecht, Blutdruckmedikation und mittlerem 24-Stunden-BD am Oberarm verglichen. Alle Patienten wiesen einen stabilen klinischen Verlauf und eine normale Linksventrikelfunktion auf. Die Messungen erfolgten mit einem oszillometrischen Oberarm-BD-Messgerät (mobilograph, i. e. m., Stolberg, Deutschland). Auf Höhe des diastolischen BD werden Pulskurven aufgezeichnet und mit den validierten ARCSolver Algorithmen die Parameter der steady-state und pulsatilen Hämodynamik automatisch ermittelt.

Ergebnisse: Beide Gruppen waren nach Alter (58,5 ± 12,1 vs 58,5 ± 12,2 Jahre, $p > 0{,}05$), Geschlecht (20 % Frauen pro Gruppe), und 24 Stunden Oberarm-BD (125/82 ± 11/8 vs 127/81 ± 11/9 mmHg, $p > 0{,}05$) gut vergleichbar. Das durchschnittliche Zeitintervall nach HTX betrug 10,1 ± 9,5 Jahre.

In der Gruppe nach HTX zeigte sich eine im Durchschnitt höhere 24-Stunden Herzfrequenz (HF) (79 ± 10 vs 71 ± 8/min; $p < 0{,}05$) im Vergleich zur Kontrollgruppe. Beide Gruppen zeigten einen signifikanten Abfall des systolischen und diastolischen BD in der Nacht, des mittleren arteriellen Druckes (MAP), des zentralen systolischen BD sowie der HF. In der Kontrollgruppe verringerte sich das HMV in der Nacht, der TPR blieb konstant. Bedingt durch eine verminderte nächtliche HF kommt es zum Anstieg des SV und parallel hierzu zu einem Anstieg der antegraden und reflektierten Wellen. In der HTX-Gruppe konnte ein Abfall des TPR bei gleichzeitigen Anstieg des SV und konstantem HMV dokumentiert werden. Als Folge des verminderten TPR nehmen die Pulswellenreflexionen in der Nacht ab.

Schlussfolgerungen: Patienten mit arterieller Hypertonie zeigen einen nächtlichen BD-Abfall mit einem Anstieg der Pulswellenreflexionen in der Nacht, bedingt durch den Rückgang der HF und die Lageänderung. Nach Herztransplantation konnte eine Veränderung der pulsatilen Hämodynamik, peripherem Widerstand und Herzminutenvolumen nachgewiesen werden. Dies ist vermutlich die Folge der kardialen Denervierung durch eine HTX und einer daraus bedingten Entkoppelung zum autonomen Nervensystem, weitere Studien in diesem Patientenkollektiv werden jedoch noch benötigt.

4-2

A comparative analysis of the novel cardiac biomarkers sST2, GDF-15, Galectin-3, suPAR, H-FABP and Fetuin-A in heart failure, STEMI and NSTEMI patients

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Background: Heart failure (HF) and myocardial infarction (MI) constitute a major therapeutic challenge in cardiology, leading to a considerable impact on morbidity, hospitalisation rates and health-care costs. Cardiac biomarkers represent an important tool for diagnostics, risk stratification and therapy monitoring in these disease entities, with increasing clinical significance over the last years.

Purpose: The aim of this analysis was to investigate the role of six novel cardiovascular biomarkers, namely sST2, GDF-15, Galectin-3, suPAR, H-FABP and Fetuin-A in patients suffering from heart failure (ischaemic cardiomyopathy, ICM and dilative cardiomyopathy, DCM) and myocardial infarction (STEMI and NSTEMI)

Methods: A total of 316 patients were enrolled in this current study. 123 patients were diagnosed with ischaemic or dilative cardiomyopathy, 61 patients were diagnosed with STEMI and 56 patients with NSTEMI. 76 patients without coronary artery disease (excluded by coronary angiography) or signs of acute or chronic heart failure were enrolled as control group. Plasma samples were drawn within the first hours of presentation (MI patients) or follow-up visits (HF and control patients) and analyzed for sST2 (hemodynamics and inflammation), GDF-15 (injury, remodeling), Galectin-3 (fibrosis, remodeling), suPAR (inflammation), H-FABP (ischemia) and Fetuin-A (vascular calcification) by using ELISA.

Results: Levels of sST2, H-FABP ($p < 0.0001$), suPAR ($p < 0.0002$) and GDF-15 ($p < 0.03$) were significantly higher in HF and MI patients compared to the control group. Galectin-3 (1792 vs. 2795 pg/ml, $p < 0.0001$) and Fetuin-A levels (76.8 vs.

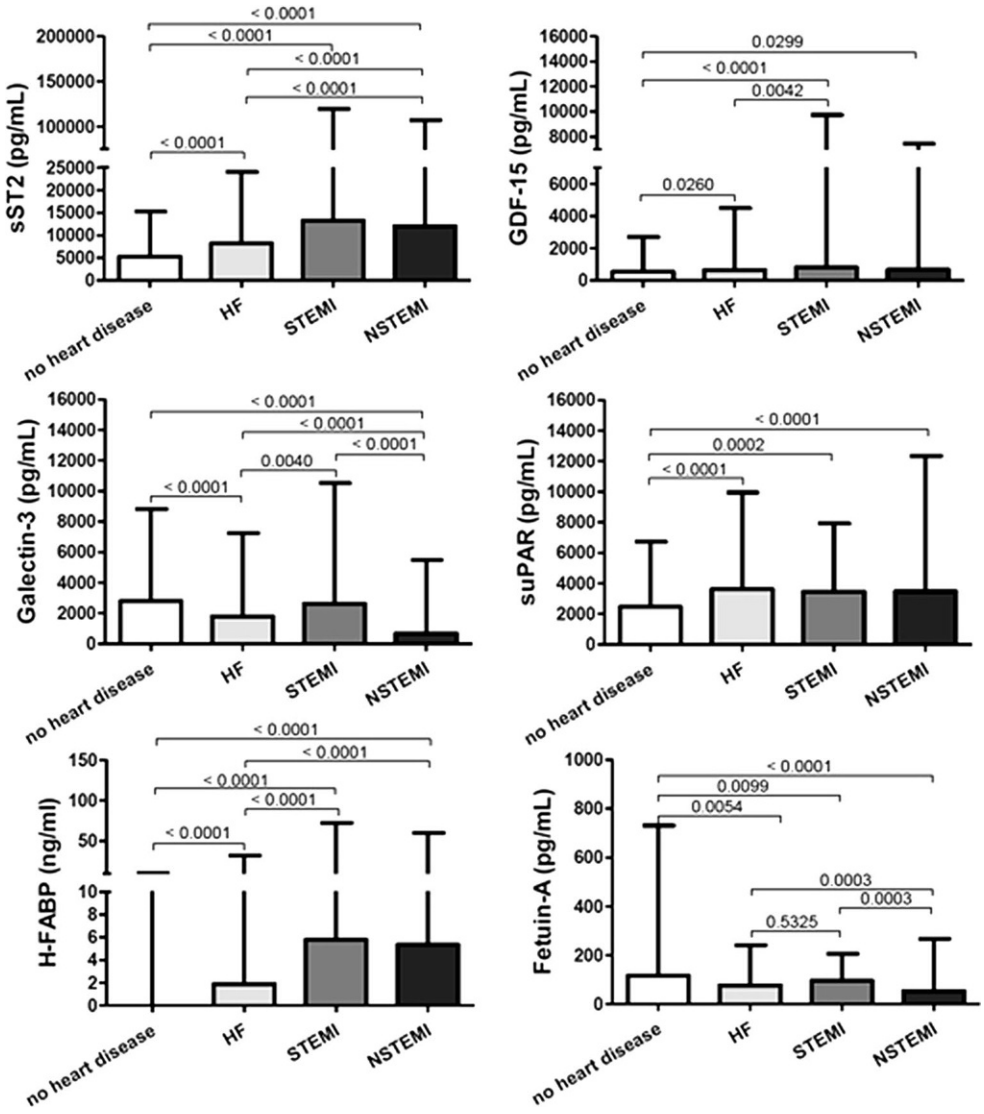

Fig. 1|4-2

116.6 pg/ml, $p = 0.001$) evidenced lower levels in HF patients and NSTEMI patients but not in STEMI patients compared to controls. STEMI and NSTEMI patients showed significantly higher levels of sST2 (13.211 vs. 8169 pg/ml, $p < 0.0001$), and H-FABP (5.78 vs. 1.89 ng/ml, $p < 0.0001$) compared to HF patients. STEMI patients additionally showed significantly higher levels of GDF-15 (818.8 vs. 666.9 pg/ml, $p = 0.004$) and Galectin-3 in comparison to HF patients. Interestingly, NSTEMI patients showed significantly lower levels of Galectin-3 compared to HF and STEMI patients as well as lower levels of Fetuin-A compared to STEMI patients.

Conclusions: By combining the information on different pathophysiological processes, novel cardiac biomarkers represent a promising tool for a more precise diagnosis, risk stratification and therapy monitoring. Furthermore, multimarker measuring could facilitate the discrimination of different cardiovascular disease entities.

4-3

Circulating Neprilysin is not a prognostic biomarker for treatment-naïve cancer patients

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Background: The membrane-bound zink-metalloendopeptidase neprilysin (NEP) is a member of a class of widely expressed cell surface proteins regulating the physiological action of many peptides. The recent introduction of NEP inhibition by the angiotensin-receptor neprilysin inhibitor (ARNI) translated into better outcomes for heart failure patients and is now clinical routine. Evidence emerges that NEP not only plays a key role in cardiovascular disease but also in tumor biology, whereas upregulation of NEP generally seems to indicate worse prognosis in most solid tumors. Nevertheless concentrations of circulating NEP (cNEP) have not yet been assessed in can-

cer patients. The aim of the study was to determine cNEP levels in an unselected cohort of treatment-naïve cancer patients, to investigate the effect of cNEP on prognosis and to assess the correlation of cNEP with established cardiac biomarkers to further characterize its role in the interdisciplinary field of cardio-oncology.

Methods: 555 consecutive patients with primary diagnosis of cancer without prior anticancer therapy were enrolled prospectively. NEP levels were determined alongside routine laboratory parameters, a set of cardiac biomarkers, i. e. N-terminal B-type natriuretic peptide (NT-proBNP), high-sensitive TroponinT (hsTnT), mid-regional pro-atrial natriuretic peptide (MR-proANP), mid-regional pro-adrenomedullin (MR-proADM) and C-terminal pro-endothelin-1 (CT-proET-1) and inflammatory parameters, i. e. C-reactive protein (CRP), interleukin-6 (IL-6) and serum amyloid A (SAA), in venous plasma samples. All-cause mortality was defined as primary endpoint.

Results: cNEP showed a wide distribution in the total cohort with a median of 276 pg/ml (IQR 0–5981) and comparable levels between different tumor entities and stages (Fig. 1). cNEP displayed a weak correlation with age (r = –0.12, $p = 0.023$) and a modest but consequent inverse correlation with inflammatory status (r = –0.14, $p = 0.007$ for CRP; r = –0.20, $p < 0.001$ for IL-6 and r = –0.18, $p < 0.001$ for SAA), however seemed not to be related to the functional parameters of other organ systems as the kidney, the liver and especially the heart (r = –0.05, $p = 0.367$ for NT-proBNP; r = –0.10, $p = 0.075$ for hsTnT; r = –0.03, r = –0.02, $p = 0.664$ for MR-proANP; r = –0.05, $p = 0.387$ for MR-proADM and r = 0.07, $p = 0.168$ for CT-proET1). cNEP was not associated with overall survival in the total cohort (adj.HR for ln(cNEP) 1.00, 95%CI:0.94–1.06, $p = 0.887$), and neither in the subgoups of solid tumors nor myeloproliferative disease, but in myelodysplatic malignancies (adj.HR for ln(cNEP) 1.27, 95%CI:1.01–1.61, $p = 0.044$). Kaplan Meier curves and log-rank analysis confirmed the missing discriminatory power of cNEP on overall survival for the unselected population of treatment-naïve cancer patients according to tertiles (Fig. 2).

Conclusions: cNEP shows a wide distribution in human plasma of cancer patients. cNEP levels are comparable between different tumor entities and stages and lack association with outcome but for myelodysplastic disease. cNEP levels do not correlate with established cardiac biomarkers generally associated with disease severity in cancer.

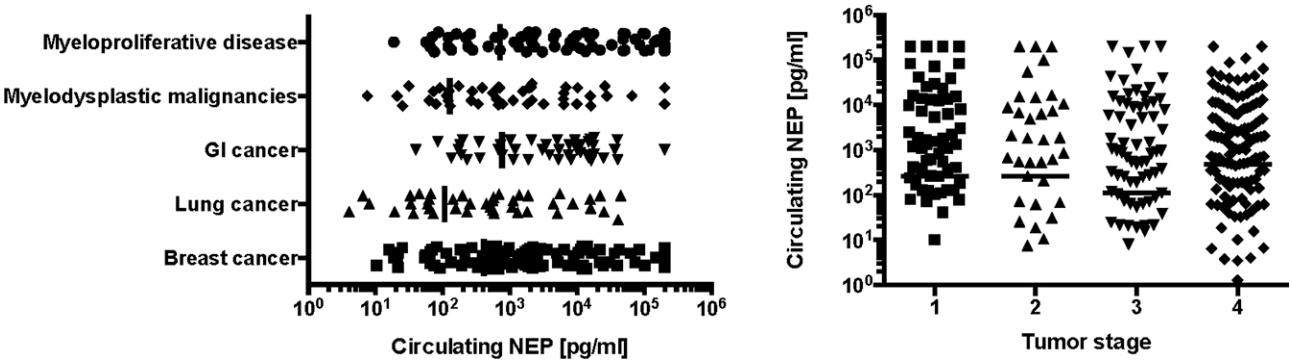
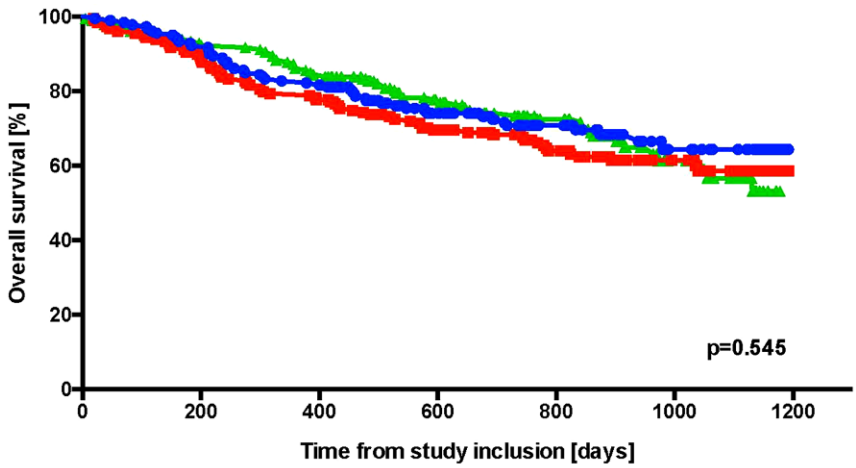


Fig. 1|4-3 Circulating NEP levels according to tumor entities and disease stage in an unselected cohort of treatment-naïve cancer patients



No. of patients at risk							1200 days estimate
Tertile 1	179	165	147	102	73	25	64.3%
Tertile 2	179	160	139	115	87	46	58.5%
Tertile 3	179	160	151	115	87	30	53.1%

Fig. 2|4-3 Association of circulating NEP with all-cause mortality according to tertiles

4-4

Gender-related differences in the clinical presentation of hypertrophic cardiomyopathy—a single-centre experience

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Background: Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disease characterized by extreme heterogeneity in clinical features. Disease-related variables have been shown to potentially impact diagnosis, risk stratification, and prognosis in HCM patients, butlittle information is available on gender differences.The goal of this study was to assess gender-related differences in a single-centre cohort with hypertrophic cardiomyopathy (HCM).

Methods: We studied 69 consecutive HCM patients from the Innsbruck Hypertrophic Cardiomyopathy Program. Standard T-Test, Mann- Whitney U-Test, Chi-square test and Fisher's exact test were used to evaluate differences between groups.

Results: Male patients had a 3:1 predominance (65%). Female patients were older and more symptomatic than male patients (63 ± 11 years vs. 52 ± 14 years; $p < 0.001$; mean New York Heart Association [NYHA] functional class 2.3 ± 0.7 vs. 1.9 ± 0.9; $p = 0.04$). By contrast, NTproBNP (ng/L) and troponin T (ng/L) were not different between groups (796[128–2007] vs. 412[147–1240], and 15.4[7–20] vs. 16.2[11–29], respectively).

Also, no differences were seen in phenotypic disease manifestation: left ventricular outflow tract obstruction (LVOTO), mid-ventricular obstruction (MVO), apical hypertrophic CMP (AHCM), non-obstructive hypertrophic CMP (HCM), and apical aneurysm formation. Maximal LVOT gradient (mmHg) was slightly higher in female patients (100[70–120] vs. 70[10–124]) but did not reach statistical significance. Similarly, calculated SCD risk score was not different between groups (2.95[1.98–4.9] vs. 2.49[1.6–4.5]).

Interestingly, LV hypertrophy on ECG was more frequent in male patients, whereas no differences were seen foratrial fibrillation, pacemaker and ICD implantation. Likewise, in patients with CMR available late gadolinium enhancement was predominant in male patients. Causal and possible causal genetic mutations were equally distributed.

Of note, interventional therapy including surgical myectomy, alcohol septal ablation, and heart transplantation was applied more often in female patients.

Conclusions: In this single-centre cohort women with HCM were under-represented, older, and more symptomatic than men resulting in more invasive therapy. Early diagnosis in women may be deferred by non-characteristic ECG appearance.

4-5

Unexpected blood flow from pulmonary veins during cardiopulmonary bypass for mitral valve surgery in a 62-year-old woman

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Background: A 62-year-old lady was acutely referred from an external surgery department where open mitral valve annuloplasty had been cancelled directly after cardiopulmonary bypass connection and cardioplegia because the pulmonary veins had continued to deliver blood into the left atrium. At admission she reported about breathlessness on exertion equivalent to NYHA class III-IV, despite optimal medical therapy for heart failure including a loop diuretic.

Methods and Results: Auscultation revealed a grade 2/6 systolic-diastolic murmur in the aortic area. She had signs of cardiopulmonary congestion (elevated jugular venous pulse, leg edema). Further comorbidities included osteoporosis and depressive mood disorder.

Office blood pressure and heart rate were 160/60 mmHg and 81 bpm, respectively. An electrocardiogram showed atrial fibrillation and complete left bundle branch block and was otherwise unremarkable. Echocardiography showed a dilated and diffuse hypokinetic left ventricle (end-diastolic diameter 66 mm, left-ventricular ejection-fraction 39%, global longitudinal strain –12.6%) and severe mitral regurgitation (MR) secondary to mitral annulus dilatation. The right ventricle had normal dimension and mildly reduced function (end-diastolic diameter 35 mm, TAPSE 15 mm) and estimated systolic pulmonary artery pressure (sPAP) was 46 mmHg. In parasternal short axis view with focus on the RVOT, the pulmonary trunk was severely dilated (41 mm). Color Doppler revealed a massive regurgita-

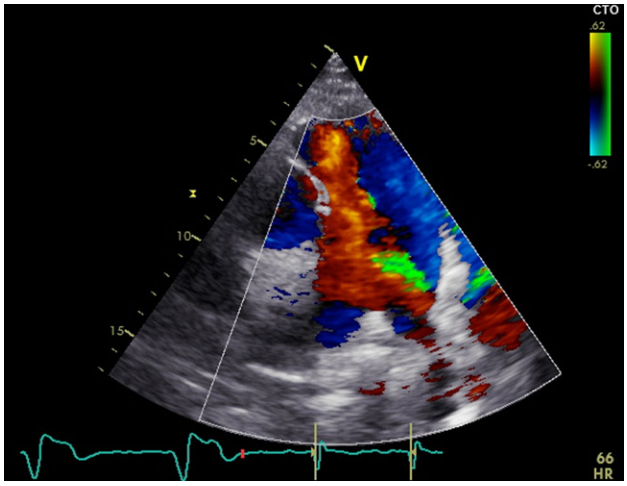

Fig. 1|4-5 Parasternal short axis view with focus on RVOT and pulmonary trunk. Color Doppler revealing a massive regurgitation jet originating from the left-sided wall of the pulmonary trunk

Clinical features of HCM patients according to gender

	All patients n (%)	Male n (% of male)	Female n (% of female)	p values
Gender	69 (100)	45 (65)	24 (35)	
Age (yrs.)	56 +/- 14	53 +/-14	63 +/-11	0,001
Phenotypic manifestation				
LVOTO	40 (58)	26 (57,8)	14 (58,3)	ns
MVO	3 (4,3)	2 (4,4)	1 (4,2)	ns
AHCM	3 (4,3)	2 (4,4)	1 (4,2)	ns
HCM	18 (26)	13 (28,9)	5 (20,8)	ns
LV apical aneurysm	2 (2,9)	2 (4,4)	0 (0.0)	ns
Clinical presentation				
NYHA I	22 (31,9)	19 (42,2)	3 (12,5)	0,039
NYHA II	23 (33,3)	12 (26,7)	11 (45,8)	
NYHA III/IV	24 (25)	14 (31)	10 (41,7)	
Syncope	12 (17,4)	6 (13,3)	6 (25)	ns
Coronary artery disease	8 (11,6)	3 (6,7)	5 (20,8)	ns
SCD Risk score	2,75 (1,83-4,61)	2,95 (1,98-4,88)	2,49 (1,60-4,54)	ns
NTproBNP (ng/L)	494 (140-1445)	412 (147 - 1240)	796 (128 - 2007)	ns
TropT (ng/L)	16,1 (9,2-24,0)	16,2 (10,8 - 28,9)	15,4 (7,05 - 20,3)	ns
Echo measurments				
LV outflow tract gradient (max.) (mmHg)	79 (0- 131)	70 (10 -124)	100 (70 - 120)	ns
Septal thickness (mm)	17,8 (15,1- 21,8)	18,1(15,7-22,6)	17 (13,0-21,3)	ns
Left atrial diameter (mm)	45,43 +/- 8,13	45,69 +/-8,01	44,95 +/- 8,49	ns
SAM	30 (43,5)	21 (46,7)	9 (37,5)	ns
Subvalvular membrane	6 (8,7)	3 (6,7)	3 (12,5)	ns
CMR available	42 (61)	27 (60)	15 (62,5)	ns
Late gadolinium enhancem.	26(37,7)	21 (46,7)	5 (20,8)	0,008
ECG				
ECG pathologic	60 (87)	40 (88,9)	20 (83,3)	ns
Atrial fibrillation	9 (13)	7 (15,6)	2 (8,3)	ns
LVH	39 (56,5)	31 (77,5)	8 (33,3)	0,006
PM	9 (13,0)	5 (11,1)	4 (16,7)	ns
ICD	12 (17,4)	8 (17,8)	4 (16,7)	ns
Genetics				
Genetic available	31 (44,9)	21 (46,7)	10 (41,6)	ns
Causal mutation	11 (15,9)	8 (17,8)	3 (12,5)	ns
Possible causal mutation	9 (13,0)	5 (11,1)	4 (16,7)	ns
No mutation	11 (15,9)	8 (17,8)	3 (12,5)	ns
Therapy				
Surgical myectomy	15 (21,7)	7 (15,6)	8 (33,3)	ns
Alcohol septal ablation	13 (18,8)	6 (13,3)	7 (29,2)	ns
Heart transplantation	5 (7,2)	3 (6,7)	2 (8,3)	ns
Medical therapy	37 (53,6)	28 (62,2)	9 (37,5)	0,05

Fig. 1|4-4

tion jet originating from the left-sided wall of the pulmonary trunk (Fig. 1).

A patent ductus arteriosus Botalli (PDA) was confirmed by computed tomography. Simultaneous right and left heart catheterization revealed both post-capillary pulmonary hypertension (mean pulmonary capillary wedge pressure 22 mmHg), as a consequence of dilated cardiomyopathy and MR, and pre-capillary pulmonary hypertension (PAP 67/27 [mean 47] mmHg), due to chronic volume overload of the pulmonary arterial system. Surgical PDA closure and concomitant mitral valve annuloplasty were successfully performed. Three months after surgery the patient's symptoms were markedly improved and estimated sPAP declined to 34 mmHg.

Conclusions: This case illustrates congenital heart disease as a rare and potentially reversible cause of dilated cardiomyopathy and functional MR underlining the importance to perform a comprehensive echocardiographic examination in the early diagnostic work-up of heart failure.

4-6

The inflammation based prognostic score mGPS predicts survival in stable heart failure patients

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Background: The progression of heart failure is presumed to be linked to inflammatory host response. The combination of the inflammatory markers albumin and C-reactive protein (CRP), termed modified Glasgow Prognostic Score (mGPS), has been derived from cancer patients and validated in multiple cohorts. This study aimed to investigate the impact of the easy leviable mGPS on survival of stable patients with heart failure with reduced ejection fraction (HFrEF).

Methods: HFrEF patients under routine ambulatory care at the heart failure unit of the Medical University of Vienna between January 2011 and November 2017 were retrospectively identified. Comorbidities and laboratory data at baseline were assessed. All-cause mortality was defined as the primary study endpoint. The mGPS score and its impact on overall survival were determined.

Results: Data was complete and analyzed for a total of 301 patients. The mGPS score was 0 for 245 (81%), 1 for 43 (14%) and 2 for 13 (4%) patients, respectively. The three groups showed significant differences in other routine laboratory parameters associated with survival, especially NT-proBNP [1895 pg/ml (IQR 834–3462) vs. 3852 pg/ml (IQR 2312–7232) vs. 9935 pg/ml (IQR 4082–19.821) for mGPS score 0, 1 and 2 respectively; $p<0.001$]. In the Cox regression analysis, increasing mGPS was associated with adverse outcome in the univariate analysis [crude HR 2.43 (95%CI 1.60–3.69), $p<0.001$] and after adjustment for age and NT-proBNP [adj. HR 1.79 (95%CI 1.02–3.12), $p=0.042$]. Kaplan-Meier analysis confirmed the high discriminatory power of the mGPS score ($p<0.001$) (Fig. 1).

Conclusions: The inflammation based score mGPS predicts survival in HFrEF patients. The association underlines the age independent impact of the inflammatory response in heart failure Inflammatory response appear to be most relevant in patients with advanced heart failure.

4-7

The outcomes of „Code STEMI" implementation in indonesian referral center hospitals

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Background: International guidelines recommend the reduction of door to balloon time in the delivery of primary percutaneous coronary intervention (PCI) to patients presenting with ST-segment Elevation Myocardial Infarction (STEMI) to no longer than 90 minutes. However, the variety and complexity of cases admitted to general hospitals made the management of STEMI to be more prone to delay compared to that in hospitals specialized in cardiovascular medicine. Therefore, Cipto Mangunkusomo Hospital, as national referral center, pioneered the implementation of Code STEMI as a new protocol in Indonesia

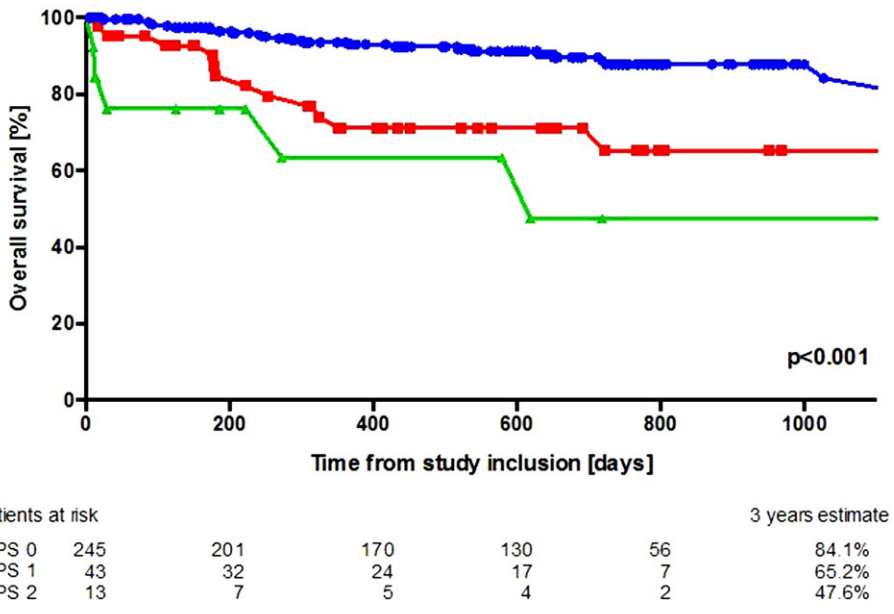

Fig. 1|4-6

referral center hospitals starting from 2017. This study aims to evaluate the impact of the new system on door-to-balloon time, length of stay, and all-cause in-hospital mortality of STEMI patients undergoing primary PCI in general hospital.

Methods: This retrospective cohort study involved all STEMI patients undergoing primary PCI admitted from January 2016 to December 2017 in Cipto Mangunkusumo National Hospital. Patients in 2017 were compared with patients in 2016, in which Code STEMI had not been implemented. The primary outcome was to measure door-to-balloon time, length of stay, and all-cause in-hospital mortality between both groups.

Results: Median door-to-balloon time was shown to decrease significantly from 272 minutes in 2016 to 184 minutes in 2017 ($p<0.001$). A decrease in median hospital length of stay from 6 days in 2016 to 5 days in 2017 was also observed ($p=0.023$). However, the difference of all-cause in-hospital mortality between the two periods was not found to be statistically significant ($p=1.000$).

Conclusions: Time delay between patient admission and balloon inflation still becomes a problem in implementing effective primary PCI for STEMI patients in Indonesia. Code STEMI protocol implementation in Indonesia Referral Center Hospitals has brought an 88 minutes reduction of median door-to-balloon time. Besides, the length of stay of STEMI patients was also significantly reduced. Despite the decrease, the national standard of care that aims to reduce door-to-balloon time to 90 minutes has not been met.

The decrease in door-to-balloon time and hospital length of stay may be attributed to the solution offered by "Code STEMI" for the problems contributing to the delay of STEMI management. Code STEMI provides a solid mechanism that facilitates the access to the catheterization laboratory for STEMI patients admitted to the emergency department. The increase in the number of staff in charge of triage and the number of ECG available in the emergency department was implemented in "Code STEMI" in order to solve the delay in diagnosis. Another solution offered by "Code STEMI" is the use of telemedicine in the form of chat group in instant messaging application that allows communication between medical units without having the patient burdened to walk around the hospital for administrative reasons.

4-8

Relationship between parathyroid hormone and cardiac function and congestion in chronic heart failure: a prospective cohort study

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Background: Chronic heart failure (CHF) is often accompanied by disturbed bone metabolism, but potential mechanistic links are unclear in large parts. High parathyroid hormone (PTH) levels increase the risk of CHF and hyperparathyroidism is common in CHF patients. Few clinical studies aimed to elucidate the role of PTH in CHF, but their majority was limited by the retrospective character and very low sample sizes prohibiting multivariate analyses.

We aimed to correlate plasma PTH levels with echocardiographic and laboratory parameters reflecting both cardiac systolic or diastolic function and congestion in CHF patients.

Methods: Subjects were enrolled between September 2016 and December 2017, as part of a single-center prospective cohort study. Main inclusion criteria were age over 18 years, CHF according to the ESC CHF guidelines 2016 and left ventricular ejection fraction (LVEF) < 50%. Stable disease was defined as absence of unplanned hospitalization or change in medication or device therapy within the previous month or major surgery within the previous 3 months. Exclusion criteria were any acute illnesses or more than moderate primary valvular disease. Blood samples were taken after an overnight fast and all laboratory parameters were determined immediately.

Results: We enrolled 99 patients (mean age 64.8 ± SD 9.6 years, 79% males). Mean LVEF was 35.9 +/– 9.0% and median NT-proBNP was 1301 [IQR 349–2750] pg/ml. Hyperparathyroidism was present in 50% of patients and median PTH was 65.0 [47.0–94.6] pg/ml.

PTH correlated significantly with NT-proBNP (Pearson $r=0.467$, $p<0.001$), but not with LVEF, tricuspid annular plane systolic excursion or e'. In multivariate linear regression analyses with adjustment for age, sex, estimated glomerular filtration rate, 25-hydroxyvitamin D and body mass index, PTH remained significantly associated with NT-proBNP (adjusted beta-coefficient 0.331, $p=0.004$).

Conclusions: In 99 patients with CHF, PTH was significantly correlated with NT-proBNP, but not with parameters of cardiac function, independently of important potential confounding variables. This observation is in line with previous studies and suggests a mechanistic interweavement between cardiac congestion and PTH secretion. Further investigation will be necessary to elucidate the impact of this possible interaction on bone health in CHF patients.

POSTERSITZUNG 5 – Rhythmologie 1

5-1

Detektion von Vorhofflimmern nach einem embolischen Schlaganfall unklarer Ursache

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Grundlagen: Aktuell erleiden etwa 26 Millionen Menschen weltweit jährlich einen Schlaganfall. In 1/3 der Patienten kann trotz umfangreicher Abklärung kein eindeutiger pathogenetischer Mechanismus verantwortlich gemacht werden. Obwohl in vielen Fällen eine kardioembolische Genese verdächtigt wird (ESUS, embolic stroke of undetermined source), konnte Vorhofflimmern als wichtige Ursache in großen randomisierten Studien trotz kontinuierlichem Monitoring nur in einem geringen Prozentsatz nachgewiesen werden (EMBRACE 16,1 %, CRYSATAL-AF 12,4 %). Fraglich bleibt, ob verbesserte Detek-

tionsalgorithmen diese Rate erhöhen. Ziel unserer Studie ist der Nachweis von Vorhofflimmern nach ESUS in einem „real world" Patientenkollektiv.

Methodik: In dieses uni-zentrische Register wurden alle Patienten mit einem ESUS, die anschließend einen Loop Recorder (Medtronic, Reveal Linq©) erhielten, zwischen 09/2014 und 09/2017 eingeschlossen. Die Daten des Loop Recorders wurden alle 4 Monate ausgelesen. Die Dauer der Nachsorge wurde auf 3 Jahre begrenzt.

Am Ende der Einschlussphase wurde eine Zwischenanalyse durchgeführt. Die wichtigsten Endpunkte waren der Nachweis von Vorhofflimmern, eines neuerlichen Schlaganfalls, Tod und Komplikationen durch den Loop Recorder.

Ergebnisse: Insgesamt wurden 87 Patienten analysiert (mittl. Alter: 65,3 +/– 12,6). Die Loop Recorder Implantation fand nach durchschnittlich 20 d (19,9 +/–34,4 d) statt. 23 % ($n=20$) der Patienten wurden mit einer therapeutischen Antikoagulation entlassen, während der Großteil der Patienten (73,6 %, $n=64$) eine Thrombozytenaggregationshemmung erhielt. Zum Zeitpunkt der Auswertung wurden 74,7 % ($n=65$) zumindest 1 Jahr nachverfolgt. Bei 21,8 % ($n=19$) der Patienten wurde Vorhofflimmern detektiert, wobei dieses in der Mehrzahl der Fälle (73,7 %, $n=14$) innerhalb der ersten 6 Monate nach Diagnosestellung auftrat. Das durchschnittliche Alter der Patienten mit Vorhofflimmern (72,2 +/– 7,9LJ vs. 63,2 +/–13,1LJ), als auch das kardioembolische Risiko (CHADsVASC ≥4, 94,7 % vs. 67,6 %) waren höher als das der AF-freien Vergleichsgruppe. Bei keinem Patienten kam es zu einem neuerlichen Schlaganfall oder Tod. Bei 1 Patienten musste der Loop Recorder aufgrund einer Taschеninfektion vorzeitig explantiert werden.

Schlussfolgerungen: In dieser „real world" Patientenkohorte lag die Detektionsrate von Vorhofflimmern bei ESUS-Patienten etwas höher als in rezenten randomisierten Studien wie Crystal-AF. Bei einem Großteil der Patienten trat Vorhofflimmern in den ersten Monaten nach Schlaganfall auf.

5-2

Feasibility study of the MRI compatibility of a Leadless Pacemaker System

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Background: As in vivo real-life data are still scarce, we conducted a study to assess the safety and feasibility of cardiac MRI in patients with a leadless pacemaker system.

Methods: In this prospective non-randomized interventional trial, we enrolled 15 patients with an MRI conditional Micra® leadless pacemaker system to undergo either a 1.5 T or 3.0 T cardiac MRI scan. Clinical adverse events as well as device parameters such as pacing threshold, sensing, impedance and battery life were assessed at baseline as well as 1 and 3 months after the scan. Device parameter changes between different time points were tested for statistical significance and compared with pre-set cut-off values.

Results: Fourteen patients underwent the cardiac MRI scan according to the protocol as well as the scheduled follow-up visits. One participant was excluded from analysis, as the MRI scan was not possible because of severe claustrophobia. Other clinical events did not occur during the scan and the follow-up period. Device parameters stayed stable and changes during the observational period were statistically not significant (pacing threshold: 0.01 ± 0.05 V, $p=0.308$, 0.01 ± 0.07 V, $p=0.419$, sensing: –0.15 ± 1.11 mV, $p=0.658$, –0.19 ± 1.17 mV, $p=0.800$, impedance: –7.86 ± 30.7 Ohm, $p=0.447$, –7.86 ± 25.77 Ohm, $p=0.183$, at 1- and 3-months follow-up, respectively). Parameter changes were not statistically different between patients who underwent imaging at 1.5 T ($n=7$) or 3.0 T ($n=7$).

Conclusions: In our set of patients with a Micra® leadless pacemaker, cardiac magnetic resonance imaging at either 1.5 T or 3.0 T proved feasible and safe with no relevant changes in device parameters within 3 months of follow-up.

5-3

High-frequency jet ventilation during atrial fibrillation ablation: safety, efficacy and feasibility

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Background: High-frequency jet ventilation (HFJV) is used to decrease respiratory motion and augment precision during atrial fibrillation (AF) ablations; however, the patient safety and efficacy of HFJV has not been extensively studied. The aim of this study was to evaluate the safety, efficacy and feasibility of HFJV during radiofrequency ablation in patients with atrial fibrillation.

Methods: We studied nineteen consecutive patients who underwent AF-ablation under general anesthesia (GA), ablated by the same operator at our institution during the last 18

Patient characteristics

Patient characteristics	All patients (N=19)	CV (N=10)	HFJV (N=9)	p-value
Age (years)	57,5±9,3 years	55,8±8,8	59,5±10	NS
Gender M/F (%)	11/8 (58%/42%)	8/2 (80%/20%)	3/6 (33%/66%)	0,04
Significant Obesity (BMI>30)	11/19 (58%)	7/10 (70%)	4/9 (44,4%)	NS
Sleep apnea syndrome (%)	7/19 (37%)	3/10 (30%)	4/9 (44,4%)	NS
First ablation procedure (%)	16/19 (84%)	8/10 (80%)	8/9 (89%)	NS
Paroxysmal AF (%)	10/19 (53%)	6/10 (60%)	4/9 (44%)	NS
PVI + CT-Isthmus Ablation (%)	5/19 (26%)	2/10 (20%)	3/9 (33%)	NS
Mean procedural time (min)	174±36	176±36	173±38	NS
Mean ablation time (min)	39±9	39±9	40±10	NS
Mean fluoroscopy time (min)	12±6,5	11±5	14±7,5	NS
Mean fluoroscopy dose (mGym²)	3249±3219	3227±2250	3273±4230	NS
Procedural success rate (%)	19/19 (100%)	10/10 (100%)	9/9 (100%)	NS
Major complication rate (%)	0/19 (0%)	0/10 (0%)	0/9 (0%)	NS
Minor complication rate (%)	1/19 (5%)	0/10 (0%)	1/9 (11%)	NS

Fig. 1 | 5-3

months (November 2016—March 2018). Patients were divided in 2 groups: conventional ventilation (CV) group (N = 10) and high-frequency jet ventilation (HFJV) group (N = 9).

Results: The overall mean age of patients (N = 19) was 57.5 ± 9.3 years (CV: 55.8 ± 8.8 years, HFJV: 59.5 ± 10 years, p = NS), 58% were men (CV:80%, HFJV:33%, p = 0.04). The main reason for ablation under GA was significant obesity with BMI > 30 kg/m² (58%—CV: 70%, HFJV: 44.4%, p = NS), followed by significant obstructive sleep apnea syndrome (37%—CV: 30%, HFJV: 44.4%, p = NS). Paroxysmal AF was diagnosed in 53% of the patients (CV: 60%, HFJV: 44%, p = NS), while a cavotricuspid isthmus (CTI) ablation was planned or required during the procedure in 26% of patients (CV: 20%, HFJV: 33%). Mean procedural time was 174 ± 36 min (CV: 176 ± 36 min, HFJV: 173 ± 38 min, p = NS), mean ablation time was 39 ± 9 min (CV: 39 ± 9 min, HFJV: 40 ± 10 min, p = NS), mean fluoroscopy time was 12 ± 6.5 min (CV: 11 ± 5 min, HFJV: 14 ± 7.5 min, p = NS) and mean fluoroscopy dose was 3249 ± 3219 mGym² (CV: 3227 ± 2250 mGym², HFJV: 3273 ± 4230 mGym², p = NS). Procedural success rate was 100% (CV: 100%, HFJV: 100%, p = NS), periprocedural major complication rate was 0% (CV: 0%, HFJV: 0%, p = NS) and periprocedural minor complication rate was 5% (CV: 0%, HFJV: 11%—merely one patient with minor groin hematoma, p = NS). Long-term (1-year) procedural success rates are not yet available.

Conclusions: The use of high-frequency jet ventilation during AF-ablation is safe, well-tolerated and efficacious, with ablation duration and procedural success rates similar to conventional ventilation in patients requiring GA during the ablation procedure.

5-4

Major complications following pulmonary vein ablation with cryotechnology in atrial fibrillation—a single center report

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Background: Treatment of atrial fibrillation (AF) is an ongoing topic, as it is believed that one in four middle-aged adults in the US and in Europe will suffer from AF. With a total amount of almost 35 million people worldwide and a prevalence of around 3%, it is one of the most important supraventricular tachycardia.

In 1998, M. Haisseguerre could show in his publication the pulmonary veins (PVs) as main origin of AF. Since this time circumferential ablation of the PVs has become an auspicious option for treating AF besides the well-established treatment options with antiarrhythmic drugs, especially in patients with paroxysmal AF and if its's patients choice—underlined by the latest ESC guidelines.

Since the Fire and Ice trial published in 2016, cryoablation has shown a non inferiority to the widely used treatment strategy with point by point radiofrequency ablation. Multiple clinical trials have shown arrhythmia free survival of 50 to 75% at 1-year post ablation.

Nevertheless, AF ablation involves certain risks of major complications due to the procedure itself and especially in regard to the vulnerable thin-walled atria, the anatomic vicinity to adjacent structures such as nerves, blood vessels and other organs.

Methods: Between 2009 and 2017 there were 507 pulmonary vein isolations (PVIs) performed in our center, using the different technical developments of Medtronic Cryoballoon. All patients were analyzed through retrograde evaluation of peri- and postinterventional complications. Before every procedure, transesophageal echocardiography was executed to rule out left atrial appendage thrombus and a cardiac CT was done to visualize pulmonary vein anatomy. As standard, the ablation was performed in sedoanalgesia using fentanyl and propofol under hemodynamical monitoring. All procedures were carried out by one of six interventionists. After procedure, every patient was observed for 24 hours on our cardiac care unit. All complications were documented in the patient's history.

For statistical analysis, Microsoft Excel 2016 MSO and Graph Pad Prism 7 was used.

Results: From a cohort of 507 patients undergoing PVI, the mean age was 59.15 ± 10.71 years. There were 144 (28.54%) women.

Complications during the procedure or within the length of hospital stay were documented in 47 (9.27%) patients. The most frequent complication was vascular injury at the venous access site at the inguinal region. In total 18 (3.55%) vascular associated complications were documented of which 12 (2.37%) were hematomata, three (0.59%) patients suffered from spurious aneurysm, two patients (0.39%) developed an AV- fistula and one (0.20%) patient reported severe persistent pain. In 15 (2.96%) patients, phrenic nerve palsy was apparent in a routinely performed chest x-ray on the day after the procedure. In five (0.99%) cases a cerebrovascular accident (TIA/stroke) occurred. Pericarditis was evident in four (0.79%) patients. Three patients (0.59%) developed a cardiac tamponade and were in need of echocardiographically- guided pericardiocentesis. One (0.20%) patient showed a pneumothorax after ablation. One patient (0.20%) suffered from massive cervical hemorrhage two days after PVI resulting in death.

Conclusions: Pulmonary vein ablation using cryotechnology in atrial fibrillation is associated with a low rate of serious complications like stroke or death and therefore a feasible treatment option of AF especially in younger patients.

5-5

Pulmonary vein isolation by cryotechnology in patients with atrial fibrillation—evaluation of total procedure duration and fluoroscopy time in a long-term follow up

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Background: Atrial Fibrillation (AF) has become the most important supraventricular arrhythmia in the last years. An incidence of 2–3% in adults and the aging population underlines the high clinical relevance of AF concerning a significant higher risk for stroke and death.

The relevance of pulmonary vein isolation (PVI) increased in the last years next to pharmacological treatment. Therefore, the ESC Guidelines on the "Management of Atrial Fibrillation" indicated PVI as a treatment option after failure of medi-

cal treatment and as first line therapy, mainly in patients with paroxysmal AF on their choice. The data of the Fire and Ice trial published in 2016 by Krum et al. showed, that PVI by cryotechnology (CRYO) was non-inferior to point-by-point ablation performed by radiofrequency technology. The need for only one transseptal puncture and the short duration of the procedure are important advantages of CRYO. However, we have to keep in mind the need for longer fluoroscopy time for navigation of the cryoballon. Therefore, we performed an analysis of procedure and fluoroscopy time of all patients treated with PVI by CRYO at our department.

Methods: All patients with AF treated with PVI by CRYO (Medtronic Cryoballon®) were analysed due retrograde evaluation of the procedure and fluoroscopy times in dependence of different Cryoballon catheters and in dependence of different operators.

Cardiac CT for evaluation of pulmonary vein anatomy and transesophageal echocardiography for exclusion of left atrial appendage thrombus were done before PVI. Procedures were performed under sedanalgesia and all pulmonary veins were treated with at least one freeze, until electrical isolation was achieved. For statistical analysis Graph Pad Prism 7 was used.

Results: Since 2009 519 patients were treated for AF with PVI using CRYO. Mean age was 59 10.68 years and 29.09% of patients were female. Main comorbidities were hypercholesteremia ($n=345/66.47\%$), hypertension ($n=270/52.02\%$) and coronary artery disease ($n=228/43.93\%$). First generation cryoballon was used in 145 patients while PVI with second generation cryoballon was done in 340 patients. The cryoballon ST catheter was used in 34 patients. In total, the mean procedure and fluoroscopy time for all procedures was 107.42 49.16 and 22.9 13.22 minutes. A first analysis of procedure and fluoroscopy times by the different generations revealed a constant decrease of both over years due to technical improvements of newer generation devices.

(First generation cryoballon: mean procedure time: 161.9 46.73 minutes and mean fluoroscopy time 35.54 14.9 minutes; second generation cryoballon (mean procedure time: 87.13 30.33 minutes and mean fluoroscopy time 17.62 7.95 minutes, $p<0.0001$); cryoballon ST catheter (mean procedure time: 73.16 24.44 minutes and mean fluoroscopy time 20.78 10.07 minutes ($p<0.0001$)). In a second analysis total procedure and fluoroscopy times were evaluated in dependence of the operators over the last years. Thereby we also found a decrease of both times, as a result of the learning curve of the devices. The procedure duration decreased from 190.4 33.54 minutes in 2009 to 87.5 35.95 minutes in 2017 ($p<0.0001$) and fluoroscopy time decreased from 48.62 15.4 minutes to 21.07 9.73 minutes in 2017 ($p<0.0001$).

Conclusions: We were able to show a significant decrease of procedure duration and of fluoroscopy time in PVI with CRYO due to improvements of devises and a high operator experience.

5-6

Reversal of systolic dysfunction in a male adolescent with left ventricular hypertrabeculation/noncompaction and Wolff-Parkinson-White syndrome after accessory pathway ablation

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Background: Recurrent or incessant tachycardia may occur in symptomatic Wolff-Parkinson-White (WPW) syndrome, leading to ventricular dysfunction, tachycardia-induced cardiomyopathy (TIC). Asymptomatic WPW syndrome-induced TIC has rarely been reported, with incidence rates higher in pediatric patients than in adults. Left ventricular hypertrabeculation/noncompaction (LVHT) is a cardiac abnormality of unknown etiology and is found in normally sized, well contracting left ventricles as well as in dilated ventricles with systolic dysfunction. LVHT associated with WPW has been reported several times, however reversal of systolic dysfunction after ablation has not been described so far.

Description of the patient: A previously healthy 17-years old male underwent the first electrocardiogram (ECG) of his life at the conscription for military service. ECG showed WPW-syndrome with overt pre-excitation, and he was referred for cardiological investigation. He reported no cardiac symptoms and was an active soccer player. Clinical investigation was normal. Echocardiography revealed an enlarged left ventricle (enddiastolic diameter 59 mm), a reduced ejection fraction (14%) and LVHT of the apex and lateral wall. Resting ECG and 24-hour Holter monitoring disclosed multiple episodes of atrial tachycardias with a heart rate of 110/min. After repeated inquiries the patient admitted that he felt frequently "rapid heart beats", but this was so normal that it did not bother him.

Patient management: Cardiac magnetic resonance (CMRI) imaging was planned but could not be carried out because of atrial arrhythmias. Electrophysiological examination disclosed an epicardial left posteroseptal accessory pathway with ante- and retrograde conduction. Radiofrequency ablation was carried out in October 2017. After 16 radiofrequency deliveries in the left atrium and in the coronary sinus, the retrograde conduction was completely blocked and the anterograde conduction was blocked intermittently. The postinterventional ECG did not show Delta waves any more. Two months later, in December 2017, echocardiography showed a normally sized left ventricle (enddiastolic diameter 56 mm) with normal systolic function (EF 60%) and unchanged LVHT. The patient did not receive any pharmacotherapy except acetylsalicylic acid 100 mg/d for 4 weeks after ablation. The patient is continuously in NYHA I class of heart failure and reports that he feels no "rapid heart beats" any more. CMRI is scheduled for February 2018. Genetic testing is under way.

Conclusions and implications for clinical practice: WPW-induced TIC may even occur in asymptomatic patients, who are so adapted to their arrhythmias that they do not recognize them. Ablation of the accessory pathway leads to reversal of systolic dysfunction without necessity for neurohumoral therapy. Since the further course of the cardiac situation including LVHT is uncertain, the patient remains under cardiologic observation.

5-7

Level of Vitamin D predicts occurrence of atrial high rate episodes in patients with chronic heart failure

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Background: Chronic heart failure (CHF) is one of the most important risk factors for the development of atrial fibrillation (AF). Recent studies have shown that low 25-hydroxyvitamin D (25(OH)D) levels are associated with the presence of AF and may be involved in its pathogenesis.

In this study, we aimed to investigate the relation of low Vitamin D levels on the prevalence of AF in patients with CHF.

Methods: Participants of the prospective "Role of Comorbidities in Chronic Heart Failure" (RoC-HF) single-center cohort study (Registry number NCT02922478) were included between September 2016 and December 2017. Main inclusion criteria were age over 18 years, CHF according to the ESC CHF guidelines 2016 and left ventricular ejection fraction (EF) < 50%. Stable disease was defined as absence of unplanned hospitalization or change in medication or device therapy in the previous month or major surgery in the previous 3 months. Patients with any acute illnesses or more than moderate primary valvular disease were excluded. Blood samples were obtained after an overnight fast laboratory parameters used in the present analyses were determined immediately. Device interrogations were performed to screen for the presence of atrial high rate episodes (AHRE) lasting longer than 30 s that occurred within one year prior to the respective blood sampling.

Results: We enrolled 99 patients (mean age 65 ± 10 years, 79% males). Mean EF was 35.9 ± 9.0%. Complete data from device interrogations were available in 54 patients, 31 (57%) of these patients had dilative cardiomyopathy and 20 (37%) ischemic cardiomyopathy. CRT-D devices were implanted in 34 patients (63%), single or dual chamber defibrillators in 17 patients (32%), the other patients had pacemakers or CRT-pacemakers. Median (range) 25(OH)D was 22.3 (6.9–87.8) ng/ml.

AHRE occurred in 25 (46%) of the 54 patients. There were no significant differences between patients with or without AHRE considering age (64 (49–76) vs. 64 (47–76) years, $p = 0.508$), female gender (20 vs. 31%, $p = 0.535$), arterial hypertension (64 vs. 71%, $p = 0.761$), diabetes mellitus (42 vs. 38%, $p = 1.0$), NYHA class (2 (2–4) vs. 2 (2–4), $p = 0.283$), left atrial diameter in parasternal long axis (42 vs. 38 mm, $p = 0.304$) or EF (35.8 ± 10 vs. 34.5 ± 10, $p = 0.676$).

Patients with AHRE had significantly lower levels of 25(OH)D 20.9 ± 9 vs. 30.1 ± 19.1 ng/mL ($p = 0.02$) in univariate analyses.

Conclusions: In this study with 54 CHF patients, device interrogations revealed that lower levels of 25(OH)D were associated with AHRE episodes. Further investigation will be necessary to elucidate, whether substitution of Vitamin D may have an additional benefit for rhythm control in patients with CHF.

POSTERSITZUNG 6 – Risikofaktoren/ Stoffwechsel/Lipide 1

6-1

C-reactive protein significantly predicts cardiovascular events both in peripheral artery disease patients with and in those without type 2 Diabetes

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Background: The power of C-reactive protein (CRP) to predict cardiovascular events in the extremely high-risk population of patients with the combination of peripheral artery disease (PAD) and type 2 diabetes (T2 DM) is unclear and is investigated in this study.

Methods: We measured serum CRP in 319 consecutive patients with sonographically proven PAD. T2 DM was diagnosed according to the American Diabetes Association definition. Prospectively, cardiovascular events were recorded over a mean follow-up time of 4.2 ± 3.0 years.

Results: At baseline, CRP in our cohort of PAD patients did not differ significantly between patients with T2 DM and nondiabetic subjects (1.0 ± 1.7 vs. 0.8 ± 1.8 mg/dl; $p = 0.122$). Prospectively, 194 patients, i. e. 60.8% of the total study cohort suffered cardiovascular events, and CRP after multivariate adjustment was a significant predictor of cardiovascular event risk in the total patient cohort, with a standardized adjusted hazard ratio (HR) of 1.25 [1.43–1.63]; $p < 0.001$. Considering diabetes status, the cardiovascular event rate was even higher in PAD patients with T2 DM than in those who did not have diabetes (68.4 vs. 55.2%; $p < 0.001$). CRP significantly predicted cardiovascular events both in PAD patients with T2 DM and in those who did not have T2 DM, with standardized adjusted HRs of 1.36 [1.08–1.70]; $p < 0.001$ and 1.52 [1.28–1.81]; $p < 0.001$, respectively.

Conclusions: We conclude that CRP significantly predicts cardiovascular events both in PAD patients with and in PAD patients without T2 DM.

6-2

Impact of past and current smoking on mortality risk in angiographied coronary patients with Type 2 Diabetes

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Background: The impact of smoking on mortality risk in angiographied coronary patients is unclear and is addressed in the present study.

Methods: We enrolled 1804 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary disease (CAD). Patients who had smoked within 30 days prior to angiography were considered current smokers. Prospectively, mortality was recorded over a mean follow-up time of 7.6 ± 2.8 years.

Results: At baseline, both in patients with T2 DM ($n = 522$; 28.9% of the study cohort) and in non-diabetic subjects the prevalence of a past (44.1 and 39.5%; $p = 0.035$) and, albeit less so, of current smoking (18.0 and 17.7%; $p = 0.247$) was high. Prospectively, current smoking independently predicted cardiovascular events after multivariate adjustment including baseline

CAD in patients with diabetes (HR 1.78 [1.16–2.74]; $p=0.009$) as well as in non-diabetic patients (HR 1.68 [1.12–2.52]; $p=0.013$), whereas past smoking neither in patients with T2 DM nor in non-diabetic subjects was associated with cardiovascular events (HRs 0.77 [0.54–1.10]; $p=0.152$ and HR 1.16 [0.87–1.53]; $p=0.313$, respectively). An interaction term diabetes x current smoking was not significant ($p=0.564$), indicating that current smoking was equally predictive of mortality in patients with T2 DM and in nondiabetic subjects.

Conclusions: We conclude that current but not past smoking strongly increases mortality risk angiographied coronary patients with T2 DM independently from the baseline CAD state.

6-3

Single and combined effects of peripheral artery disease and of Type 2 Diabetes Mellitus on the risk of cardiovascular events in women

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Background: Both peripheral artery disease (PAD) and type 2 diabetes (T2 DM) are associated with a high risk of cardiovascular events. However, the single and combined effects of PAD and of T2 DM in women have not been investigated yet and are addressed in the present study.

Methods: We prospectively recorded cardiovascular events in a series of 436 women of whom 94 had PAD and 342 did not have PAD.

Results: At baseline, the prevalence of diabetes was higher in women with PAD than in those who did have PAD (41.5 vs. 21.6%, $p<0.001$). Over a mean follow-up period of 7.2 years we recorded 108 cardiovascular events. When compared to the event rate in women with neither PAD nor T2 DM (14.9%) the event rate was not significantly increased in those with T2 DM but without PAD (16.2%; $p=0.972$) but was significantly higher in non-diabetic women with PAD (47.3%; $p<0.001$) and further increased in those with both PAD and T2 DM (76.9%; $p<0.001$). Nondiabetic women with PAD were at a significantly higher cardiovascular risk than women with T2 DM who did not have PAD ($p=0.001$). When compared to women with neither PAD nor T2 DM, adjusted hazard ratios were 0.93 [0.48–1.80]; $p=0.831$, 3.80 [2.02–7.13]; $p<0.001$, and 7.41 [3.87–14.19]; $p<0.001$ for women with T2 DM only, for those with PAD only and for those with the combination of PAD plus T2 DM, respectively.

Conclusions: We conclude that T2 DM strongly increases the risk of future cardiovascular events in women with PAD. However, type 2 diabetic women who do not have PAD are at a significantly lower cardiovascular event risk than non-diabetic women with PAD. PAD in women is a stronger risk factor than T2 DM.

6-4

The Visceral Adiposity Index predicts cardiovascular events both in cardiovascular disease patients with and in those without diabetes

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Background: The Visceral Adiposity Index Predicts Cardiovascular Events Both in Cardiovascular Disease Patients With and in those Without Diabetes. The visceral adiposity index (VAI) is a validated tool for the evaluation of visceral adiposity, using waist circumference, serum triglycerides, age and gender to diagnose this metabolic abnormality. It has recently been associated with cardiovascular risk in primary care patients. No data are available on the association of the VAI with mortality in patients with cardiovascular disease (CVD).

Methods: We therefore prospectively recorded the incidence of cardiovascular events over a mean follow-up period of 7.9 ± 3.1 years in a large cohort of 1858 consecutive patients with established cardiovascular disease (1599 patients with angiographically proven coronary artery disease and 259 patients with sonographically proven peripheral artery disease). The VAI was calculated according to the Amato formula; type 2 diabetes (T2 DM) was defined according to the ADA definition.

Results: At baseline, the VAI was significantly higher in CVD patients with T2 DM than in those who did not have diabetes (347 ± 331 vs. 228 ± 200; $p<0.001$). Prospectively, 585 vascular events occurred; the event rate was significantly higher in patients with T2 DM than in those who did not have diabetes (46.8% vs. 31.3%; $p<0.001$). After multivariate adjustment, the VAI significantly predicted cardiovascular events in CVD patients with T2 DM (standardized adjusted hazard ratio (HR) 1.24 [1.09–1.42]; $p=0.007$) as well as in those who did not have T2 DM (HR 1.18 [1.06–1.31]; $p=0.014$).

Conclusions: We conclude that the VAI predicts cardiovascular events both in CVD patients with and in those without diabetes.

6-5

Einsatz von PCSK9-Inhibitoren bei therapieresistenter Hyperlipidämie nach Herztransplantation

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Grundlagen: Die Hyperlipidämie ist ein wesentlicher Risikofaktor für die Entstehung der Graftvaskulopathie (GVP) nach

Herztransplantation. Unter der immunsuppressiven Therapie beträgt die Inzidenz der Hyperlipidämie bei herztransplantierten (HTX-)Patienten im ersten Jahr 74 % und 91 % innerhalb von 5 Jahren. Die lipidsenkende Therapie mit Statinen stellt aufgrund von Medikamenteninteraktionen und Verstärkung der Nebenwirkungen eine große Herausforderung dar. Proproteinkonvertase Subtilisin/Kexin Typ 9 (PCSK9)-Inhibitoren haben sich bereits bei kardiovaskulären Hochrisikogruppen als sehr effektiv erwiesen. In unserem Zentrum haben wir erstmalig PCSK9-Inhibitoren bei ausgewählten HTX-Patienten eingesetzt, die einerseits mit zumutbarer Statindosis und/oder mit Etizimib nicht die angestrebten LDL-Cholesterin-Zielwerte von 100 mg/dl erreichen konnten.

Methodik: Im Zeitraum 02/2017 bis 12/2017 wurden 13 erwachsene HTX-Patienten (Alter: 60,4 ± 10,9, 30,8 % weiblich) ausgewählt. Die Patienten waren 54,3 ± 40,1 Monate post-HTX. Die ausgewählten Patienten wurden gemeinsam mit der für PCSK9-Anwendung zugelassen Lipidambulanz begutachtet und die Therapie initiiert. Die Patienten erhielten Alirocumab 75 mg s. c. alle 2 Wochen. Observationszeit war 6 Monate vor Konversion bis 6 Monate nach Konversion. Veränderungen in der Statintherapie wurden bei Änderungen der Lipidwerte bzw. Nebenwirkungen durchgeführt und dokumentiert. Um die Inzidenz und Prävalenz von Myopathie und Hepatoxizität zu evaluieren wurden 1, 3 und 6 Monate post Konversion CK und Leberenzyme gemessen. Effektivitätsanalysen wurden mittels serieller Messungen von Blutlipiden (LDL, HDL, Cholesterin, Triglyceride und LP(a)) durchgeführt.

Ergebnisse: Gesamt Cholesterin (228,9 ± 37,4 vs. 136,1 ± 42,5 mg/dl; $p < 0{,}001$), LDL Cholesterin (140,4 ± 27,6 vs. 53,6 ± 24,1 mg/dl; $p < 0{,}001$) und Lipoprotein (a) (69,7 ± 71,9 vs. 46,4 ± 54,8 mg/dl; $p = 0{,}002$) zeigten signifikant niedrigere Werte nach Therapiestart und blieben signifikant niedriger bis zum Ende des Beobachtungszeitraums. Triglyceride (165,9 ± 45,9 vs.157,8 ± 75,5 mg/dl, p = n.s.) und HDL Cholesterin (55,2 ± 11,6 vs. 53,2 ± 19,6 mg/dl; p = n.s.) änderten sich nicht. Die Prävalenz von CK und Transaminasen Erhöhungen änderten sich nicht. (CK: 46,2 %, GPT: 7,7 %, GOT: 7,7 %, GGT: 23,1 %). Jeweils 4 Patienten (30,7 %) hatten Rosuvastatin, Atorvastatin oder kein Statin vor dem Therapiestart. Ein Patient wurde mit Pravastatin behandelt. In 77,8 % ($n = 7$) Patienten wurde die Statintherapie nach Therapiestart geändert. In 4 Patienten wurden Statine gestoppt, bei 2 Patienten wurde die Dosis reduziert und in einem Patienten wurde von Rosuvastatin auf Atorvastatin konvertiert. PCSK9 assoziierte Nebenwirkungen (Nervensystem, Schmerzsymptome) traten bei keinem der behandelten Patienten auf und bei keinem Patienten musste die Therapie abgebrochen werden.

Schlussfolgerungen: Die Therapie mit PCSK9-Inhibitor (Alirocumab) stellt eine effektive und sichere Option in der Therapie der Hyperlipidämie nach Herztransplantation dar. Unter der Therapie blieben die Leber- und Nierenfunktionsparameter stabil, während eine signifikante Reduktion der Lipidwerte erreicht wurde. Ob die PCSK9-Therapie langfristig auch einen positiven Einfluss auf die Entstehung bzw. Progredienz der GVP haben wird, muss in einem längeren Beobachtungszeitraum ermittelt werden.

6-6

Betatrophin predicts cardiovascular events independently from the presence of Type 2 Diabetes and coronary artery disease

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Background: Betatrophin, also known as ANGPTL8 or lipasin is a nutritionally-regulated protein secreted by the liver and adipose tissue. It is associated with type 2 diabetes mellitus (T2 DM) and lipid metabolism. Whether betatrophin is associated with the risk for cardiovascular events is unknown and is addressed in the present study.

Methods: We measured betatrophin in 553 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD) and prospectively recorded cardiovascular events in these patients during a follow-up period of up to 8 years.

Results: During follow-up, 301 cardiovascular events occurred. The incidence of cardiovascular events was significantly higher in patients with T2 DM ($n = 161$) than in those who did not have diabetes (47.2% vs. 34.4%; $p = 0.005$). Betatrophin was significantly and inversely associated with cardiovascular events both univariately (HR 0.64 [95%CI 0.47–0.87], $p = 0.004$) and after full adjustment including T2 DM and baseline CAD (HR 0.55 [95%CI 0.40–0.76], $p < 0.001$). The inclusion of betatrophin to a basic prediction model for the cardiovascular event risk significantly increased model performance (NRI = 0.188, $p < 0.01$).

Conclusions: In conclusion, this study for the first time shows that betatrophin predicts cardiovascular events independently from conventional risk factors including the presence of T2 DM.

6-7

Disease-specific characteristics of vascular cell adhesion molecule-1 levels in patients with peripheral artery disease

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Background: Peripheral arterial disease (PAD) is one of the most common manifestations of systemic atherosclerosis. Inflammatory processes play an important role in the disease initiation as well as in its progression. Vascular cell adhesion molecule 1 (VCAM-1), a biomarker of endothelial dysfunction appears to be an important mediator in these inflammatory processes. Therefore, we hypothesized that, in patients with PAD, circulating VCAM-1 might be elevated due to its function in mediating adhesion of immune cells to the vascular endothelium in the process of endothelial dysfunction and inflammation.

Methods: A total of 106 non-consecutive patients were enrolled at the University clinic Jena in this study, of whom 51 patients had typical clinical manifestations of PAD and as controls 55 patients with no history of PAD or cardiovascular disease. All serum samples were obtained either during hospitalization or during out-patient visits and were analyzed for VCAM-1 by the use of ELISA.

Results: Compared with controls, median levels of VCAM-1 were significantly elevated in patients suffering from PAD (953 vs. 1352 pg/ml; $p < 0.001$).

Furthermore VCAM-1 appeared to be highly discriminative for the detection of PAD (AUC = 0.76; CI 0.67–0.83). We could not observe dynamics related to increasing disease stages according to Rutherford classes in patients with apparent PAD.

Conclusions: VCAM-1 was shown to be a potential discriminator and biomarker for systemic atherosclerosis. In a logistic regression analysis, VCAM-1 was robustly associated with diagnosis of PAD, even after correction for clinically relevant confounders (namely age, arterial hypertension, diabetes and LDL-levels). Thus, VCAM-1 might serve as a biomarker for PAD screening and detection.

6-8

Unusual cause of secondary hypertension

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Background: Patients who have severe or resistant hypertension should be screened for secondary hypertension. The simultaneous intake of an adequate dose of three different antihypertensive agents (inlcuding one diuretic) is defined as a resistant hypertension. Electrolyte disorders like hypokalemia with concomitant metabolic alkalosis could be a clue for secondary hypertension. If the underlying cause is cured, the blood pressure will normalize completely. We present a patient with a reninoma, which is a very unusual benign tumor of the juxtaglomerular apparatus, as the underlying cause for secondary hypertension.

Case Report: A 43 y/o female patient was referred to our hospital with acute chest pain radiating to the left arm. The medical history was remarkable for diabetes and for severe hypertension since young adulthood. An extensive increased blood pressure (240/120 mmHg) was causal for these symptoms. The blood test analysis showed a hypokalemia (2.9 mmol/l) with a concomitant metabolic alkalosis (pH 7.528, BE 5.8) under ACE inhibitor drug therapy. This constellation is suspicious for a primary hyperaldosteronism. Nevertheless we ruled out Cushing's syndrome, pheochromocytoma and renal artery stenosis. The results of the determination of aldosterone and renin was unexpected. Renin was elevated 42 times over the upper normal limit and lead to a secondary hyperaldosteronism. Through MRI we were able to detect a 10 × 15 mm tumor in the left kidney. For the final diagnoses we arranged a selective renal vein renin sampling to verify a lateralization of renin. A renin lateralization ratio > 1.5 is specific for a renin producing tumor. With a ratio of 1.58 to the left kidney our result was matching to the lesion in the MRI. Consequently, kidney surgery as a curative intervention was recommended.

Conclusions: A Renin producing juxtaglomerular cell tumor is a very unusual but curable cause of secondary hypertension. To make the final diagnosis a selective renal vein renin sampling following a strict protocol is necessary. Surgical removal by partial nephrectomy is the treatment of choice.

POSTERSITZUNG 7 – Basic Science 2

7-1

Cardiac fibrosis induced by cardiac remodeling, hypertrophy, or cardiotoxicity is characterized by distinct alterations in transcriptomic profiles in pigs

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Background: Myocardial fibrosis is characterized by a profound qualitative and quantitative alteration of the interstitial collagen network in the heart and promotes the development of cardiac dysfunctions. Fibrosis can be caused by a variety of different diseases or cardiac insults, resulting in similar symptoms of systolic and/or diastolic heart failure. Despite shared phenotypes, we hypothesized that distinct triggers of fibrosis would result in different alterations in the transcriptome of affected porcine hearts. We investigated fibrotic porcine myocardial samples from the remodeled remote zone of myocardial infarction (FIBRO), of animals treated with cardiotoxic drugs (doxorubicin/DOX/and liposomal doxorubicin/MYO/), and of hypertrophic hearts (HYPI; developed by experimental artificial aortic stenosis). Subtle differences in molecular mechanisms may significantly affect severity, reversibility, and individual disease-specific treatment strategies for cardiac fibrosis.

Methods: The transcriptomes of these samples were analyzed by next generation sequencing (NGS). For RNA-sequencing, strand specific libraries of 500 ng total RNA for paired end sequencing were prepared and mapped to the Sus scrofa genome. We analysed data using moderated statistics, principal component analyses (PCA), and signaling pathway impact analyses (SPIA), and constructed heat maps for result presentation.

Results: Myocardial infarction, hypertrophy and cardiotoxicity led to predominantly systolic, diastolic and combined systolic/diastolic heart failure, respectively. PCA indicated several common similarities of myocardial fibrosis that are independ-

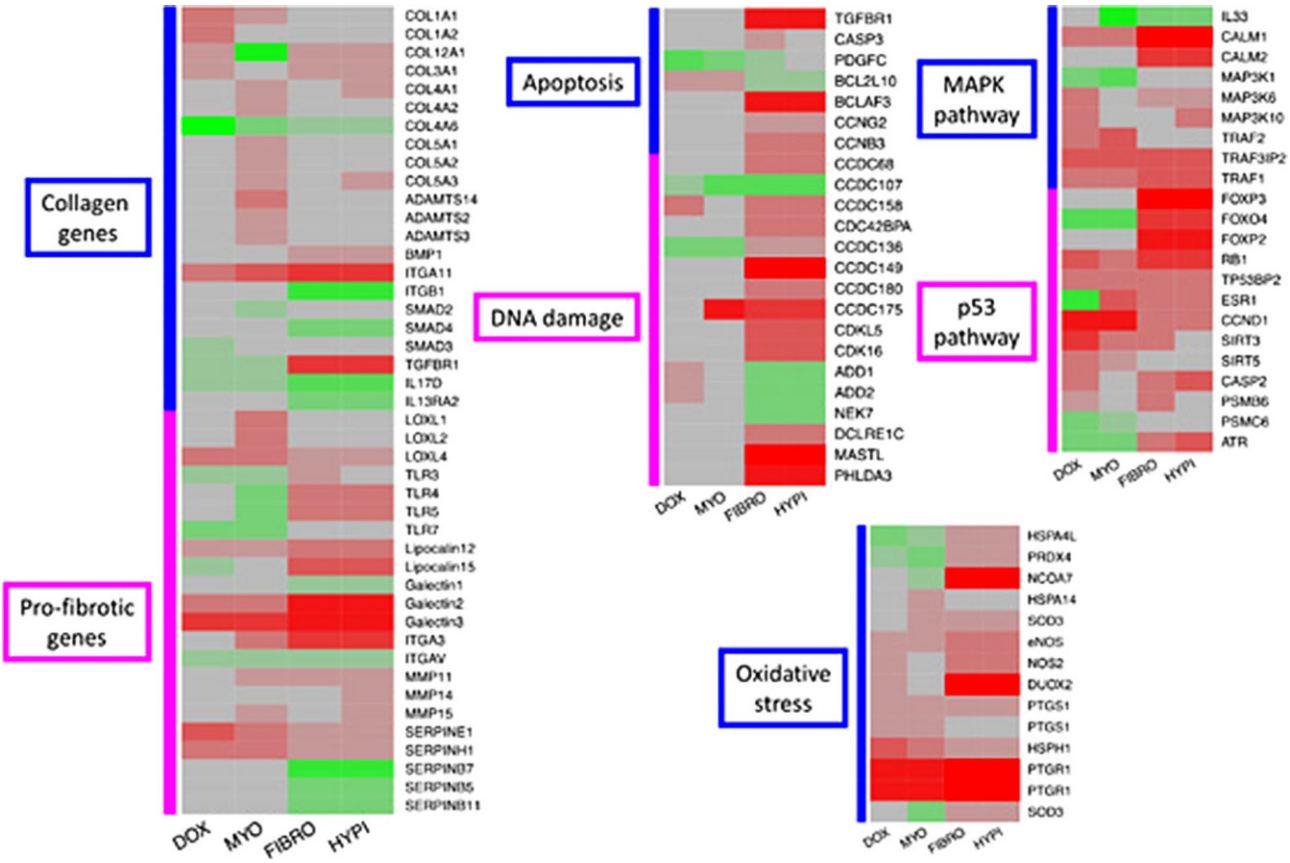

Fig. 1|7-1

ent of the underlying cause, highlighting shared mechanisms. However, cardiac remodelling after AMI and cardiac hypertrophy were characterized by more significant overlap, while the transcriptome of hearts treated with the cardiotoxic agents DOX and MYO differed to a higher extent (Fig. 1). These data indicate a varying mechanism and/or a distinct stage of fibrosis. In particular, the p53 and MAPK pathways, as well as genes involved in DNA damage and oxidative stress were more strongly induced in FIBRO and HYPI compared to DOX and MYO. Collagens and collagen processing enzymes were moderately upregulated in all groups, reflecting fibrosis on the transcriptional level.

Conclusions: Transcriptomic analyses revealed distinct mechanisms of myocardial fibrosis upon cardiotoxic drug treatment compared to cardiac remodeling after AMI or hypertrophy. The results highlighted common characteristics of fibrosis, and might facilitate the development of precision medicine approaches for cardiac fibrosis associated with a distinct mechanism.

7-2

Heart failure with reduced ejection fraction is characterized by systemic NEP downregulation

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Background: Inhibition of the ubiquitously expressed membrane-bound zink-metalloendopeptidase neprilysin (NEP) with sacubitril within the new class of drug angiotensin-receptor neprilysin inhibitor (ARNI) resulted in improved outcome of patients with heart failure (HF) with reduced ejection fraction (HFrEF) and is currently standard of care. NEP is implicated in the homeostasis of vasoactive peptides however neither the exact mechanisms, pathophysiologic alterations accompanying the condition of heart failure nor the contribution of the different organ systems are elucidated. The aim of this study was to investigate differential NEP expression, i. e. mRNA levels, NEP content, i. e. protein concentrations, and enzymatic NEP activity of various tissues in a translational model of chronic heart failure.

Methods: Ten pigs were randomized either to control ($n=5$, C-group) or HF groups ($n=5$, HF-group) at an age of three months. The animals of the HF-group underwent reperfused myocardial infarction of 90 minutes via percutaneous balloon occlusion of the mid left anterior descending coronary artery. At day three and at six months cardiac magnetic-resonance-imaging (cMRI) was performed to determine the infarction size and confirm impaired left ventricular (LV) function. At six months the animals were sacrificed and tissues of the main organs and different cardiac regions were harvested. NEP concentrations and activity were measured from fresh-frozen samples using a specific ELISA (R&D systems, UK) and a fluorimetric peptide cleavage assay, NEP expression was determined from RNA-later samples by performing duplex real-time polymerase-chain-reaction (qPCR). NEP concentrations and activities were equally determined in plasma and liquor samples. Relative values for all organs of pooled samples of the HF and control animals were compared by a non-parametric test and linear

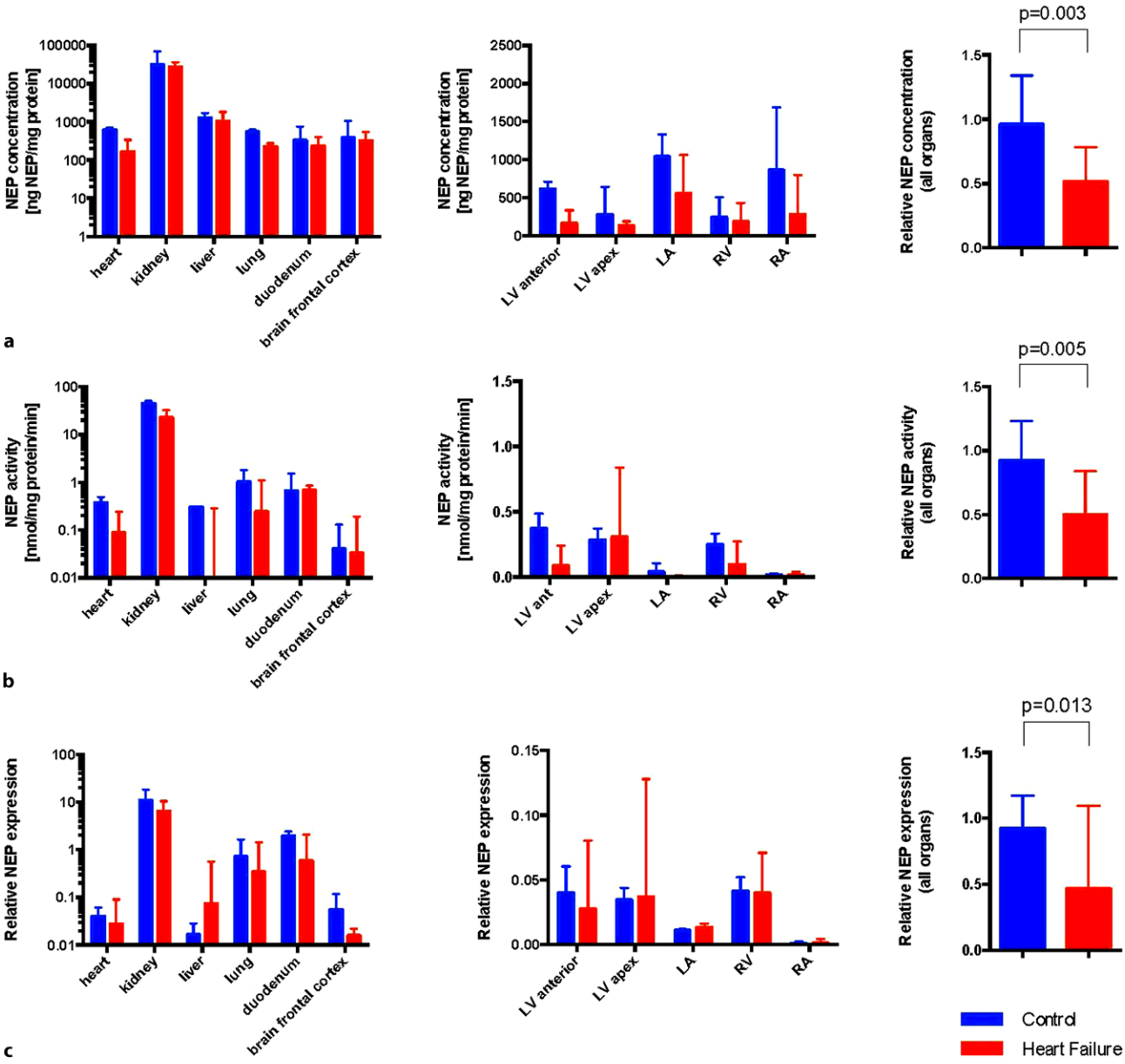

Fig. 1|7-2

regression models were calculated between NEP expression, concentration and activities.

Results: cMRI confirmed myocardial infarction with a scar area of 21.5% (IQR 20.2–22.4) of the LV at day 3 and a higher end-diastolic volume of 100.8 ml (IQR 95.2–110.2) and reduced LV EF of 41.8% (IQR 41.3–44.1) at 6 months of the HF-group compared to 79.0 ml (IQR 78.9–82.9) and 53.0% (IQR 51.8–55.0) of the C-group. NEP expression was downregulated and translated into reduced protein concentrations and activity for the sampled organ systems in the HF animals [$p=0.003$, $p=0.005$ and $p=0.013$] (Fig. 1 a–c). Control and HF hearts showed clearly detectable NEP measures with different patterns for ventricles and atria. NEP concentrations and activity between plasma and liquor samples were comparable. Tissue NEP expression and tissue NEP concentrations showed modest correlation [R2 = 0.284, $p<0.001$], tissue NEP concentrations and tissue NEP activity however an excellent correlation [R2 = 0.727, $p<0.001$] (Fig. 2 a). Plasma NEP concentrations and activity however could not be correlated to their tissue equivalents (Fig. 2 b). NEP kidney levels were 20- to 100-fold higher compared to all other organs, such as heart, abdominal organs, brain or lungs.

Conclusions: The condition of HF is characterized by a systemic downregulation alongside reduced concentrations and activity of NEP in various organs. The success of ARNI in HF might lie in the enhancement of the already initiated pathophysiological counter regulation of natural NEP action. Plasma NEP is assumably not a good biomarker.

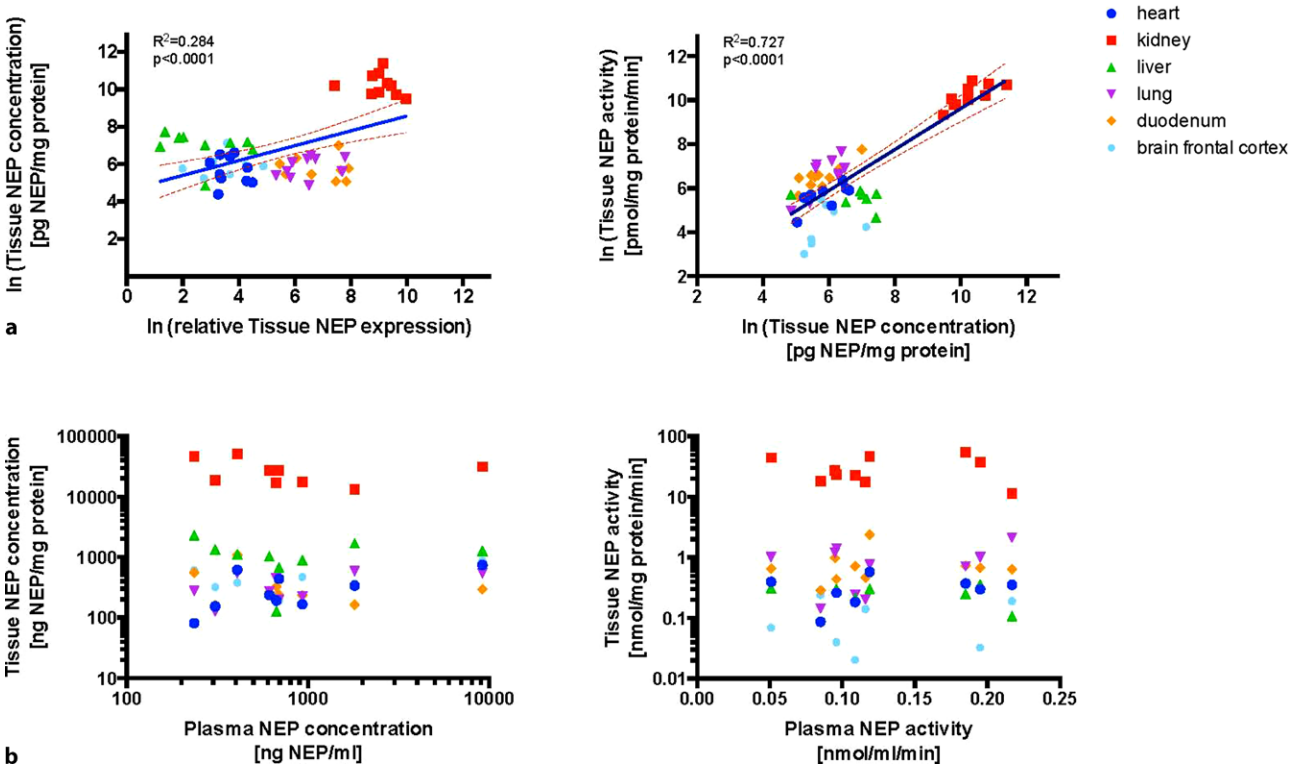

Fig. 217-2

7-3

In vitro differentiation of porcine cardiac progenitor cells to cardiomyocytes with 5-azacytitine and TGF-β1 stimulation

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Background: The conduction of porcine translational model experiments is a suitable strategy to study therapeutic approaches in basic research. Nevertheless the reduction of animal experiments has to be striven in regards to the 3 R Principle of Russell and Burch.

Therefore cell culture experiments are an alternative for the investigation of fundamental processes of cardiac issues. Since there is no purchasable porcine primary cardiomyocyte and cardiac progenitor cell line available on the market, we aimed to establish a porcine cardiac progenitor (pCPC) cell culture. This gives us the opportunity to differentiate the cells into multiple cardiac cell lineages—including cardiomyocytes—for the exploration of different physiological and pathological processes. In this study we tested the differentiation capability of pCPC to cardiomyocytes.

Methods: pCPC were isolated out of the left ventricle of porcine hearts, propagated and then characterized with cardiac progenitor cell markers islet-1 (isl-1), stem cells antigen-1 (sca-1) and tyrosine kinase KIT (c-kit or CD117). For the differentiation procedure 1 × 105 cells were seeded to each well in a 6-well-plate and medium was changed to differentiation medium (IMDM and Hams F12 supplemented with horse serum, non essential amino acids, insulin, transferrin, selenium, penicillin-streptomycin). 5-azacytidine was used in a concentration of 5 μM per well on three consecutive days for the initiation of differentiation. Cells were cultured for 3 weeks and supplemented every 2 days with fresh medium and ascorbic acid, twice a week with TGF-β1. At different time points cells were stained with immunofluorescence and mRNA was isolated to determine the state of differentiation with q-PCR quantification of sca-1 (ATXN-1), isl-1, GATA-4, MYH7 (myosin heavy chain beta), TNI (cardiac troponin I).

Results: Cardiomyocyte specific markers like cardiac TNI (3.99 +/– 0.24 log fold change) and GATA-4 (17.46 +/– 0.07 log fold change) had their highest expression on day 14 after differentiation compared to control pCPCs, with a drastically decrease of expression after day 17 (TNI 1.46 +/– 0.05; GATA-4 0.91 +/– 0.003) (Fig. 1, Fig. 4). The expression of MYH7 increased directly after 5-azacytidine stimulation to a fold change of 17.7 +/– 0.13 compared to the control cells, decreased between day 7 and day 10 with a slight increase of expression on day 14 again (1.72 +/– 0.82) (Fig. 2, Fig. 4).

Interestingly, pCPC specific markers further increased their expression after 5-azacytidine differentiation with a peak at day 14 (sca-1 4.68 +/– 0.126; isl-1 40.91 +/– 0.08).

The cultivation of pCPC together with TGF-β1 seems to inhibit the expression of cardiac specific markers TNI and GATA-4, as well as MYH7, sca-1 and isl-1.

Conclusions: In summary it can be stated that the highest expression of cardiac specific markers was observed at day 14 after differentiation induction with 5-azacytidine. TGF-β1 had no positive effect on differentiation capacity.

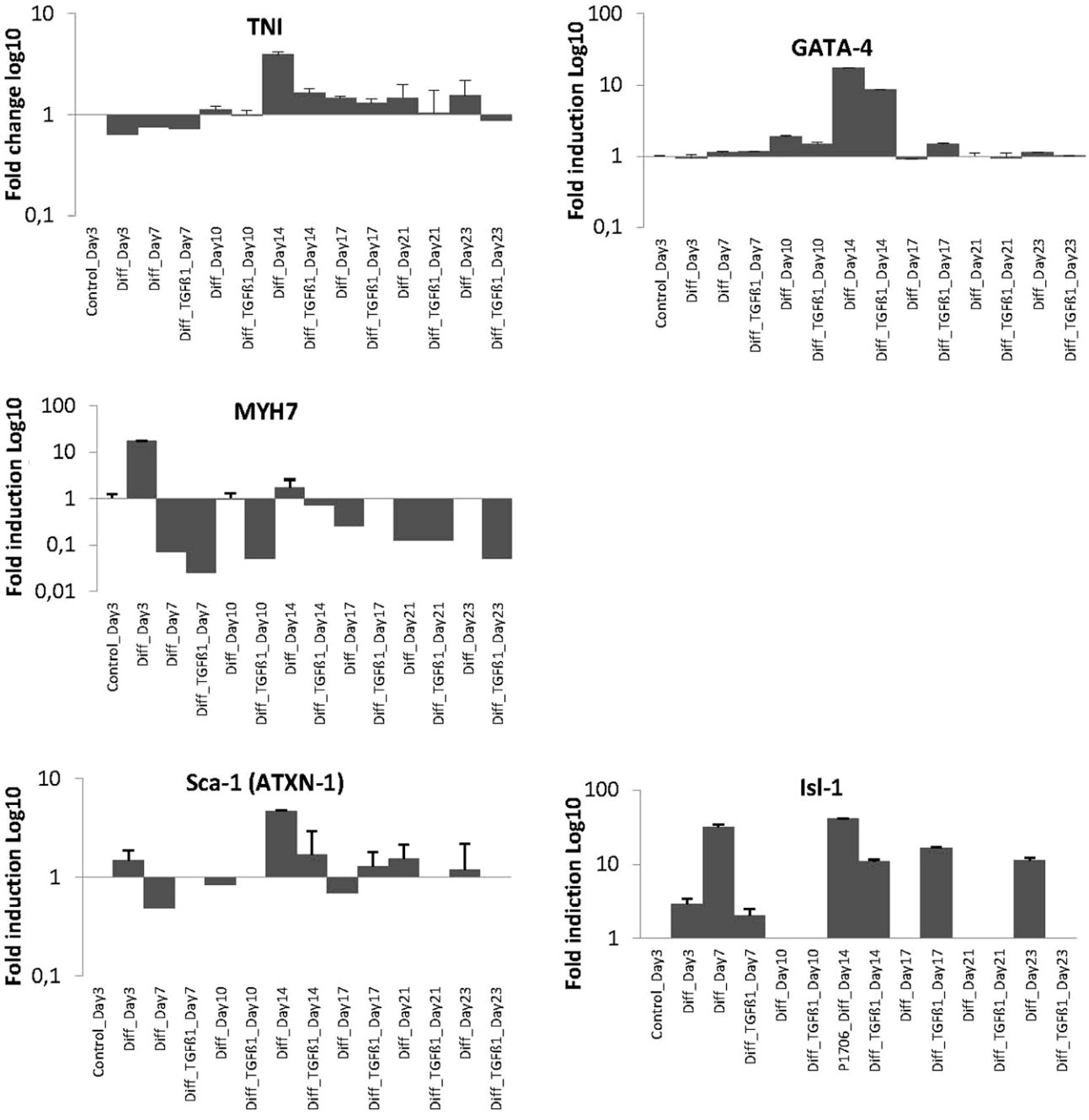

Fig. 1|7-3

7-4

Neprilysin (CD10) expression on peripheral leukocytes in chronic heart failure patients

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Background: Neprilysin inhibition (NEPi) has been shown to reduce hospitalization and all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF). Since then circulating NEP concentration (sNEP) has been discussed controversially as a biomarker. Neprilysin (CD10) is known to be present on the surface of monocytes and lymphocytes as well as at higher levels on neutrophils in healthy subjects and implicated in the inflammatory response. The possible impact of NEP expression on peripheral leukocytes on sNEP levels and prognostic measures in HFrEF have not been investigated yet.

Methods: We prospectively enrolled 99 consecutive patients with stable HFrEF, who were clinically followed-up routinely. Laboratory markers including NT-proBNP were assessed. sNEP and NEP (CD10) expression on peripheral blood cells were measured by FACS analysis for all patients. The association between NEP expression and laboratory parameters as well as with sNEP levels were determined.

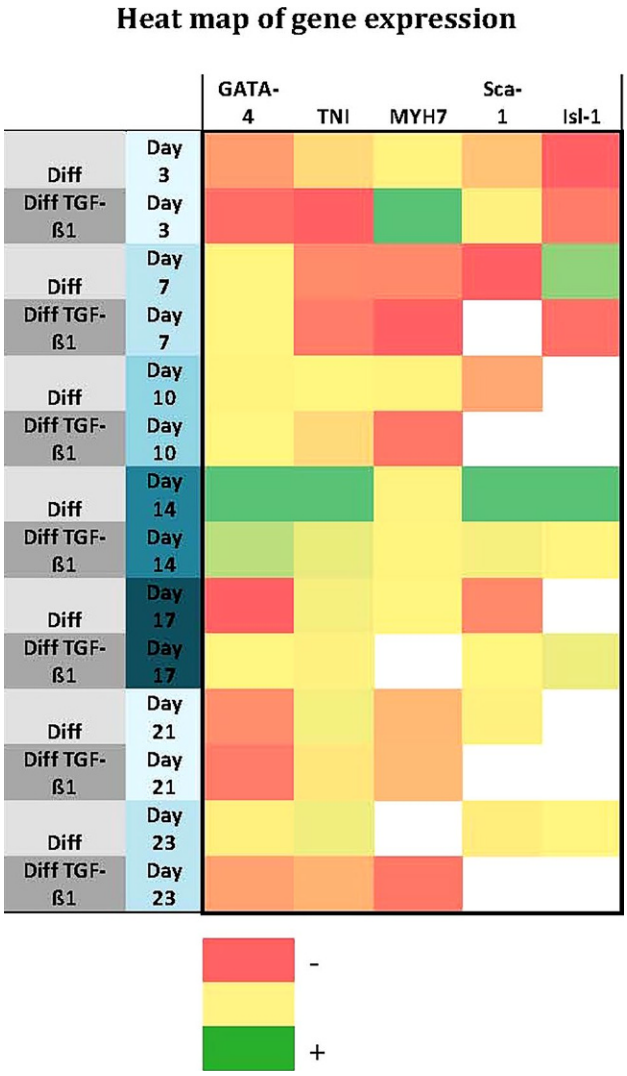

Fig. 2|7-3 Heat map of gene expression

Results: Fig. 1 shows characteristic FACS expression results for patients with HFrEF with high and low expression intensities of CD10. NEP was markedly expressed on granulocytes with 94.8% (IQR 90.5–97.4) and measureable on B-cells and monocytes with 8.5% (IQR 5.3–13.5) and 0.8% (IQR 0.4–1.5) of CD10 + cells of the respective leukocyte subtype. NEP expression on T-cells was not detectable. The mean fluorescence intensity (MFI) of CD10 was 5461 (IQR 4028–6904) for granulocytes, 640 (IQR 535–740) for B-cells and 1589 (IQR 1395–1975) for monocytes. An inverse correlation of NT-proBNP could be proven with the MFI of CD10 + granulocytes (r = –0.46, p&lt: 0.001) but not with the MFI of CD10 + B-cells (r = –0.13, $p = 0.191$) or CD10 + monocytes (r = 0.07, $p = 0.477$). Fig. 2 depicts differences in MFI for CD10+granulocytes according to tertiles of selected variables, i. e. NT-proBNP, albumin, hemoglobin and butyrylcholinesterase. sNEP concentrations were 2425 pg/ml (IQR 1559–3349). sNEP concentrations correlated positively with the expression of CD10 on granulocytes (r = 0.22, $p = 0.030$) and with the MFI of CD10 + granulocytes (r = 0.306, $p = 0.003$).

Conclusions: CD10 expression levels on neutrophils might reflect a distinct systemic inflammatory disposition, with low expression levels accompanying a more severe disease state reflected by NT-proBNP. Granulocyte CD10 expression correlates to measurable sNEP levels.

7-5

Toll-Like receptor 3 mediates radiation induced heart failure

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Background: Cardiovascular disease after adjuvant thoracic radiation has become the leading nonmalignant cause of death in cancer survivors. Radiation causes microvascular endothelial injury resulting in impaired cardiac function. The molecular mechanism of radiation induced microvascular damage remains unknown. Danger associated molecular patterns (DAMPs) are released from stressed cells and are known to activate Toll-like receptor 3 (TLR3), a receptor of the innate immune system. We hypothesized that radiation leads to release of DAMPs with subsequent activation of TLR3. Concomitant inflammation causes endothelial injury resulting in impaired myocardial function.

Methods: Endothelial cells were isolated from healthy donors undergoing heart transplantation and treated with radiation therapy (10 Gy). Expression levels of TLR3 and inflammatory cytokines were compared with cells treated either with TLR3 agonist poly (I:C) or a TLR3/dsRNA complex inhibitor. Cell cycle analysis via flow cytometry was performed after radiation. ApoE-/- and ApoE-/-/TLR3-/- mice underwent thoracic radiation (15 Gy). Heart function and morphology was analyzed via echocardiography and histological evaluation

Results: Radiation of endothelial cells resulted in activation of the TLR3 pathway, endothelial apoptosis and upregulation of the calcification marker RunX2. TLR3 inhibition abrogated radiation-dependent apoptosis of endothelial cells and resulted in a cell cycle G2 arrest. In vivo, thoracic radiation resulted in impairment of left ventricular function with reduced ejection fraction in ApoE-/- mice (LVEF %: 44.96 ± 1.70). However, left ventricular ejection fraction of ApoE-/-/TLR3-/- mice was clearly less affected by radiation (LVEF %: 50.08 ± 1.48, $p = 0.0401$).

Conclusions: Radiation leads to endothelial injury and activation of TLR3. Inhibition of TLR3 prevents from inflammation and endothelial apoptosis. ApoE-/-/TLR3-/- show superior left ventricular function after thoracic radiation compared to ApoE-/- mice. We show major involvement of TLR3 in the pathogenesis of radiation induced heart failure. TLR3 could become an effective therapeutic target for the prevention of heart disease after radiation.

7-6

Tenascin C upregulation under hyperglycemic and hypertrophic conditions in H9c2 rat cardiomyoblasts

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Background: Tenascin C (TN-C) is an important glycoprotein, which is part of the extracellular matrix and upregulated after myocardial infarction and hypertension. However, there is still limited evidence of TN-C expression and the interaction of TN-C on metalloproteinases (Mmps) and integrins in cardiomyocytes, caused by high glucose and cellular hypertrophy stressors. Therefore, the present study pursued to 1) establish in vitro experimental conditions on H9c2 rat cardiomyoblasts to upregulate TN-C expression and 2) to investigate the effect of TN-C on Mmps and integrins.

Methods: H9c2 rat cardiomyoblasts were exposed to three different conditions 1) standard control (5.6 mM glucose) and high glucose condition (35 mM glucose), 2) incubation with Angiotensin II (Ang II) and Endothelin-1 (ET-1) and 3) also cultured with human TN-C (1 and 10 ug/mL). Furthermore, total RNA was isolated and RT-qPCR was performed to value the expression levels of Tnc, Mmps, integrins and Erbbs (normalized to Gapdh).

Results: All experimental conditions showed that the mRNA expression of TNC is increased ($p<0.05$, respectively). Also, hyperglycemia increased the expression of TNC ($p<0.05$) remarkably compared to the controls, but downregulated both Mmps and integrins expression ($p<0.05$). When H9c2 cells were exposed to hypertrophic stressors such as Ang II or ET-1 cellular hypertrophy was revealed, associated with an increase

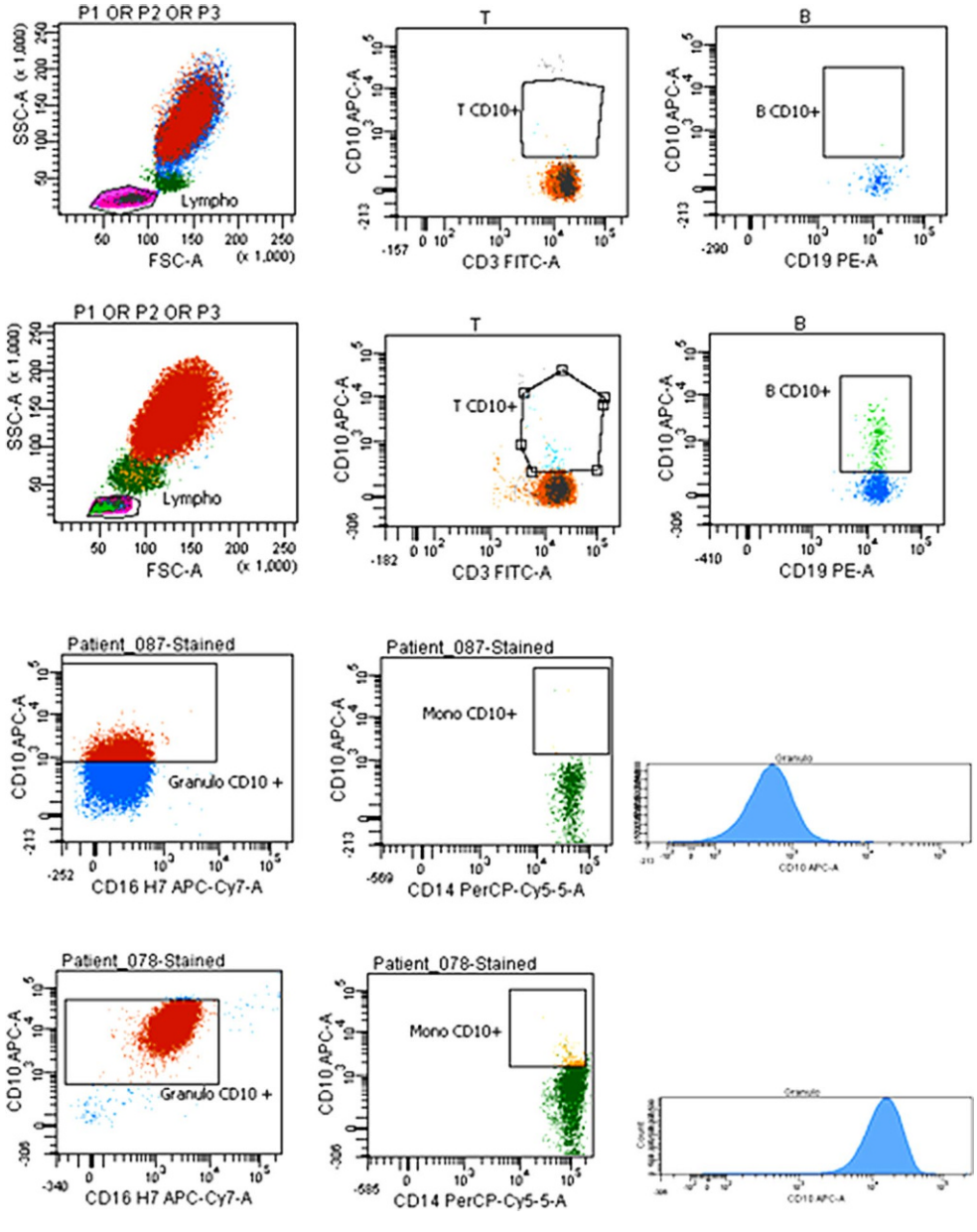

Fig. 1|7-4 NEP (CD10) expression on peripheral blood leukocytes. Characteristic FACS analysis for patients with HFrEF with A. low and B. high levels of CD10 expression on granulocytes as well as detectable expressions on monocytes, B-cells but not on T-cells

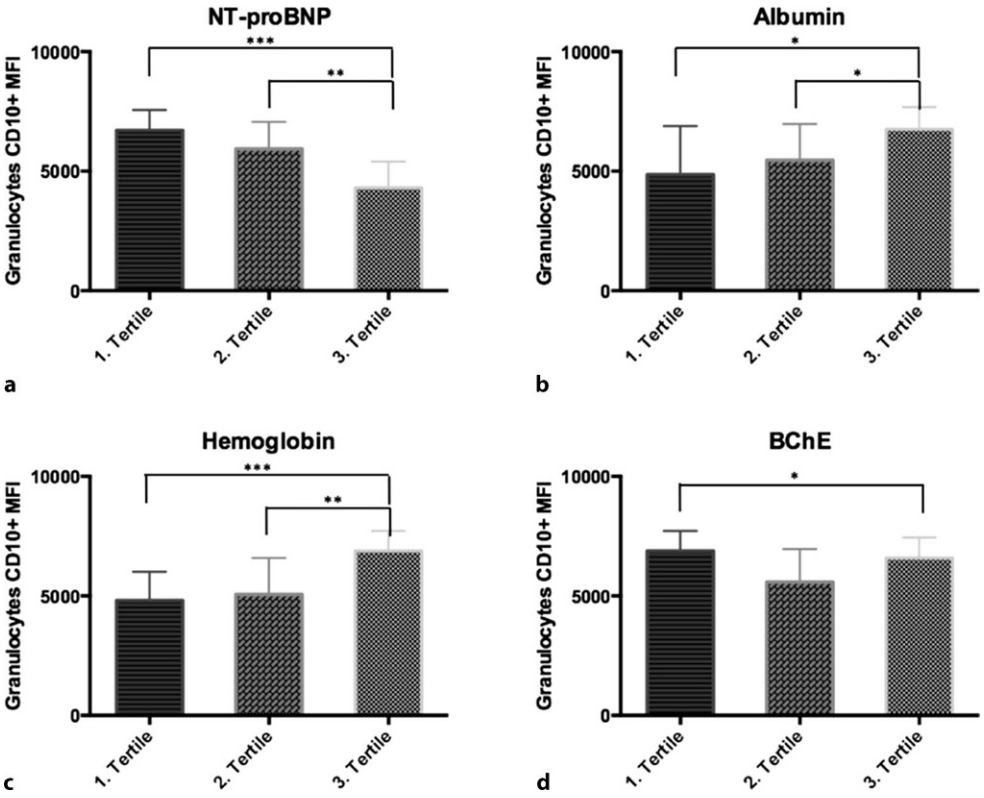

Fig. 2|7-4 NEP expression on granulocytes. Mean fluorescence intensity (*MFI*) values for NEP (CD10) expression on CD10+granulocytes of HFrEF patients ($n = 99$) according to tertiles of the respective variables (**a**) NT-proBNP, (**b**) Albumin, (**c**) Hemoglobin and (**d**) Butyryl-cholinesterase. Differences between the groups were compared by means of the Mann-Whitney-U-test

of Tnc expression compared to controls ($P < 0.05$). Moreover, human TN-C significantly increased the expression of BNP and decreased Mmps ($P < 0.05$ vs control, respectively) as well as time and dose dependently modified the expression of integrins.

Conclusions: This study shows successful results on the upregulation of TN-C in H9c2 cardiomyoblasts. From all tested conditions, TN-C mRNA expression was markedly upregulated. Of note, TN-C plays a potential role on fibrotic and hypertrophic markers regulation.

7-7

Neurohormonal profile in patients with non-ischaemic, dilated cardiomyopathy and its relationship to causes of death after 10 years of follow-up

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Background: The prognostic and diagnostic value of natriuretic prohormones is widely accepted in acute and chronic heart failure. However, their value in arrhythmic risk stratification in patients with non-ischaemic, dilated cardiomyopathy (DCM) is still unknown.

Methods: We measured midregional (MR) pro-atrial natriuretic peptide (proANP), MR-pro-adrenomedullin (proADM), C-terminal proendothelin-1 (CT-proET-1) and N-terminal pro-B natriuretic peptide (NT-proBNP) in 52 patients with DCM and left ventricular ejection fraction (LVEF) ≤ 50% and 30 control subjects without heart disease and normal LVEF. Primary end-points were time to arrhythmic death (AD) or resuscitated cardiac arrest (RCA), and secondary end-point was all-cause mortality.

Results: After 10 years (median 7 years) of follow-up 21/52 DCM patients (40.4%) died. A cardiac death was observed in 20 patients, where 10 patients had an AD and 2 patients had a RCA. The remaining 8 patients died from progressive heart failure. One patient died a non-cardiac death. MR-proANP, MR-proADM, CT-proET-1, and NT-proBNP were significantly higher in patients with DCM compared to controls ($p < 0.001$ for all markers). After adjustment for age, sex, LVEF and New York Heart Association functional class, MR-proANP (HR = 2.2, 95% CI 1.2–3.8, $p = 0.008$), MR-proADM (HR = 2.4, 95% CI 1.1–5.2, $p = 0.038$) and CT-proET-1 (HR = 2.7, 95% CI 1.3–5.6, $p = 0.009$) were independent predictors for all-cause mortality but were non-predictive for AD and RCA. In a model including all three biomarkers, only MR-proANP remained significant predicive for all-cause mortality in DCM (HR = 2.3, 95% CI 1.2–4.3, $p = 0.007$). However, when NT-proBNP was added to a multivariable model, MR-proANP was not significantly associated with all-cause mortality (HR = 2.2, 95% CI 0.6–7.8, $p = 0.226$).

Conclusions: Patients with DCM showed neurohormonal activation. MR-proANP, MR-proADM, and CT-proET-1 were predictive for all-cause mortality but not for arrhythmic death. None of the three biomarkers added additional prognostic information on top of NT-proBNP in DCM patients.

POSTERSITZUNG 8 – Bildgebung 1

8-1

2D echocardiography versus cardiac MRI after acute ST-elevation myocardial infarction: a real world comparison

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Background: Several studies have compared left-ventricular volumes and ejection fraction determined by 2D echocardiography and cardiac MRI. No study is available in the acute post-infarct period after ST-elevation myocardial infarction.

Methods: We have retrospectively analyzed 217 2D-echocardiograms performed in routine clinical practice and compared results to CMR data obtained from STEMI patients treated by primary percutaneous coronary intervention enrolled in a prospective database. Patients were stratified according to location of myocardial infarction (anterior; non-anterior) and 2D-echocardiography image quality. Echocardiograms were performed a median of 3 days after STEMI and CMR was performed at a median of 2 days.

Results: 2D-echocardiography significantly underestimated end-diastolic volumes (131+/–30 vs. 149+/–34 ml), end-systolic volumes (64+/–20 vs. 71+/–27 ml) and ejection fraction (51+/–8 vs. 53+/–11%) when compared to cardiac MRI (all $p<0.01$). In patients with good or excellent 2D echocardiography image quality, ejection fraction was not different (51+/–8 vs. 51+/–12%, $p=0.7$; $n=87$); the same applies to patients with anterior myocardial infarction, independent of image quality (49+/–8 vs. 50+/–11%; $p=0.4$; $n=96$).

Conclusions: Echocardiography significantly underestimated volumes and ejection fraction in an acute STEMI-population compared to CMR in a retrospective analysis of real world echocardiography data. In patients with high 2D echocardiography image quality or with anterior myocardial infarction ejection fraction was not significantly different and with acceptable limits of agreement.

8-2

Atrial remodeling in patients with repeated atrial fibrillation ablation

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Background: Atrial fibrillation (AF) is the most common arrhythmia and is associated with significant morbidity and mortality. Structural atrial remodeling triggers increased automaticity and is important for AF recurrence and persistence. We evaluated patients with computed tomography before repeated AF ablation redo.

Methods: Thirty-five patients with non-valvular, drug-resistant AF and without significant comorbidities underwent repeated AF ablation (min. difference 12 months). All patients underwent prior cardiac CT before the procedures. We evaluated all exams in a paired-samples fashion for left and right atrial (RA) diameters, left atrial (LA) wall thickness (LAWT, anterior, posterior and lateral), left and right ventricular epicardial adipose tissue diameter (EAT) and epicardial fat density in the interventricular sulcus. Interrater variability was assessed.

Results: Redo procedures were performed after a mean of 30.9 months (12–75 months). Serial CT exams of the 35 patients (mean age 54y, 25% female) showed a significant increase in left (50.8 ± 14.8 ml/m^2 vs. 45.0 ± 14.0 ml/m^2, $p=0.003$) and right atrial volume (42.1 ± 14.8 ml/m^2 vs. 38.5 ± 13.6 ml/m^2, $p=0.047$). Left anterior wall thickness increased significantly (2.31 ± 0.7 mm vs. 2.04 ± 0.6 mm, $p=0.007$) while posterior and lateral wall thickness was unaffected ($p=0.4$).

Epicardial adipose tissue increased significantly at the right ventricular base (4.21 ± 1.6 mm vs. 3.71 ± 1.7 mm, $p=0.041$) and apex (4.08 ± 1.8 mm vs. 3.51 ± 1.2 mm, $p=0.046$) with a similar trend mid-ventricular ($p=0.2$) and left-sided ($p=0.5$).

Lipid density values were significantly lower (-98.9 ± 13.4 HU vs. -110.5 ± 13.4 HU, $p=0.001$) before repeated ablation.

Conclusions: Structural biatrial remodeling and epicardial fat increase can be observed in patients with repeated atrial fibrillation ablation using CT.

8-3

Cardiac disease progression in Fabry Disease

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Background: Fabry Disease is a lysosomal storage disorder caused by a mutation of the GLA Gene on the X-Chromosome, containing the encoding area of the enzyme Alpha-Galactosidase A. This leads to a lack of Alpha-Galactosidase A and to the accumulation of Sphingolipids, in particular Globotriaosylceramid (GB3) in all cells containing lysosomes.

Cardiac involvement is found in more than 50% of cases and is characterized by concentric left ventricular hypertrophy typically without outflow tract obstruction, initially preserved global systolic ejection fraction combined with early stages of diastolic dysfunction, and myocardial fibrosis in end-stages.

Although awareness of Fabry Disease (FD) is increasing, and enzyme substitution is available, life expectancy is still shorter than the average, mainly due to late diagnosis of heart involvement. In Austria, it is estimated that 111 patients are affected by FD. However, little is known about the natural course of the disease.

We utilized Cardiac MRI to understand myocardial disease progression in patients with FD.

Methods: Cardiac MRI including T1 mapping was performed as part of the FD routine four-year-follow-up, where

every patient underwent echocardiography, ECG, Holter monitoring, bicycle stress test, blood sampling and physical examination. MRI functional parameters, T1 times and extracellular volume measures were obtained.

Results: Analysis of baseline values ($n=25$, 16 females, 9 males) showed a high prevalence of positive Late Gadolinium Enhancement (7 of 25=28%) representing fibrosis. In the cohort of patients who underwent a second cardiac MRI after 3–4 years ($n=17$), mean end-diastolic Left ventricular mass was unchanged, while right ventricular mass had increased by 14.8 grams ($p=0.044$). NT-proBNP and left ventricular ejection fraction remained stable. Mean native T1 values declined from 936 ms to 852 ms ($p=0.000$). No correlations were found with NYHA stage or the pattern of the underlying genetic mutation.

Conclusions: The data demonstrate that within four years, significant increase of interstitial myocardial disease occurs in FD, in the absence of measurable clinical worsening, Cardiac MRI is a sensitive technique for assessment of disease progression in interstitial heart disease.

8-4

Echocardiographic assessment of right ventricular function: Current clinical practice in Austria and Germany

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Background: Due to the complex anatomy of the right ventricle, echocardiographic evaluation of right ventricular function is a challenge. Several echocardiographic methods of quantification have been described and compared with magnetic resonance imaging derived right ventricular ejection fraction. However, many of the parameters are complex and have numerous limitations. Therefore, we suspected that many of the parameters are not widely used. To test if the parameters are actually used in clinical routine we performed an online survey.

Methods: The registered users of an ultrasound teaching platform (123sonography) were asked to participate in this online survey-based study. The participants were asked which of the parameters (eyeballing, TAPSE, S', fractional area change, RIMP, 3D-EF, dp/dt, longitudinal strain) they apply in clinical practice.

Results: A total of 127 participants from Austria ($n=55$, 43%), and Germany ($n=72$, 57%) completed the survey. Only eyeballing (80%), TAPSE (72%), and S' (19%) were commonly applied in clinical routine. New technologies such as global longitudinal strain and 3D echocardiography were rarely applied by the participants.

Conclusions: In the year 2017, eyeballing and TAPSE are the methods used in routine echocardiography in Austria and Germany for the assessment of right ventricular function. When it comes to routine use, longitudinal strain and volume assessment of the right ventricle by 3D echocardiography do not play a role. Even though advanced parameters have been shown to be highly accurate, they are rarely used in clinical practice.

8-5

Myocardial strain analysis by 2D Speckle Tracking for detection of obstructive coronary artery disease

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Background: Echocardiography plays a key role in diagnosis of suspected cardiac disease. However, conventional resting echocardiography has a limited role in the diagnostic armamentarium for obstructive coronary artery disease in stable patients without regional wall motion abnormalities. 2D-strain echocardiography evolved as a promising tool for detection of subtle myocardial dysfunction. The aim of this study was to assess if 2D strain imaging by speckle tracking can provide additional information on the diagnosis of obstructive coronary artery disease in patients with normal left ventricular function and stable angina pectoris.

Methods: We included patients without a history of coronary artery disease, scheduled for coronary angiography due to suspected angina pectoris. Echocardiography was performed prior to coronary angiography and global longitudinal strain (GLS), regional strain and Postsystolic shortening Index (PSI) were obtained, accomplished by 2D speckle tracking Imaging. We compared strain patterns and strain values of patients with coronary artery disease (CAD group), confirmed by coronary angiography and patients without coronary artery disease. (non CAD group).

Results: 18 patients with a mean age of 67.5 years were included. 11 patients had coronary artery disease (CAD group), whereas 7 had no obstructive coronary arteries (non CAD group). All patients were in sinus rhythm. Mean left ventricular ejection fraction was 58.2+3.4% in patients of CAD group and 59.3+1.9% in the non CAD group. In 10 of 11 (90.1%) patients with obstructive coronary stenosis Postsystolic shortening was detected. Median PSI was 20.2+12.5%. In contrast, just in 1 of 7 patients without coronary artery disease Postsytolic shortening was observed with a PSI of 7.6%. Mean GLS in the CAD and non CAD group was –18.3+1.7% and 20.3+2.6% respectively. Furthermore we observed a high probability for CAD in the presence of strain dispersion. Despite a trend to lower GLS and higher PSI values in patients with CAD, there was no significant difference between the two groups, probably due to the small number of patients.

Conclusions: Analysis of strain patterns including Postsystolic shortening, strain dispersion and Global longitudinal strain assessed by 2D strain Imaging may extend the accuracy of non-invasive detection of coronary artery disease in stable patients without wall motion abnormalities.

8-6

Speckle tracking derived longitudinal strain—validation and influence of scanner settings

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Background: Speckle tracking based strain analysis is on the verge of clinical routine for the assessment of left ventricular function. However, it is unclear if the methodology is affected by factors other than myocardial mechanics. We evaluated the impact of ultrasound machine settings on the quality and reliability of strain measurement in routine clinical practice.

Methods: We recruited 35 consecutive patients with various degrees of left ventricular function and cardiac diagnoses. In each patient the four chamber view was recorded several times with different ultrasound settings (modification of gain, frame rate, depth, and transducer frequency) with a commercially available ultrasound imaging system (Vivid 7; GE Healthcare). In addition, inter- and intra-observer variability was assessed. Global longitudinal peak systolic strain (GLPSS) values were calculated offline (EchoPac® software, GE Healthcare). For each modified variable, we estimated a linear regression model with a random intercept and a random slope. The two observers were compared via Bland-Altman analysis.

Results: Ejection fraction ranged between 10% and 76% and correlated well with GLPSS (r = –0.70). Modification of gain (mean effect: –0.019%, 95% CI: –0.112% to 0.073%, p-value = 0.680) and frame rate (mean effect: 0.002%, 95% CI: –0.011% to 0.015%, p-value = 0.747) exhibited no effect on measurements of GLPSS. Conversely, a higher depth setting led to slightly higher GLPSS values (mean effect: –0.156%, 95% CI: –0.239% to –0.072%, p-value < 0.001). Higher harmonic and fundamental imaging transducer frequencies were associated with lower GLPSS values (mean effect: 1.102%, 95% CI: 0.605% to 1.600%, p-value < 0.001, and mean effect: 0.522%, 95% CI: 0.172% to 0.872%, p-value = 0.003, respectively). Bland-Altman analysis did not indicate statistically significant differences in variances between two measurements of a single observer (observer A: mean difference: –0.200%, 95% CI: –0.609 to 0.209, and observer B: mean difference: –0.103%, 95% CI: –0.871 to 0.664, respectively) or between measurements of two skilled observers in the same patient (observer A vs. B: mean difference: –0.527%, 95% CI: –1.116% to 0.062%).

Conclusions: Speckle tracking based GLPSS analysis provides reproducible and robust parameters of left ventricular function if extreme depth and transducer settings are avoided.

POSTERSITZUNG 9 – Interventionelle Kardiologie 1

9-1

Normal values for doppler Echocardiographic Assessment of prosthetic valve function after TAVR—A systematic review and meta-analysis

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Background: Transcatheter aortic valve replacement (TAVR) has emerged as an attractive, minimally invasive alternative to surgical AVR in patients at high and intermediate surgical risk. Particularities specific to TAVR and a rapidly growing number of available prosthesis make post-procedural assessment of valve function challenging. Aim of the present analysis was to collect and pool all available data cin the literature regarding normal doppler values for transcatheter prosthetic heart valves and to provide a comprehensive overview.

Methods: A PRISMA checklist-guided systematic review and meta-analysis of prospective observational studies or national and device specific registries or randomized clinical trials was conducted. Studies were identified by searching PUBMED, SCOPUS, Cochrane Central Register of Controlled Trials and LILACs from 01/2000 to 03/2017.

Results: Out of 240 abstracts, 155 studies (entailing a total of 27,159 patients) reported echocardiographic parameters. 55 studies in 7778 patients for the CoreValve®, SAPIEN valve: 35 studies with 4942 patients, SAPIEN XT: 32 studies with 3557, SAPIEN III:12 studies with 6231 patients, Direct Flow Medical Transcatheter valve: 12 studies with 816 patients, LOTUS™ Valve: 8 studies with 984 patients, Evolut™ R valve:4 studies with 872 patients, JenaValve™: 4 studies with 206 patients, ACURATE TA™:10 studies with 1161 patients, ACURATE neo™ valve: 5 studies with 273 patients, Portico™ valve: 4 studies with 191 patients for the and the Engager™ valve:4 studies with 148 patients. The pooled means and standard deviations for all available TAVR prosthesis were classified according to implanted valve size and time since implantation. We observed a mild increase in the different doppler indices from the discharge to the long term follow up (Fig. 1). However the changes were minor reassuring the stable haemodynamic performance of the different TAVR prosthesis. Second and third generation successors of the available TAVR prosthesis tended to show superior hemodynamic characteristics as compared to the first generation devices. We found no significant difference in mean transprosthetic gradient between the Edwards Sapien and the Sapien XT (9.85 ± 4.19 mmHg, vs. 9.94 ± 4.7 mmHg, p = 0.40). Interestingly the analysis revealed a significant higher mean gradient of the Edwards Sapien III valve as compared to the Edwards Sapien (10.45 ± 4.91 vs. 9.85 ± 4.19 mmHg. P < 0.001) and the Edwards Sapien XT (10.45 ± 4.91 vs. 9.94 ± 4.7 mmHg, p < 0.001). In contrast to this, the newer Medtronic EvolutTM R showed significant lower mean gradients at baseline as compared to the Medtronic CoreValve® (7.41 ± 4.7 vs. 8.53 ± 4.7, p < 0.001).

Conclusions: The present study firstly describes a pooled analysis of normal values for all available TAVR prosthesis to empower physicians with a reliable tool to perform follow-up echocardiographic assessment in TAVR patients and to safely identify patients with prostheses dysfunction.

9-2

Hämodynamische Parameter nach „Valve-in-Valve“ transkatheter Aortenklappenimplantation (VIV-TAVR)

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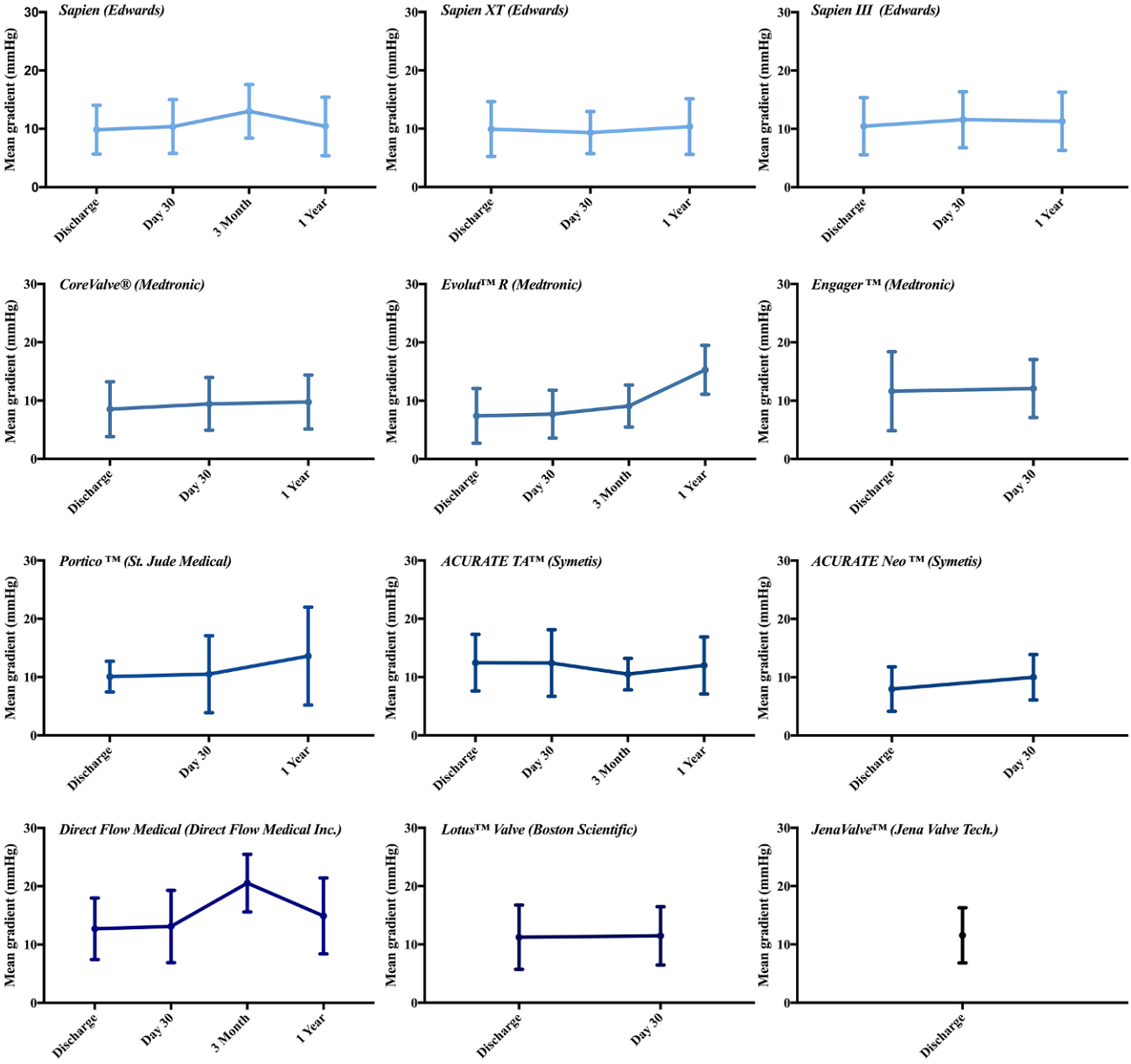

Fig. 1 | 9-1 Mean Doppler gradients for transcatheter aortic valve prosthesis according to valve type

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Ziele der Studie: Erstens klinische und hämodynamische Parameter nach „Valve-in-Valve" transkatheter Aortenklappenimplantation (VIV-TAVI) in Patienten mit dysfunktionalen chirurgischen Bioklappenprothesen (BV) zu beschreiben. Zweitens die Analyse von Prädiktoren der Ein-Jahres-Mortalität nach VIV-TAVI, mit besonderem Augenmerk auf das Phänomen der residualen Stenose (mittlerer Druckgradient >20 mmHg).

Methodik: 223 Patienten mit symptomatischer, dysfunktionaler BV (Restenose oder Insuffizienz) die eine VIV-TAVI erhielten wurden in diese Studie eingeschlossen.

Ergebnisse: Die Patienten waren alt (76 ± 11 Jahre) und hatten hohe EuroSCORE (27 ± 17 Punkte) und STS-Scores (8,3 ± 10,1 Punkte). Die meisten Patienten waren in NYHA III (64 %) and NYHA IV (24 %) Stadium. 85 Patienten erhielten VIV-TAVI aufgrund einer restenosierten BV, 76 Patienten aufgrund einer insuffizienten BV, die restlichen 62 Patienten aufgrund einer kombinierten Stenose und Insuffizienz. 115 Patienten wurden mit einer TAVI der ersten Generation (Sapien XT oder CoreValve) behandelt. Konversion zu einer chirugischen Sanierung war in 3 (1 %) Patienten notwendig. 4 (2 %) Patienten erlitten periinterventionell einen Schlaganfall, in 6 Patienten (3 %) war postinterventionell ein neuer Schrittmacher notwendig.

Die 30-Tage-Mortalität war 11 % (22 von 206) und die Ein-Jahres-Mortalität 24 % (37 von 155). Patienten mit einer kleinen BV (Bioprothese <23 mm) hatten postinterventionell öfter eine residualen Stenose (mittlerer Druckgradient >20 mmHg) (33 % vs. 17 %; $p = 0{,}04$). Patienten mit kleinen BV (<23 mm), welche mit einer TAVI der ersten Generation versus der zweiten Generation behandelt wurden, wiesen öfter eine residuale Stenose (67 % vs. 10 %; $p = 0{,}001$) auf. Weder eine kleine BV noch eine residuale Stenose noch die Implantation einer TAVI der ersten Generation waren mit der Ein-Jahres-Mortalität assoziiert. Im Gegensatz zum EuroSCORE war der STS-Score ein Prädiktor für

die Ein-Jahres-Mortalität (HR 1,05 95 %CI 1,01–1,09; $p=0,01$; AUC 0,63 95 %CI 0,54–0,71).

Schlussfolgerungen: Patienten, die einer VIV-TAVI unterzogen werden, weisen postinterventionell relativ häufig formal eine residuale Stenose auf, insbesondere wenn eine TAVI-Klappe der ersten Generation verwendet wird. Da diese Kondition jedoch nicht mit der Mortalität nach einem Monat oder einem Jahr assoziiert ist, stellt die Antizipation einer residualen Stenose keine Kontraindikation für eine VIV-TAVI dar. VIV-TAVI ist somit eine valide Behandlungsoption für alle Patienten mit einer dysfunktionalen BV.

9-3

Transkatheter Aortenklappenimplantation als Behandlungsoption für reine Aortenklappeninsuffizienz

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Grundlagen: Die transkatheter Aortenklappenimplantation (TAVI) ist mittlerweile fester Bestandteil der Behandlung der hochgradigen, symptomatischen Aortenklappenstenose für Patienten mit hohem oder auch intermediären Risiko für einen herzchirurgischen Aortenklappenersatz (SAVR). Bisher galt die reine Aortenklappeninsuffizienz (PAR) als Kontraindikation für eine interventionelle Behandlung, doch für Patienten mit zu hohem Risiko für SAVR sind innovative Transkatheterverfahren notwendig. Ziel unserer Analyse war es daher, die verfügbaren Daten von TAVI aufgrund PAR zu analysieren.

Methodik und Ergebnisse: Mittels PubMed-Analyse konnten wir 12 hochqualitative (>5 Patienten; Suche bis 16.12.2017) Studien von Patienten, welche eine TAVI aufgrund PAR erhielten, identifizieren. Insgesamt wurden Daten von 640 Patienten evaluiert. Es wurden gepoolte Eventraten kalkuliert, der primäre Endpunkt war die Mortalität nach 30 Tagen.

TAVI-Klappen der ersten Generation (CoreValve or Sapien XT) wurden in 39 % ($n=247$) und TAVI-Klappen der zweiten Generation (J-Valve, JenaValve, DirectFlow, Acurate TA, Evolut R, Lotus, Sapien 3, Engager, Portico) in 61 % ($n=393$) der Fälle implantiert.

In der Gesamtkohorte war die 30-Tage-Mortalität 12,2 % (95 %CI 8,7 %–16,2 %; I^2 31 %), die Schlaganfallrate 3,5 % (95 %CI 2,2 %–5,0 %; I^2 0 %), eine mehr als erstgradige residuale Aortenklappeninsuffizienz lag in 9,9 % (95 %CI 2,6 %–21,1 %; I^2 91 %) vor und die Implantation war in 89,5 % (95 %CI 81,7 %–95,3 %; I^2 82 %) erfolgreich.

In der Subgruppe der Patienten, welche mit einer TAVI der ersten Generation behandelt worden waren, betrug die 30-Tage-Mortalität 16,6 % (95 %CI 11,7 %–22,2 %; I^2 17 %), in 68,0 % (95 %CI 58,5 %–76,8 %; I^2 54 %) war die Implantation erfolgreich und die Schlaganfallrate war 2,8 % (95 %CI 1,2 %–5,3 %; I^2 0 %). Eine mehr als erstgradige Aortenklappeninsuffizienz lag in 37,8 % (95 %CI 12,9 %–66,8 %; I^2 94 %) der Patienten vor.

Die 30-Tage-Mortalität in der Subgruppe der Patienten behandelt mit einer TAVI der zweiten Generation war 9,2 % (95 %CI 6,3 %–12,7 %; I^2 9 %), die Schlaganfallrate war 3,9 % (95 %CI 2,2 %–6,0 %; I^2 0 %), die Implantation war in 92,2 % (95 %CI 85,9 %–96,7 %; I^2 64 %) erfolgreich, und eine mehr als erstgradige residuale Aortenklappeninsuffizienz lag in 3,1 % (95 %CI 1,6 %–5,0 %; I^2 0 %) vor.

Die 30-Tage-Mortalität in der Subgruppe der Patienten behandelt mit einer JenaValve, der einzigen Klappe zugelassen für PAR, war 14,1 % (95 %CI 8,8 %–20,4 %, I^2 0 %), die Schlaganfallrate war 4,5 % (95 %CI 0,8–10,7 %; I^2 45 %), die Implantation war in 90,1 % (95 %CI 81,2 %–96,4 %; I^2 60 %) erfolgreich, und eine mehr als erstgradige residuale Aortenklappeninsuffizienz lag in 3,3 % (0,6 %–8,1 %; I^2 32 %) vor.

Schlussfolgerungen: Für Patienten mit PAR, die ein inakzeptabel hohes Risiko für einen konventionellen chirurgischen Aortenklappenersatz aufweisen, ist eine TAVI eine sichere Therapieoption mit relativ geringen Komplikationen und hohen Erfolgsraten bei der Implantation.

9-4

The new STS/ACC TAVI risk score and long-term outcome in TAVI patients

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Background: The new Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) risk score predicts in-hospital mortality in transcatheter aortic valve implantation (TAVI) patients. Despite a low number of variables, it was non-inferior to other risk scores. However, little is known about its accuracy in predicting long-term outcome in TAVI patients.

Methods: We compared the accuracy of 5 different scores (STS-Predicted Risk of Mortality (STS-PROM), STS-Predicted Risk of Comorbidity (STS-PROC), STS/ACC TAVI score, European System for Cardiac Operative Risk Evaluation (EuroSCORE) II and German Aortic Valve (AV) Score) in predicting 1- and 5-year survival in 515 consecutive patients with complete records undergoing TAVI at our institution from 2007 to 2015.

Results: Median follow-up was 4.3 (interquartile range 2.7–6.3) years and 1- and 5-year mortality 15% and 50.7%, respectively. ROC analysis for 1-year mortality (which was complete) showed highest AUC in STS-PROC (0.614 vs. STS-PROM 0.608, STS/ACC 0.561, EuroSCORE II 0.583, German AV score 0.609; Fig. 1). In Cox regression analysis for 5-year mortality, STS-PROC was superior to other scores ($p<0.001$, HR 1.033, 95% CI 1.018–1.048 per 1% increase). When matched for gender, age, and left ventricular function, STS-PROM outperformed other scores ($p<0.001$, HR 1.093, 95% CI 1.049–1.140, Fig. 2).

Conclusions: The new STS/ACC TAVI score was inferior to traditional STS-PROC and STS-PROM scoring systems in predicting long-term outcome in our cohort.

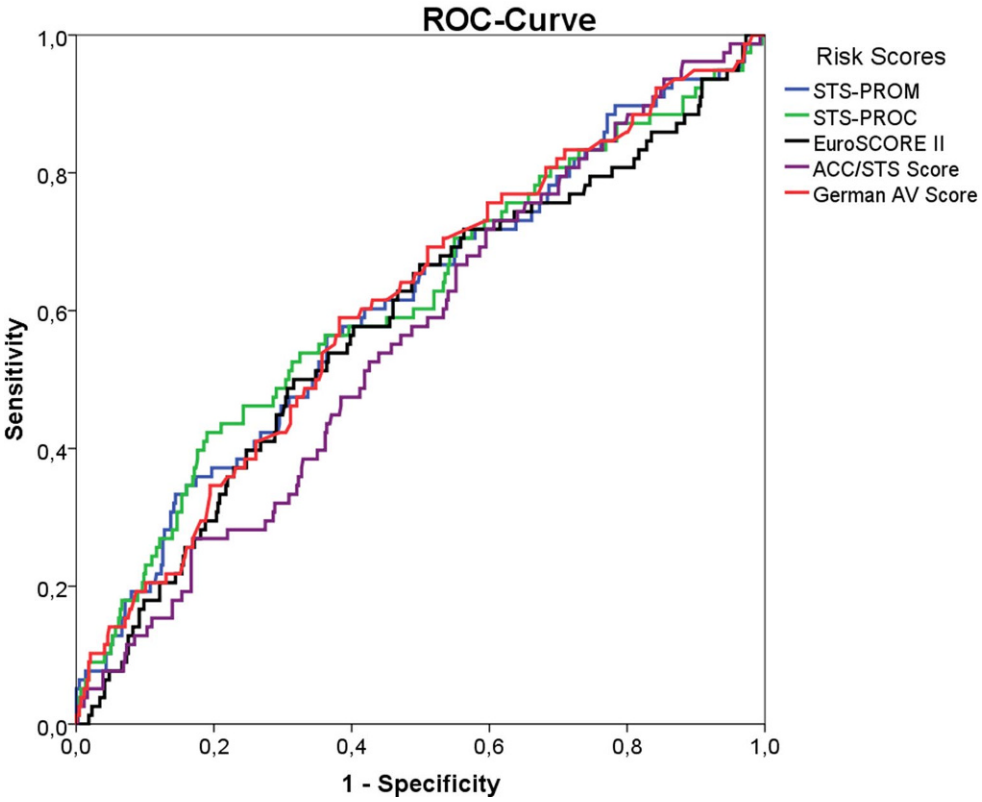

Fig. 1 | 9-4 ROC-AUC for different scores in predicting 1-year mortality. EuroSCORE: European System for Cardiac Operative Risk Evaluation; *AV:* aortic valve; *STS:* Society of Thoracic Surgeons; *PROC:* Predicted Risk of Comorbidity; *PROM:* Predicted Risk of Mortality

Risk score	1-year mortality	5-year mortality (unmatched)		5-year mortality (matched for age, sex, and LVF)	
	ROC-AUC	COX p	COX HR (95% CI)	COX p	COX HR (95% CI)
STS-PROM	0.608	0.000095	1.078 (1.038-1.119)	0.000028	1.093 (1.049-1.140)
STS-PROC	0.614	0.000014	1.033 (1.018-1.048)	0.000083	1.032 (1.016-1.049)
STS/ACC	0.561	0.003	1.120 (1.038-1.208)	0.004	1.122 (1.038-1.214)
EuroSCORE II	0.583	0.008	1.014 (1.004-1.024)	0.063	1.011 (0.999-1.023)
German AV	0.609	0.001	1.041 (1.016-1.067)	0.000110	1.063 (1.031-1.096)

Fig. 2 | 9-4 ROC-AUC for 1-year mortality and Cox regression for 5-year mortality of different scoring systems. Hazard ratios (HRs) per 1% increase are given. *EuroSCORE:* European System for Cardiac Operative Risk Evaluation; *AV:* aortic valve; *LVF:* left ventricular function; *STS:* society of Thoracic Surgeons; *PROC:* Predicted Risk of Comorbidity; *PROM:* Predicted Risk of Mortality

9-5

Indications for and outcome in patients undergoing left atrial appendage closure in Austria

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Background: According to recent ESC guidelines, left atrial appendage closure (LAAC) is an established treatment option for patients with atrial fibrillation and either contraindication to (N)OAC therapy, increased bleeding risk, ischemic stroke despite anticoagulation or non-compliance with anticoagulation (IIb B indication). The goal of the Austrian registry was to describe and assess indications, peri- and post-procedural management strategies, and short- and long-term outcomes of all LAAC patients 2012–2017.

Methods: The registry included all patients ($n=157$) undergoing LAAC procedures in Austria between 2012 and August 2017 (age 74±7 years, 38% female; median CHA2DS2-VASc score of 4, median HAS-BLED score 3). The number of proce-

dures per year increased from 3 (2012) to 47 (January-August 2017). As for the indication, 58% had a major bleeding under OAC (32% intracranial, 24% GI bleeding, 2% other), 17% had a thromboembolic event despite of OAC and 25% had other indications, such as anaemia (10%), requirement for triple therapy (5%), predisposition for bleeding (3%), or other (7%).

Results: Amplatzer® (SJM, St. Paul, MN, US) occluders were used in 84 patients (54%) and Watchman® (Boston Scientific, Malborough, MA, US) occluders in 72 patients (46%). A median size of 25 mm (IQR 22–27 mm) was used. Median duration of procedure was 65 (IQR 54–90) minutes. Procedural success defined by was 97%. Major procedural complication rate was 9%, including anaemia requiring transfusion (3%), femoral pseudoaneurysma requiring intervention (3%) or hemodynamically relevant pericardial effusion (2%), all of which were reversible. Median hospitalisation duration was 3 (IQR 2–5) days. Postprocedurally, most patients received dual antiplatelet therapy (54%) for 1.5 to 6 months and single antiplatelet therapy (48%), no antithrombotic therapy (41%), (N)OAC (6%) or other (5%) thereafter.

During follow up of 230 ± 25 days, 6% of patients experienced major bleeding, 3% major ischemic stroke, and one patient (1%) hospitalisation due to displacement of LAA occluder.

Conclusions: LAAC is increasingly adopted in Austria. The most common indication for LAAC is major bleeding. Device implantation success and complication rates are similar to the results of landmark LAAC trials.

9-6

Impact of major bleeding on long-term mortality in patients undergoing transcatheter aortic valve replacement (TAVR)

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Background: Transcatheter aortic valve replacement (TAVR) has been demonstrated to be an established therapy for high-risk, inoperable patients with severe symptomatic aortic valve stenosis (expected mortality after 2 years is 68% based on international data). The identification of modifiable risk factors for death is important to improve prognosis in such patients undergoing TAVR.

Methods: We analyzed factors associated with long-term all-cause death in patients undergoing TAVR, in particularly whether major bleeding complications before and after hospital discharge of the index admission are associated with adverse outcomes. Major bleedings were defined as Bleeding Academic Research Consortium (BARC) type 3 or greater. Multivariable adjustments were performed using a Cox proportional hazards model with backward elimination of insignificant variables at a p-value ≥0.20.

Results: In total, 157 patients with severe aortic stenosis underwent TAVR between August 2010 and December 2017 at our department, of whom 8 (5%) patients died in-hospital and were excluded for further analysis. The mean age of patients included into the analysis was 83 ± 6 years, the mean STS score was 6.1 ± 3.5% and 59% were female. During a mean follow-up of 24 ± 20 months 62 (42%) patients died. The incidence of major in-hospital bleedings as well as major bleedings during follow-up was 22%. After multivariable adjustment, factors significantly associated with all-cause death were baseline hemoglobin (before TAVR, HR 1.16, 95%CI 1.03;1.30, $p=0.02$ per g/dL decrease), angiographically proven coronary artery disease (CAD, HR 2.28, 95%CI 1.25; 4.18, $p<0.01$), chronic obstructive pulmonary disease (COPD, HR 3.99, 95%CI 2.24; 7.10, $p<0.01$), and the occurrence of a major bleeding episode during follow-up (HR 2.99, 95% CI1.66; 5.41, $p<0.01$). Major in-hospital bleeding complications ($p=0.40$), the use of initial triple antithrombotic therapy ($p=0.77$), and severely reduced left ventricular function ($p=0.21$) were not significantly associated with all-cause death.

Conclusions: In descending order for relative risk of death, COPD, the occurrence of major bleedings during follow-up, significant CAD, and anemia were associated with adverse outcomes of patients undergoing TAVR. Therefore, strategies to minimize bleeding risk seem to be an important treatment target to improve prognosis.

9-7

Der radiale Zugang ist bei Primär PCI mit einem verbesserten intra-hospitalen Outcome verbunden

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Grundlagen: Randomisierte Studien zeigten ein verbessertes Outcome durch den radialen Zugang während primärer PCI (PPCI) nach STEMI. Ziel dieser Studie war zu evaluieren, ob der radiale Zugang dem Femoralen auch in der täglichen klinischen Praxis, sowie bei Patienten mit kardiogenem Schock überlegen ist.

Methodik: Für die vorliegende Analyse wurden Patienten aus einem multi-zentrischen Register, die zwischen Jänner 2012 und Dezember 2016 eine PPCI im Rahmen eines STEMI erhielten, analysiert. Als Endpunkte wurden die intra-hospitale Mortalität sowie MACE (Kombination aus Tod, Myokardinfarkt und Schlaganfall) und NACE (Kombination aus MACE und schweren Blutungen) herangezogen.

Ergebnisse: Insgesamt wurden 7412 Patienten eingeschlossen, wobei 2765 (37,3 %) über einen radialen und 4647 Pa-

tienten (62,7 %) über einen femoralen Zugang angiographiert wurden. Die intra-hospitale Mortalität war in der radialen Gruppe niedriger als in der Femoralen (3,3 % vs. 6,7 %; $p<0,01$). In einer multivariaten Regressions-Analyse unter Berücksichtigung von Alter, Geschlecht, Diabetes, früherer kardiovaskulärer Ereignisse, Vorhofflimmern, Plättchenhemmung, Zeitverzögerung, Blutungen und Reanimation im Zuge des Ereignisses, sowie kardiogenem Schock zeigte sich ein Trend zur Mortalitätsreduktion für den radialen Zugang (OR 0,74, 95 % CI = 0,54–1,01, $p=0,06$). Sowohl die MACE- (OR 0,73, 95 % CI = 0,55–0,96, $p=0,03$), als auch NACE-Rate (OR 0,71, 95 % CI = 0,54–0,93, $p=0,01$) waren signifikant niedriger bei diesen Patienten. Bei radialem Zugang konnte für die Subgruppe ohne kardiogenen Schock eine Mortalitätsreduktion aufgezeigt werden (OR 0,55, 95 % CI = 0,36–0,85, $p=0,01$). Dies war bei Patienten mit kardiogenem Schock nicht der Fall (OR 1,14, 95 % CI = 0,70–1,87, $p=0,59$).

Schlussfolgerungen: Der radiale Zugang ist in der klinischen Praxis mit einem verbesserten Outcome nach PPCI verbunden. Verglichen mit dem femoralen Zugang kann bei Patienten ohne, nicht jedoch im kardiogenen Schock eine Mortalitätsreduktion beobachtet werden.

9-8

Significant intraprocedural alterations of HV- and QRS-intervals during transcatheter aortic valve replacement

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Background: Transcatheter aortic valve replacement (TAVR) is an established treatment option for selected patients with severe aortic valve stenosis. Despite the technological improvement of transcatheter valves, there is still a substantial rate of new-onset conduction disturbances necessitating pacemaker implantation after TAVR. Electrophysiological predictors of high grade atrioventricular conduction disorders have not been sufficiently determined yet.

Methods: Therefore, in our ongoing clinical trial, we prospectively assess intraprocedural HV- and QRS-interval dynamics as potential predictors of significant conduction disturbances by the use of a portable EP system (St. Jude Medical, WorkMate Claris 56 channel system w/EP-4 Stimulator), which is located in the cath lab. Via an additional venous puncture in the left groin, a HIS catheter is positioned in patients undergoing TAVR with consecutive real-time HV- and QRS-interval-monitoring during the procedure.

Results: After recruitment of 58 patients (36 female, 22 male) with a mean age of 80.14 years undergoing TAVR, statistical analysis of the recorded data by means of the Wilcoxon-test revealed significant intraprocedural increases of the mean HV-interval, both after balloon valvuloplasty as well as after implantation of the valve prosthesis (Fig. 1). Furthermore, similar prolongations were seen when measuring QRS-complex durations (Fig. 2). From the point of valve implantation to the end of the procedure, there was no further significant increase of the HV- or QRS-intervals (Table 1).

Conclusions: To the best of our knowledge, we are the first to measure intraprocedural changes in the cardiac conduction system by means of a portable EP-system in patients undergoing transcatheter aortic valve replacement. Evaluation of the HV-time interval has, so far, only been done by separate electrophysiology studies prior to as well as after TAVR. In the early analysis of our ongoing clinical trial, significant increases of intraprocedural HV- and QRS-intervals were observed. The main cause of these findings seems to be the direct impact of mechanical radial forces on the bundle of His as well as the left bundle branch induced by balloon dilatation as well as implantation of the valve prosthesis, as these events were significantly associated with an abrupt prolongation of HV- and QRS-intervals. As significant increases of these parameters already showed potential association with the delayed onset of conduction disorders in some of our patients, we are looking forward to the final analysis after recruitment and follow-up of the planned total study population.

9-9

Significant intraprocedural HV-time prolongation as sole predictor of late occurrence of complete atrioventricular block in a patient undergoing transcatheter aortic valve replacement

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Case Report: We report the case of an 82-year old male patient, who was scheduled for transfemoral aortic valve replacement (TAVR) for severe symptomatic aortic stenosis. His medical history included coronary heart disease, diabetes and hypertension. Electrocardiography (ECG) at baseline displayed normofrequent sinus rhythm, first degree atrioventricular (AV) block with a prolonged PR-interval of 262 ms and a QRS-duration of 100 ms. Echocardiography revealed severe aortic stenosis with a gradient of 110/70 mmHg and a valve orifice area of 0.6 cm^2.

For TAVR, initial valvuloplasty with a 20 mm balloon and subsequent implantation of a 29 mm Medtronic CoreValve Evolut-R prosthesis were performed. According to the study protocol of an ongoing trial evaluating intraprocedural HV-time changes during TAVR, a HIS catheter was positioned via an additional venous puncture in the left groin prior to balloon valvuloplasty and real-time HV-interval was monitored during the procedure. Measurement at baseline revealed a HV-duration of 60 ms with a prolongation to 95 ms after implantation of the valve prosthesis resulting in a total increase of the HV-interval by 35 ms.

Afterwards, the patient was monitored for 48 hours with no signs of second or third degree AV block or episodes of bradycardia. The ECG on the second postprocedural day showed sinus rhythm with a heart rate of 67 bpm, first degree AV block with a PR-interval of 305 ms and a QRS-duration of 91 ms. According to the study protocol a subcutaneous loop recorder was implanted before discharge.

At the first scheduled visit after one month, the patient was in good condition reporting no episodes of (pre-) syncope or vertigo. His ECG was largely unchanged with normofrequent sinus rhythm, a prolonged PR-interval of 304 ms and a QRS-complex-duration of 92 ms. Loop recorder interrogation showed no documented episodes of bradycardia or asystole. However, two

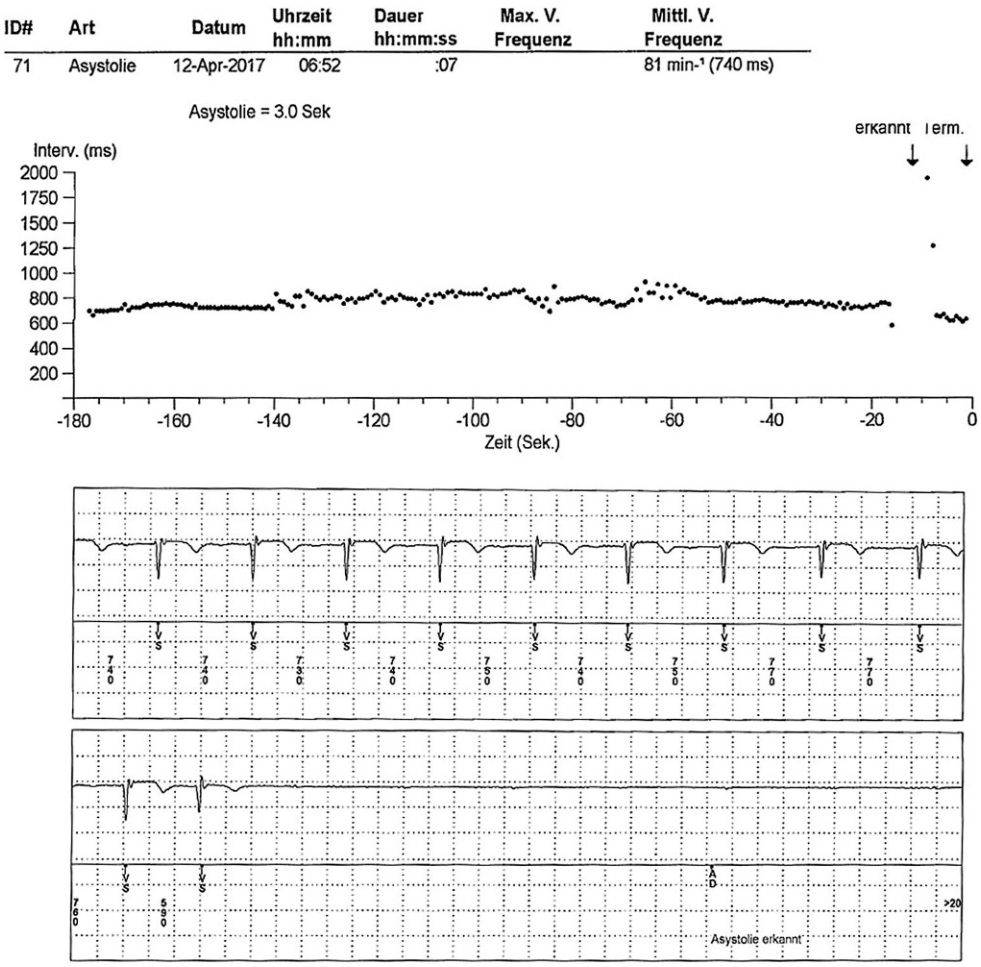

Fig. 1 | 9-9

days prior to the next scheduled visit three months after TAVR, the patient reported an episode of syncope without preceding symptoms. Device interrogation revealed intermittent complete AV block with prolonged ventricular asystole of seven seconds as the cause of this event (Fig. 1). Due to the documented conduction disturbance, the patient was admitted for permanent pacemaker implantation.

Conclusions: Approximately 90% of all conduction disturbances in patients undergoing TAVR manifest within the first week1. However, they may be transient or may appear up to one year after device implantation2. Early onset may be caused by direct mechanical injury, edema or inflammation on the His bundle or the left bundle branch. Possible reasons for a late onset may include continued calcification of the conduction pathways or continued expansion of the valve's frame 2, 3.

5.6% of all deaths after TAVR are the consequence of sudden cardiac death4. While pacemaker implantation is recommended in patients with a documented total AV block, predictive factors of high grade AV conduction disorders have not been sufficiently determined yet. In our case, the intraprocedural HV-time prolongation was the sole predictive risk factor of total AV block. Measurement of HV-time changes during TAVR may be a valuable tool to predict the occurrence of delayed postinterventional AV conduction disorders and reduce mortality due to sudden cardiac death, which is crucial especially because the indication for TAVR is expanding towards younger, intermediate-risk patients.

POSTERSITZUNG 10 – Pulmonale Hypertension

10-1

Preserved right ventricular function but increased speckle tracking-derived right atrial strain in altitude-induced pulmonary hypertension

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Background: High-altitude pulmonary hypertension exposes the right ventricle (RV) to increased afterload which is occasionally a cause of high-altitude right heart failure. This study aimed to evaluate physiologic variables and comprehensive echocardiographic indices of RV as well as RA function following rapid ascent to high altitude in healthy volunteers.

Methods: 50 subjects performed rapid (<24 hrs) and active ascent to 4559 m. All participants underwent 2D echocardiography during a baseline examination at low altitude (424 m) as well as at three study time-points (7, 20 and 44 h) after arrival

at high altitude. In addition to systolic pulmonary artery pressure (sPAP), comprehensive 2D planimetric- and tissue Doppler- indices of RV function as well as volumetric and speckle-tracking-derived strain indices of RA function were obtained.

Results: sPAP (sPAPlow: 24.4 ± 3.8 vs. sPAPhigh: 38.5 ± 8.2 mmHg, $p < .001$) increased significantly from baseline to the first altitude examination and remained elevated at high altitude. Measures of longitudinal RV systolic function (Tricuspid annular plane systolic excursion (TAPSElow: 23.3 ± 3.7 vs. TAPSEhigh: 25.0 ± 3.1 mm, $p = .016$) and peak tricuspid lateral annular systolic velocity (S'low: 12.9 ± 1.8 vs. S'high: 14.0 ± 2.0 mmHg, $p = .001$)) increased significantly from baseline to the first altitude examination and remained elevated at high altitude. RV myocardial performance index and fractional area change as global estimates of both systolic and diastolic RV function did not change. RA Reservoir Strain (ε) (εlow: 50.2 ± 12.1 vs. εhigh: 53.8 ± 11.0%, $p < .001$) increased significantly from baseline to the first altitude examination secondary to increase of RA Contraction Strain (εlow: 19.2 ± 6.4 vs. εhigh: 25.4 ± 9.6%, $p < .001$). Volumetric RA data paralleled RA strain results.

Conclusions: Rapid ascent to high altitude is associated with preserved RV systolic function but increased contractile RA demand. RA contractile functional reserve is necessary for RV diastolic filling in high-altitude pulmonary hypertension and overt functional impairment might be a risk factor for high-altitude right heart failure.

10-2

A novel index of right ventricular end-systolic remodeling in pediatric pulmonary hypertension

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Background: Echocardiographic determination of the novel right ventricular end-systolic remodeling index (RVES RI) was found to be of clinical value for assessment of pulmonary hypertension (PH) in adults. This study aims to investigate the value of the RVES RI in pediatric pulmonary hypertension and a comparison to conventional echocardiographic values of the RV in children with confirmed PH.

Methods: We suggested that a simple index that incorporates both the longitudinal component of RV adaptation and the end-systolic dimension would add significant information of RV behavior in pediatric PH. We therefore investigated 55 children with PH and in 55 matched healthy children (age range: 1 to 18 years). The RVESRI was defined by lateral length divided by septal height of the RV measured in end-systole.

Results: The RVES RI is significantly increased in children with PH compared to age-matched healthy subjects. The RVES RI correlated positively with the RV end-diastolic basal diameter, length and area, with the RV end-systolic length and area, with the right atrial (RA) area, and with the left ventricular eccentricity index (LVEI) in our PH children. RVES RI correlated negatively to tricuspid annular plane systolic excursion (TAPSE), tricuspid annular peak systolic velocity (S'), and pulmonary artery acceleration time (PAAT) in our PH patients. The RVES RI further showed a positive correlation to the invasive hemodynamic parameters mean pulmonary artery pressure (mPAP), and the pulmonary vascular resistance index (PVRi).

Conclusions: The RVES RI is a simple, reproducible echocardiographic parameter for the assessment of PH in children. The RVES RI normal values (of our healthy children group) and the increased values of our PH children will from now on be included in the battery of echocardiographic parameters to assess pediatric PH.

10-3

The selective prostacyclin (IP) receptor agonist selexipag: first sparse experience in pediatric pulmonary arterial hypertension

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Background: Pulmonary artery hypertension (PAH) is an important cause of morbidity and mortality in children. During the past few years, treatment of PAH has undergone an evolution. Additional drugs such as the selective prostacyclin (IP) receptor agonist selexipag are expected to be approved in the near future for children with PAH. However, emerging therapeutic strategies for adult PH, such as a triple oral combination therapy, have not been extensively studied in children with PAH. Herein, we present the sparse available data on the use of selexipag in children, which is currently limited on only a few patients with PAH.

Methods and Results: We report on one hand the initial experience in 6 pediatric patients on selexipag from 2 centers, which includes one case that was the first published pediatric case worldwide [1], describing clinical and hemodynamic improvements by cardiac catheterization in a 12-year old female with hereditary PAH. Another group recently published their center experience of using selexipag in 5 children with either IPAH or PAH associated with congenital heart disease (PAH-CHD) [2]. Prior to the start of an additional third agent, usually all patients were on PDE5i and ERA dual therapy. The concept of add-on oral selexipag to dual oral combination therapy (mostly PDE5i and ERA) is powered by the idea of (1) avoiding central venous lines, especially in small children or in patients who deny this approach, and/or (2) to achieve stabilization, and if necessary as a bridge to bilateral lung transplantation or Potts shunt creation.

Conclusions: As the first clinical data in PAH children are now available, oral selexipag use will increase over the next months and years in the pediatric age group. We emphasize that the add-on use of oral selexipag must still be considered "experimental therapy", and suggest a strict patient selection and enrollment in a clinical study, including regular echocardiographic evaluations plus cardiac catheterization before and 6 months after the start of selexipag. We want to address the

future decision to add selexipag as a third oral PAH agent, or to replace intravenously administered PAH drugs with oral selexipag in stable patients, may become feasible in children with significant PAH.

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10-4

Plasma ADAMTS13 activity in chronic thromboembolic pulmonary hypertension

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Background: Deficiency of ADAMTS13 activity leads to von Willebrand factor giant multimers with high affinity for platelets and high thrombotic risk. Because elevated levels of vWF are associated with thrombosis, we tested the hypothesis that low ADAMTS13 activity is associated with chronic major vessel pulmonary thrombi (chronic thromboembolic pulmonary hypertension, CTEPH) leading to pulmonary hypertension.

Methods: ADAMTS13 activity was measured in a kinetic assay using the fluorescence resonance energy transfer substrate VWF 73. ADAMTS13 antigen concentration was measured in an enzyme-linked immunosorbent assay. The specific ADAMTS13 activity was calculated as ratio of activity to antigen concentration. Plasma samples of 140 patients and 96 healthy controls were obtained.

Results: Of 140 patients, 69 patients (49%) were diagnosed with CTEPH and 71 patients (51%) were diagnosed with PH. PH patients included patients with idiopathic PAH, hereditary PAH and PAH associated with drug/toxins ($n=30$), patients with PAH associated with connective tissue disease (CTD, $n=11$), patients with portopulmonary PAH ($n=5$), patients with PAH associated with congenital heart disease (CHD, $n=7$) and patients with pulmonary hypertension (PH) due to lung disease and/or hypoxia ($n=13$).

ADAMTS13 antigen concentration was not different between patients with CTEPH and PH (0.57 ± 0.18 µg/ml and 0.56 ± 0.21 µg/ml respectively) but was elevated in both groups relative to healthy controls (0.51 ± 0.10 µg/ml, $p\leq0.02$). Specific ADAMTS13 activity was significantly reduced in patients with CTEPH and PH relative to healthy controls (1.71 ± 0.27, 1.76 ± 0.39 and 1.98 ± 0.52 respectively, $p\leq0.003$) while no differences were seen between CTEPH and PH. In a subgroup analysis ADAMTS13 antigen concentration was significantly lower in patients with PAH associated with CTD relative to patients with idiopathic PAH, hereditary PAH and PAH associated with drug/toxins (0.44 ± 0.22 µg/ml vs 0.61 ± 0.22 µg/ml, $p=0.028$) but no differences in specific ADAMTS13 activity could be observed in any PH subgroup. Operable CTEPH patients ($n=40$) and non-operable CTEPH patients ($n=28$) showed no differences in ADAMTS13 antigen concentration or specific ADAMTS13 activity (0.59 ± 0.19 vs 0.52 ± 0.14 and 1.73 ± 0.29 vs 1.69 ± 0.25 respectively).

Conclusions: Following our hypothesis we could show that patients with CTEPH and PH have significantly reduced levels of specific ADAMTS13 activity relative to healthy controls. No differences of specific ADAMTS13 activity could be shown for the PH subgroups or operable and non-operable CTEPH patients.

10-5

An uncommon case of pulmonary hypertension caused by Whipple's disease

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Background: Pulmonary hypertension is a chronic incurable disease. With this case report we present a very rare and possible reversal cause for pulmonary hypertension. We report about a significant improvement of pulmonary pressure values of a 55 year old man after a successful antibiotic and tadalafil treatment of Whipple's disease.

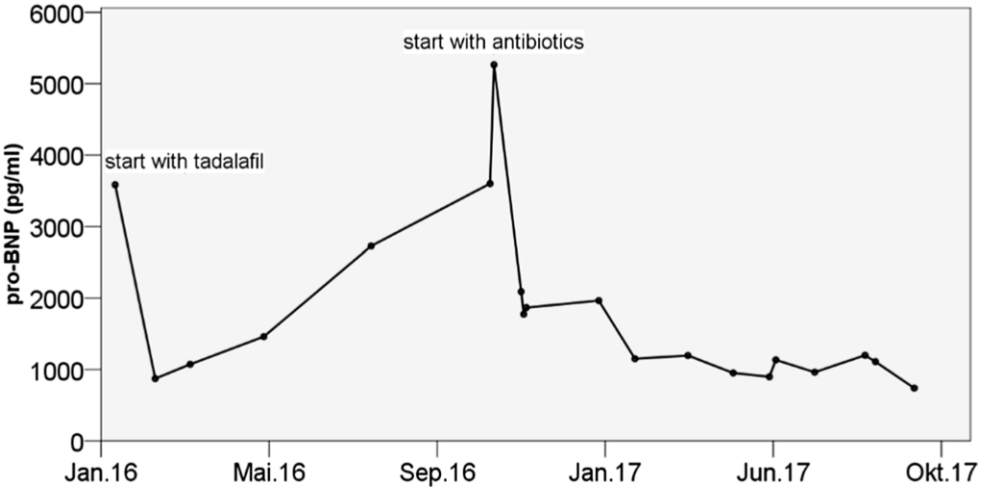
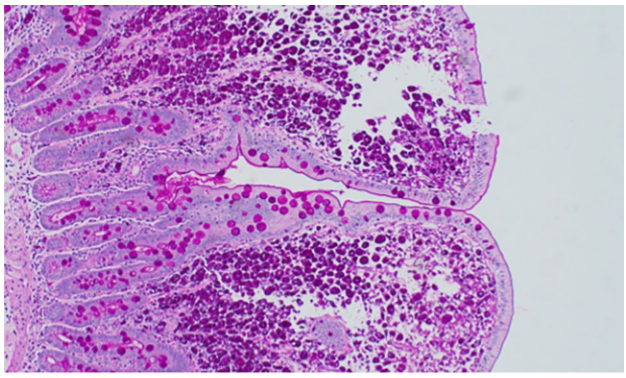


Fig. 1 | 10-5



PAS-positive macrophages in the duodenal mucosa

	sPAP mmHg	dPAP mmHg	mPAP mmHg	PCWP mmHg
Jan 2016	38	30	34	15
Jun 2017	23	10	14	11

Pressure values before treatment and under tadalafil + antibiotics

Fig. 2 | 10-5

Whipple's disease is with an incidence of 0.5–1:1.000.000 a very rare chronic infectious disease, which usually occurs in middle-aged men. It is caused by the bacterium Tropheryma Whipplei, which is known since 1992. Normally the disease leads untreated through malabsorption in the small bowel to wasting and further to death. The most common symptom is chronic diarrhoea through malabsorption following by weight loss. Joint pains could occur many years before any digestive tract symptoms develop. Beside this signs and symptoms uveitis, endocarditis and brain involvement is well known. A pulmonary manifestation of the Whipple's disease is only from individual case reports documented. The specific pathophysiology is unidentified.

Case Report: In our case we diagnosed a pulmonary hypertension in NYHA III with concomitant edema of the leg by use of echocardiography and right heart catheterization. After the diagnosis we started a specific therapy with tadalafil. Our patient reported about weight loss through diarrhoea of about 15 kg in a period of 3 months. By use of gastroscopy with gastrointestinal biopsy of the duodenum we were able to detect PAS-positive macrophages which are specific for the Whipple's disease. Also the PCR for Tropheryma Whipplei of the duodenum and cerebrospinal fluid was positive. Even some weeks after starting an antibiotic treatment with Trimethoprim/sulfamethoxazole there was an Improvement of dyspnoea, peripheral edema and diarrhea, but the patient developed ascites. The ascites was an inflammatory ascites due to an immune reconstitution inflammatory syndrome, which could misdiagnosed as a cardial ascites. Six months after initiation of the antibiotics and under tadalafil treatment the pressure values of the right heart catheterization improved significantly. A try to stop the specific treatment with tadalafil failed because of worsening dyspnoea and raise of sPAP during physical stress.

Conclusions: Whipple's disease is a very rare underlying cause for pulmonary hypertension. After an appropriate antibiotic treatment and specific therapy a significant improvement of the pulmonary pressure is possible. In the literature are some individual case reports where the pulmonary hypertension resolved completely. In a patient with elevated pulmonary pressure and concomitant weight loss with diarrhoea it could be looked for Whipple's disease as a rare underlying disease.

10-6

Differences between diffuse and limited systemic sclerosis in patients from upper Austria

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Background: Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease characterized by the excessive production and accumulation of collagen and vasculopathy. This leads to sclerosis of the skin and changes in internal organs (heart, lung, digestive tract, kidney). There are two different forms: the limited and the diffuse SSc. The aim of our work was to compare clinical and laboratory parameters of patients with diffuse SSc with those of patients with limited SSc.

Methods: The data were obtained from the network for SSc, which has been maintained at the Department of Dermatology at the Ordensklinikum Linz Elisabethinen since 2006. Pulmonary arterial hypertension (PAH) was determined by echocardiography and right-sided cardiac catheterization.

Results: Out of 54 patients with SSc, 24 patients were diagnosed with diffuse SSc (anti-Scl-70 antibodies positive in 15 patients) and 25 patients with limited SSc (Cen-B-P antibodies positive in 18 patients). PAH was present in 37.9% of patients with diffuse SSc and in 28.0% of patients with limited SSc. Pulmonary fibrosis was found in 79.3% of patients with diffuse SSc and in 36.0% of patients with limited SSc. Esophageal hypomotility had developed in 89.7% of patients with diffuse SSc and in 66.7% of patients with limited SSc. Raynaud's syndrome was present in all patients with diffuse and limited SSc. Digital ulcers were seen in 44.8% of patients with diffuse SSc and in 50.0% of patients with limited SSc.

Conclusions: PAH, pulmonary fibrosis and esophageal hypomotility occur more frequently in diffuse SSc than in limited SSc, while Raynaud's syndrome and digital ulcers are equally common in both forms of SSc.

10-7

Innovative treatment option of diuretic resistant cardiac decompensation due to right heart failure in patients with severe pulmonary hypertension

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Background: Pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH)

are severe diseases and despite nowadays good treatment options are available, in daily clinical practice we are faced to treat patients with recurrent acute cardiac decompensation quite often. Advanced cardio-renal syndrome with diuretic resistance is a very limiting factor in therapeutic methods. Recurrent abdominal paracentesis and pleural aspiration are short term and very effective treatment options but not capable as permanent therapy.

Case presentation: Our patient is a 72-year-old male with severe right ventricular dysfunction due to CTEPH receiving Riociguat and subcutaneous Treprostinil as specific medication. He presented with manifest acute heart failure NYHA IV, resulting in prominent ascites, pleural effusions and anasacra. Continuous furosemide infusion, fluid restriction and sporadic addition of xipamid showed only insufficient response. Even concomitant pleural aspiration and temporary SLED (sustained low efficiency dialysis) were not able to achieve improvement and over time significant deterioration of kidney function was monitored.

In the past we had 4 similar cases of PAH patients who suffered from diuretic refractory heart failure and who received a peritoneal dialysis catheter for continuous drainage of ascites even after hospital discharge. In cooperation with nephrologists and surgeons our patient got a PD catheter implanted in procedural sedation. Several liters of ascites could be drained every day and a visible clinical improvement was shown. During recompensation our patient lost a total of 47 kg (130 kg to 83 kg) and the renal function recovers from a glomerular filtration rate of 16 to 50 ml/min/l. A mild SBP was successfully treated with intra-abdominal instillation of Vancomycin and Ceftazidim for 2 weeks. During the further course there were no more complications. The patient was discharged from hospital continuing ascites draining himself at home. Riociguat and subcutaneous Treprostinil were pursued during the stay and afterwards. Close follow up examination is provided in the pulmonary hypertension ambulance.

Conclusions: Continuous ascites drainage via a peritoneal dialysis catheter is a very effective method in advanced cardio-renal syndrome with diuretic resistance due to right heart failure in pulmonary hypertension. It really gives the patients a better quality of life. But as these patients are a high vulnerable collective they should be referred to a center and the decision about catheter insertion has to be made in a multidisciplinary team including cardiologists, nephrologists and surgeons.

POSTERSITZUNG 11 – Rhythmologie 2

11-1

Akutoutcome der VT-Ablationen an einem tertiären Zentrum

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Grundlagen: Als Therapieoptionen für chronisch rezidivierende ventrikuläre Tachykardien (VT) stehen heute neben der medikamentösen Behandlung und der Therapie mit einem implantierbaren Cardioverter-Defibrillator (ICD) in zunehmenden Maße die Katheterablation des arrhythmogenen Substrates zur Verfügung. Wir berichten über unsere Erfahrung hinsichtlich Akuterfolg und Sicherheit dieser Therapie.

Methodik: Für die retrospektive Auswertung des VT-Ablationsoutcomes wurden alle VT-Ablationsprozeduren, welche im Zeitraum von 01.01.2014–27.09.2017 im Ordensklinikum Linz der Elisabethinen durchgeführt worden sind, herangezogen. Für die Evaluierung des Akutoutcomes wurden Erfolgsrate und Komplikationen herangezogen. Als Akuterfolg wurde die post-interventionelle Nicht-Induzierbarkeit der prä-interventionell auslösbaren VTs definiert. Als Teilerfolg wurde eine inkomplette Suppression bezeichnet, ein Misserfolg bestand aus der fehlenden Suppression der VT post-interventionell (klinische VTs nach wie vor induzierbar).

Ergebnisse: Es wurden insgesamt 180 Patienten in dem untersuchten Zeitraum behandelt. Die behandelten Patienten waren im Durchschnitt 57,3 Jahre (± 13,5) alt. Es wurden insgesamt drei Gruppen erstellt. Gruppe A: ischämische Kardiomyopathie ($n=55$, 89,0 % männlich), Gruppe B: nicht-ischämische Kardiomyopathie ($n=38$, 84,2 % männlich), Gruppe C: keine strukturelle Herzerkrankung ($n=87$, 51,7 % männlich). Folgender Anteil der Patienten hatten bereits eine oder mehrere Vorablationen (A: 21,8 % vs. B: 34,2 % vs. C: 27,6 %). Der Anteil der ICD-Träger gliedert sich wie folgt (A: 76,4 % vs. B: 86,8 % vs. C: 18,4 %).

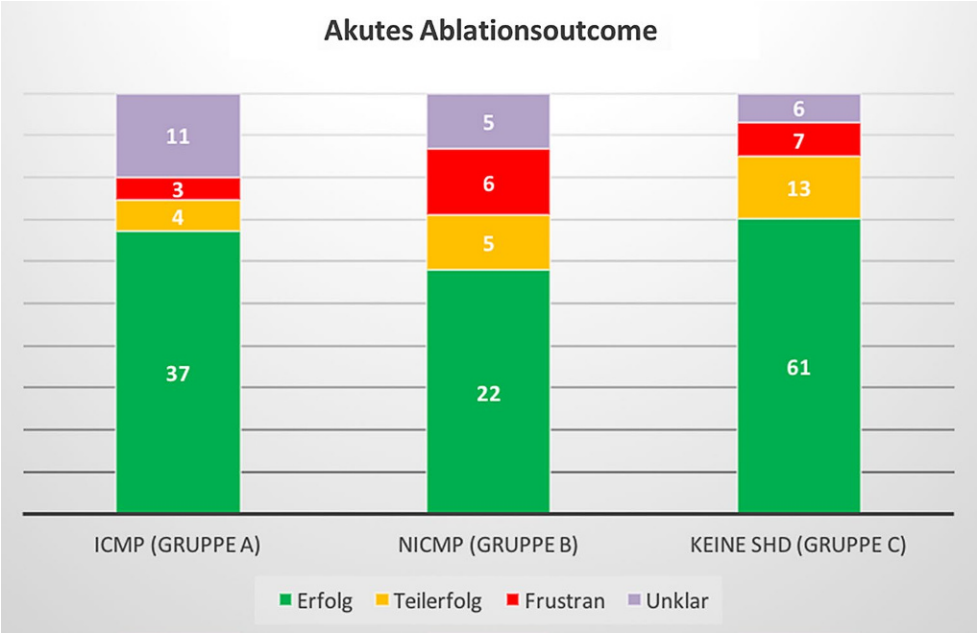

Abb. 1 | 11-1 Akutes Ablationsoutcome: ICMP 37 (67,3 %) erfolgreiche Ablationen; NICMP 22 (57,9 % erfolgreiche Ablationen; No SHD – keine strukturelle Herzerkrankung 61 (70,1 %)

Eine erfolgreiche Ablation konnte in 37 (67,3 %) vs. 22 (57,9 %) vs. 61 (70,1 %) der Fälle erzielt werden. Die Teilerfolge gliederten sich wie folgt: 4 (7,3 %) vs. 5 (13,2 %) vs. 13 (14,9 %). In 3 (5,4 %) vs. 6 (15,8 %) vs. 7 (8,0 %) der Fälle verlief die Ablation frustran. Bei 11 (20,0 %) vs. 5 (13,1 %) vs. 6 (7,0 %) konnte über das akute Ergebnis keine Aussage getroffen werden, da präinterventionell keine VT bzw. Extrasystolen induzierbar waren. 2 Patienten sind während der Prozedur verstorben (elektrischer Sturm, Perikardtamponade, Mortalität 1,1 %). Bei 2 Patienten kam es zu einem AV-Block III, welcher mit einem Schrittmacher versorgt werden musste (1,1 %). Bei einem Patienten kam es zu einem latent trifaszikulären Block bei vorbestehendem RSB. Insgesamt kam es zu 10 (5,5 %) Perikardtamponaden, welche sich im post-interventionellen Verlauf regredient zeigten.

Schlussfolgerungen: Vor allem die Gruppe der ischämischen und der nicht strukturellen Herzerkrankungen (67,3 % bzw. 70,1 %) zeigen einen guten Ablationserfolg. Nicht ischämische Substrate sind mit einer niedrigeren Erfolgsrate verbunden. Schwerwiegendere Komplikationen (v. a. Perikardtamponaden, AV-Blockierung mit Schrittmacherversorgung) traten in ca. 7–8 % auf, die Mortalität liegt bei 1,1 %. Da aber vor allem das VT-freie Überleben für den Patienten von Bedeutung ist, sind weitere Untersuchungen hinsichtlich des Longterm-Outcomes dieser Patienten notwendig.

11-2

High incidence of atrial fibrillation after successful catheter ablation of atrioventricular nodal reentrant tachycardia: a 15.5 year follow-up

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Background: Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common type of supraventricular tachycardia. Slow pathway (SP) ablation is the treatment of choice with a high acute success rate and a negligible periprocedural risk. However, long-term outcome data are scarce. The aim of this study was to assess long-term outcome, arrhythmia free survival and the incidence of pacemaker (PM) implantation after SP ablation.

Methods: In this study, 534 consecutive patients with AVNRT, who underwent SP ablation between 1994 and 1999 were included in the study. During a mean follow-up of 15.5 years, 101 (18.9%) patients died unrelated to the procedure or any arrhythmia. We could obtain information from 329 patients (61.6%). Data were collected by completing a questionnaire and/or contacting patients. Medical files were screened for documented recurrence, new-onset arrhythmias and repeat electrophysiological studies as well as PM implants.

Results: During the electrophysiological study, sustained 1:1 slow AV nodal pathway conduction was eliminated in all patients. There was no procedure-related AV-block requiring immediate pacemaker implantation. Recurrence of AVNRT was documented in 9 patients (2.7%), among those 7 patients (2.1%) underwent a successful second ablation procedure. Eleven

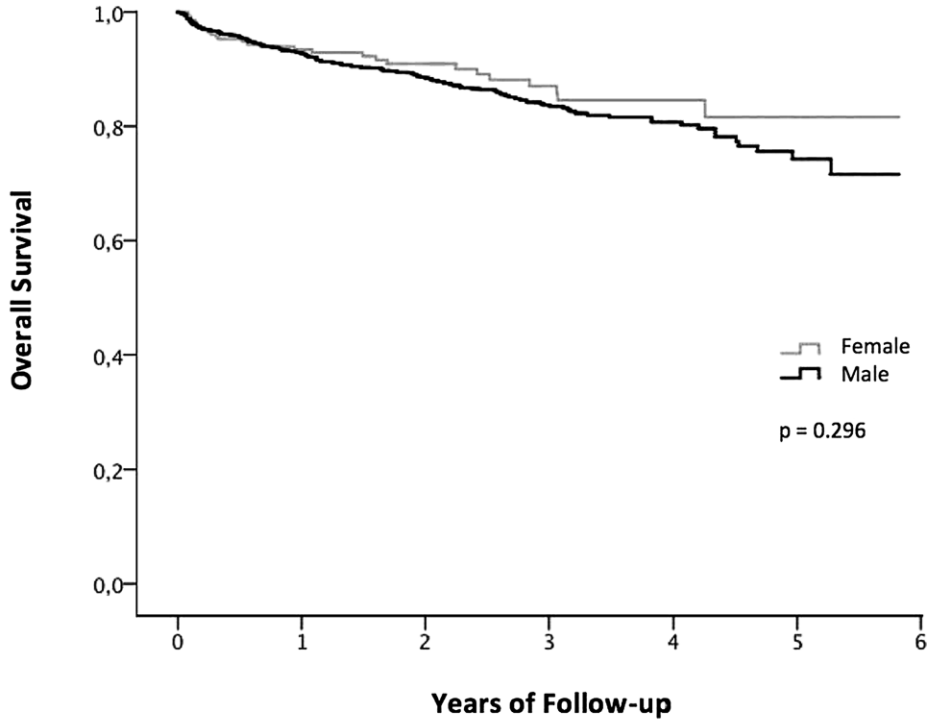

Fig. 1 | 11-3

Events and rate ratios (RR) of inappropriate and successful therapy, results of negative binomial regression analysis.

	Male (n = 1206)	Female (n = 265)	Male vs Female	
	Number of Events		RR (95% CI)	p-value
Inappropriate ATP	1010	381	2.03 (0.55-7.51)	0.288
Inappropriate Shock	486	61	0.57 (0.28-1.14)	0.111
Successful ATP	7829	1032	0.55 (0.20-1.56)	0.262
Successful Shock	928	492	2.79 (0.64-12.01)	0.171

a

Uni- and multivariate Cox Regression Analysis for predictors of overall mortality:

	Univariate			Multivariate		
	HR	95% CI	p value	HR	95% CI	p value
Age	1.04	1.03-1.06	**< 0.001**	1.04	1.03-1.06	**< 0.001**
Prim.Prev.	0.92	0.67-1.26	0.614			
AAR3	1.70	1.26-2.27	**< 0.001**	1.49	1.11-2.01	**0.008**
IND	1.11	0.81-1.52	0.511			
STD	0.81	0.59-1.11	0.186			
RED	1.12	0.82-1.53	0.465			
VVI	0.92	0.68-1.24	0.576			
DDD	0.95	0.70-1.30	0.758			
CRT-D	1.21	0.86-1.70	0.278			
EF_{normal}	0.43	0.25-0.73	**0.002**	0.71	0.40-1.27	0.245
EF_{mild}	0.89	0.57-1.41	0.632			
EF_{mod}	0.84	0.57-1.25	0.385			
EF_{sev}	1.72	1.27-2.34	**0.001**	1.49	1.07-2.08	**0.019**
ICMP	1.00	0.75-1.35	0.98			

b

Fig. 2 | 11-3

patients (3.3%) received pacemaker implantation 8.6 ± 3.5 years after ablation due to symptomatic sick-sinus syndrome ($n = 5$), symptomatic second degree AV-block ($n = 5$) and due to iatrogenic AV-block during artificial valve surgery ($n = 1$).

The relationship to atrial fibrillation (AF) in this study population seems to be twofold: in 4 out of 7 patients with pre-existing AF (57.1%), AF was eliminated by ablation of AVNRT suggesting that this arrhythmia serves as the sole AF trigger. On the long term however, patients with prior AVNRT, despite successful SP ablation, seem to be prone to develop new onset AF, as 42 patients (12.8%) developed AF during follow-up. Pre-existing arterial hypertension (odds ratio 2.6, 95% CI 1.13–5.76, $p < 0.03$), age (odds ratio 1, $p < 0.001$) and the postinterventional AH interval (odds ratio 1.02, 95% CI 1.004–1.045, $p < 0.05$) predicted the occurrence of AF, whereas the induction of AF by incremental pacing during the electrophysiological study was of no predictive value (odds ratio 1.51, 95% CI 0.77–2.95, $p = 0.23$).

Conclusions: The present long-term observational study after successful SP ablation of AVNRT confirms its clinical value reflected by a 2.7% recurrence rate. The unexpectedly high incidence of new-onset AF (12.8%) may impact long-term follow-up and requires further clinical attention.

11-3

Sex differences in inappropriate therapy and survival among 1471 implantable cardioverter defibrillator recipients

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Background and Objective: To assess a potential relationship between gender and outcome in recipients of implantable cardioverter defibrillators (ICDs).

Methods: All 1471 ICD recipients between 2000–2015 were retrospectively analyzed. Primary and secondary outcome parameters were overall survival and occurrence of inappropriate and successful antitachycardia pacing (ATP) and shock therapy.

Results: We analyzed 1206 (82.0%) male and 265 (18.0%) female ICD recipients. Mean follow-up times were 2.1 ± 1.5 years in males and 2.0 ± 1.5 years in females. Negative binomial regression analysis revealed a non-significant difference between male and female patients in inappropriate ATP (Rate Ratio (RR) = 2.03, $p = 0.288$) and in inappropriate shock therapy (RR = 0.57, $p = 0.111$) (Fig. 2a). No significant differences were observed in occurrence of successful ATP (RR = 0.55, $p = 0.262$)

and successful shock therapy (RR = 2.79, $p = 0.171$). Kaplan Meier analysis revealed that there was no significant difference in overall survival between males and females ($p = 0.296$, Fig. 1). Univariate and multivariate Cox Regression was performed to account for imbalances in patient's baseline characteristics and to determine predictors of overall mortality (Fig. 2b). In the multivariate model, age (HR = 1.04, $p = < 0.001$), treatment with antiarrhythmic drugs Class 3 (HR = 1.49, $p = 0.008$) and severely reduced ejection fraction (HR = 1.49, $p = 0.019$) remained predictors of overall mortality. After adjustment for age, treatment with antiarrhythmic drugs Class 3 and severely reduced ejection fraction, gender remained a non-significant predictor of overall mortality (HR (male) = 1.21, $p = 0.389$).

Conclusions: Female and male patients equally benefit from ICD therapy. The current analysis could not identify a possible relationship between gender and outcomes of device therapy.

11-4

Is there a difference in rhythm outcome between patients undergoing first line versus second line paroxysmal atrial fibrillation ablation?—Results of the EORP Atrial Fibrillation Ablation Long-Term Registry

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Background: Catheter ablation of atrial fibrillation is an established second line therapy for patients with symptomatic paroxysmal AF (PAF) and may be considered as a first line therapy in selected patients who are highly symptomatic, considering patient choice, benefit, and risk, according to recent ESC guidelines. Our study investigated whether a first line vs. second line ablation approach may result in improved sinus rhythm maintenance after ablation.

Methods: The EORP registry collected data in 27 European countries at 104 centres (including three Austria centres) in a prospective fashion. A total of 1922 patients undergoing their first PAF ablation were included in this study (36% female; median age 59 (52–65) years; median CHA2DS2-VASc Score 1). Of those, 196 (10%) underwent first line PAF ablation, whereas 1726 (90%) underwent second line PAF ablation after failure of ≥1 class I or III antiarrhythmic drug (AAD). There was no significant difference in baseline characteristics such as age, gender, co-morbidities, EHRA score, left atrial size or LVEF between groups. However, the first line group had a shorter time since first diagnosis of AF (1.1 (0.5–3.0) in first line patients vs. 2.4 (1.1–5.0) years in second line patients; $p < 0.001$) and a lower BMI (26.3 vs. 27.6; $p < 0.01$).

Results: There was no difference in ablation modalities such as the use of RF ablation (76.5 vs. 74.6%, $p =$ n.s.) or ablation strategy (PVI only in 69.7 vs. 66.9, $p =$ n.s.) between groups. Over 12.4 months of FU and after 1.1 ablation procedures, 73.1% vs. 69% of patients were free of arrhythmia recurrence in the first vs. second line ablation group ($p =$ n.s.). However, a higher number of patients were on AADs in the second line group (26.9% vs. 45.6%; $p < 0.001$). There was no significant difference in major adverse events (cardiovascular, peripheral vascular, neurological) (7.2 vs. 6%, $p =$ n.s.)

Conclusions: Success of AF ablation did not differ between patients who received ablation as first vs. second line therapy. A higher number of patients in the second-line group were still on AADs. Based on these data from a multicentre prospective registry, a trial of AAD therapy before AF ablation may be justified in most patients with symptomatic PAF eligible for rhythm control.

11-5

Potential local inflammation in individuals implanted with a leadless pacemaker systems: an experimental in vitro study

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Background: Leadless pacemaker technology is a promising upcoming field in clinical rhythmology. Currently, there are two different available products. Currently, the most commonly used system in the clinical setting is the Micra system (Medtronic).

According to the companies, the devices are usually expected to remain floating within the right ventricle, while fixation to the myocardium is achieved by the use of tines.

For both devices, an unexpected ingrowth/encapsulation within the wall of the right ventricle with signs of inlammatory cell infiltration was reported, which could be found during autopsies in some patients that witnessed non-pacemaker associated death.

Even though technical parameters of these pacemakers remained stable during follow-ups, the occurrence of a complete encapsulation was not expected and the processes of endothelialisation remained unclear. We hypothesized that a local inflammatory response might be the cause of these findings and could eventually be measurable.

The aim of our study was to investigate the effect of the Micra system and its materials/components on the immune responde and whether inflammatory processes take place in vitro.

Methods: For this purpose, whole Micra pacemakers were incubated in 9 ml heparinized plasma from 25 healthy volunteers for 48 h at 37 °C and 5% CO_2. Furthermore, 0.5 g gold, steel, titanium and tungsten wires were incubated in 9 ml heparinized plasma for 48 h at 37 °C and 5% CO_2 as well ($n = 10$).

To detect eventual inflammatory processes, the cytokines of systemic inflammation, e. g. interleukin- (IL) 1β, IL-6, and tumor necrosis factor alpha (TNF-α) and the chemokine IL-8

were measured using enzyme-linked immunosorbent assay (ELISA). Additionally, the level of transforming growth factor beta 1 (TGF-β1) and vascular endothelial growth factor (VEGF) were analysed.

Results: ELISA analyses showed that the whole Micra system leads to a significant increase of the inflammatory cytokine IL-6 which correlates with the data gained by the incubation of whole blood with the different wires. In particular, 0.5 g of tungsten showed a significant rise of IL-6 which was also found for IL-1β and IL-8. The other wires only had a marginal effect on the different cytokines and chemokines.

Conclusions: In this in vitro study analyzing effects of the Micra system it could be shown that the material composition of the pacemaker system led to an onset of inflammatory processes in whole blood through the increase of IL-6, IL-1β and IL-8. Consequently, through these findings one may speculate that the composition of Micra pacemaker may have an inflammatory effect on patients with Micra implants, nevertheless this effect might only be very localized and should not affect pacemaker function.

11-6

Risk factor assessment for survival in pacemaker patients in a single center large-scale study

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Background: Improving pacing technology justifies regular reevaluation of survival and influencing factors in patients with pacemakers (PM). The aim of this study was to investigate clinical factors with possible impact on survival in PM patients.

Methods: This retrospective study is based on PM patients of the Medical University of Vienna between 2000 and 2015. In total, 2930 patients with completed 10-year follow-up or death within 10 years were included in a multivariate COX regression. 10-year follow-up period started with patients' first PM implantation. Implantation indication (AV-block, sick sinus syndrome, atrial fibrillation, bundle branch block or unspecified) and mortality risk factors, such as male sex, age at first PM implantation, history of myocardial infarction, symptoms of heart failure, diabetes, hypertension or hyperlipidemia as confounding factors were adjusted to survival.

Results: 10 years after PM implantation 1311 of 2930 patients (44.74%) were still alive. Estimated mean survival was 6.8 years (95% confidence interval 6.72–6.98 years, Kaplan-Meier method). Fig. 1 shows hazard ratios and 95% confidence intervals for tested covariates. Independent risk factors for mortality in PM patients were male sex ($P<0.001$), higher age at first PM implantation ($P<0.001$), symptoms of heart failure ($P<0.001$) or diabetes ($P=0.001$). Treated hyperlipidemia was identified as a beneficial factor for survival ($P=0.002$), most probably due to intensive primary and secondary prevention of cardiovascular diseases. Index arrhythmia (indication for PM implantation) or history of myocardial infarction did not affect mortality. Implantation of dual chamber PM was not associated with better survival outcome compared to single chamber PM, although a borderline significance was found ($P=0.06$).

Conclusions: Male sex, higher age at first PM implantation, heart failure and diabetes were identified as independent risk factors for mortality in a 10-year follow-up. Index arrhythmia or implantation of single or dual chamber PM did not affect mortality.

11-7

Wearable cardioverter defibrillator (WCD) as a monitoring tool—results of the Austrian WCD Registry

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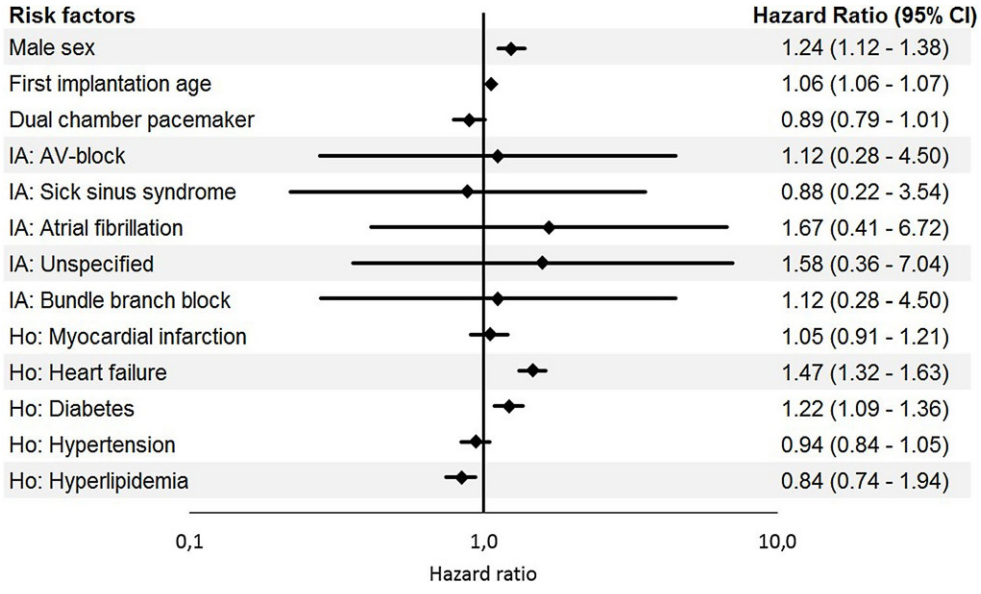

Fig. 1 | 11-6 Results of multivariate COX regression. *CI:* Confidence interval; *IA:* Index arrhythmia/implantation indication; *Ho:* History of

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Background: The wearable cardioverter defibrillator (WCD) is a treatment option for patients at temporarily high risk for ventricular arrhythmias. Beside the shock function the WCD allows continuous ECG monitoring either automatically triggered or initiated by the patient when symptoms occur.

Methods: Analysis of all automatically and manually recorded WCD ECGs of 448 patients in 48 Austrian centers who received a WCD from 2009–2016

Results: 448 Patients were analyzed (59 ± 14 years, 24% female). The median duration of WCD use was 54 [1–436] days. The daily wearing compliance was in median 23 hours [1–24]. Patients did not differ in daily wearing compliance regardless of age quartile, gender or WCD indication.

Among all 448 enrolled patients 10.201 ECGs in 300 patients (67%) (median 6 [1–964]) were automatically recorded by the WCD. Of those, 165 (1.6%) (median 2 [1–37]) ECGs in 44 patients (10%) showed a ventricular arrhythmia: 16 shocked VT/VF (8VT/8VF) events (10%) in 16 patients, 35 sustained hemodynamically stable and tolerated VTs (21%) in 15 patients, one VF event (1%) in one patient, 107 nsVTs (65%) in 28 patients, two bradycardia events (2%) in two patients and one asystole event (1%) in one patient, and therefore were classified as appropriate automatically recorded ECG.

The remaining 10.036 automatically recorded ECGs in 290 patients (median 6 [1–963] showed artefacts (97%), supraventricular tachycardia (1%), atrial fibrilation (1%) or pacemaker oversensing (1%).

The WCD as possible eventrecorder in case of symptoms was used by 248 patients, who induced 2787 manually recorded ECGs (median 3 [1–579]). Of those, 56 (2%) were classified as appropriate containing atrial fibrillation ($n = 23$; 41%), nsVTs ($n = 27$; 48%), slow sustained VTs ($n = 3$; 5.5%) or bradycardia ($n = 3$; 5.5%). Atrial fibrillation was newly detected in 3 patients.

The remaining 2731 ECGs were classified as inappropriate. The reason for inappropriate manual ECGs were ventricular extrasystole in 16 ECGs (0.6%), sinus tachycardia in two ECGs (0.1%) or 2713 (99%) ECGs showing a normal rhythm.

Eleven of the 448 patients (2.5%) received 22 appropriate WCD shocks for 19 VT/VF events (9 VT and 10 VF events). The median time from WCD prescription to a shock event was 7 days [2–151]. Eight out of eleven patients (73%) received their first WCD shock within 30 days.

Conclusions: The WCD as effective treatment option in patients at high risk for ventricular arrhythmia triggers a vast amount of alarms. Automated and patient-triggered recordings may lead to detection of severe arrhythmias. However, the vast majority of automated alarms is due to artefacts.

11-8

Safety profile of near-zero fluoroscopy atrial fibrillation ablation with non-fluoroscopic catheter visualization: experience from 1000 consecutive procedures

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Background: Efforts to reduce radiation exposure during catheter ablation procedures have included the use of various technological measures. Significant results have been achieved to the point where near lead-free procedures in routine clinical practice has become a realistic goal. The integration of MediGuide technology [non-fluoroscopic catheter visualization technology (NFCV)] and three-dimensional electroanatomical mapping is one of the methods developed in response to radiation reduction initiatives. We aimed to evaluate the impact of this NFCV technology on atrial fibrillation (AF) catheter ablation in terms of reduction in procedural and radiation time as well as safety aspects.

Methods and Results: Between March 2012 and March 2017, a total of 1000 patients underwent AF ablation using NFCV. Patient and procedural data and complications within the first 3 months were entered into a prospective registry and analysed. We assessed procedure time, fluoroscopy time, and dose and complications. In a cohort of 1000 patients (62.9 ± 11 years; 72% men; left ventricular ejection fraction 57%; and left atrial diameter 43.2 mm), the median procedure time was 120 min, median fluoroscopy time was 0.90 min, and the median fluoroscopy dose of was 345.1 cGy _ cm^2. Stratification of the first (Group 1) and the last 250 (Group 2) cases showed significant improvement in the median procedure time (140–110 min) and reduction in the median fluoroscopy time (6–0.5 min) and the median dose (2263–151.9 cGy _ cm^2). The overall complication rate was 2.0%.

Conclusions: The use of NFCV technology enables safe, consistent, and 'near lead-free' performance of AF ablation in routine clinical practice.

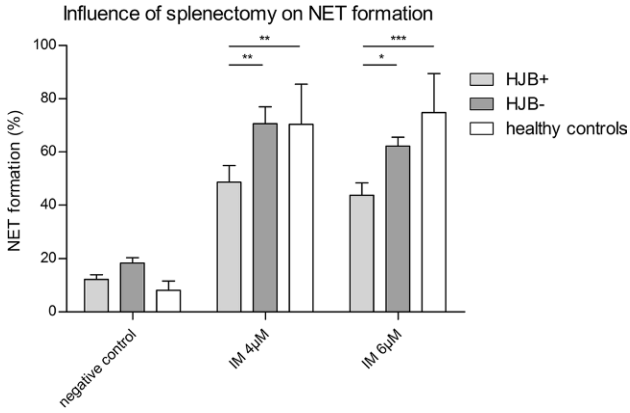

Fig. 1 | 12-1

POSTERSITZUNG 12 – Basic Science 3

12-1

Neutrophil extracellular trap formation is impaired in patients with Howell Jolly body-positive splenectomy

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Background: Neutrophils are able to release their nuclear content into the extracellular space by formation of neutrophil extracellular traps (NETs). NETs have a role in host defense, but are also implicated in thrombotic and autoimmune diseases. Splenectomy is a risk factor for the development of bacterial infections of chronic thromboembolic pulmonary hypertension (CTEPH). In splenectomized patients, dysfunction of neutrophils has been reported with regards to bactericidal function and reactive oxygen species formation. NETosis in splenectomy has not been investigated. We hypothesized that NETosis was altered in splenectomized patients.

Methods: We drew venous blood from patients with a history of splenectomy ($n=16$, 50% female, mean age 57 ± 12 years). Howell Jolly bodies (HJB), nuclear remnants in erythrocytes considered to be indicative of severe splenic dysfunction, were detected by microscopy. Ex vivo NET formation of isolated neutrophils upon stimulation with ionomycin was measured using Sytox® Green, a dye exclusively staining extracellular DNA released in the course of NETosis.

Results: Five (31%) patients had relative neutropenia; eight (50%) patients were HJB+. In HJB+ patients, NET formation ex vivo was significantly decreased compared to HJB- patients (Figure). Interestingly, spontaneous NET formation in the absence of ionomycin was also decreased.

Conclusions: Our findings indicate impaired NETosis, an important effector mechanism of neutrophils, in in HJB-positive splenectomy patients. This could be one factor explaining increased susceptibility to bacterial infection.

12-2

Non-classical monocytes at the culprit lesion site of ST elevation myocardial infarction patients ameliorate outcome via CX3CR1

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Background: Myocardial infarction (MI) is a major cause of acute and chronic heart failure. The pathomechanisms of myocardial salvage and scar formation are incompletely understood. We have previously shown that neutrophils release neutrophil extracellular traps (NETs) at the culprit lesion site (CLS). Coronary NET burden correlated significantly with increased infarct size in ST elevation MI (STEMI) patients. It was shown that macrophages are critical for the clearance of NETs. Monocytes are circulating macrophage precursors and play a critical role after myocardial ischemia/necrosis. Monocytes are sub-grouped according to their CD14/CD16 expression into classical (CD14++CD16-), intermediate (CD14++CD16+) and non-classical (CD14+CD16++) monocytes. These subsets fulfill diverging roles in inflammation; especially patrolling non-classical monocytes are important for the efficient removal of cell debris after tissue damage. The chemotactic fractalkine receptor CX3CR1 is highly expressed on non-classical monocytes. We sought to investigate monocyte subsets at the CLS of STEMI patients.

Methods: In the course of a clinical trial, in which out of hospital-initiated therapeutic hypothermia was tested in STEMI patients (STATIM trial, $n=120$, submitted), we determined monocyte subsets in thrombectomy specimens from the CLS compared to femoral blood samples ($n=30$) using flow cytometry. Cardiac magnet resonance (CMR) was performed in these patients 4 ± 2 days after STEMI. The primary endpoint of this trial was myocardial salvage index (MSI). In a second STEMI population ($n=36$), we performed a detailed expression marker analysis of respective subsets at the CLS compared to the femoral site. NET surrogate markers (citrullinated histone 3 [citH3], double-stranded deoxyribonucleic acid [dsDNA]) were measured in CLS and femoral plasma using immunometric assays.

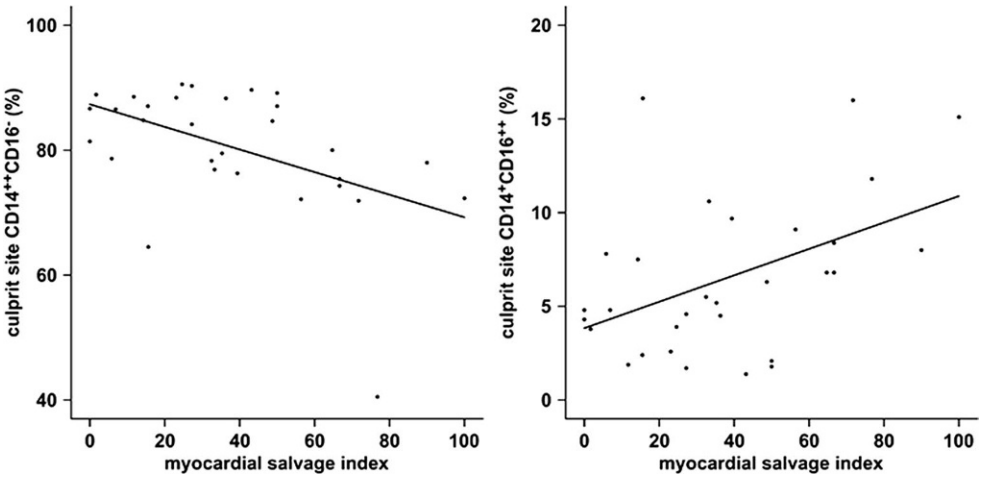

Fig. 1 | 12-2

Enzymatic infarct size (CK-MB area under the curve [CK-MB AUC]) was determined in all patients.

Results: Therapeutic hypothermia had no effect on MSI or other outcome measures. Classical monocytes were significantly decreased at the CLS and correlated negatively with MSI, whereas non-classical monocytes where significantly increased and correlated positively with MSI (Fig. 1). In the second STEMI population, CX3CR1 expression of non-classical monocytes correlated negatively with CK-MB AUC and with citH3 and dsDNA. These NET surrogate markers correlated positively with CK-MB AUC, as previously published.

Conclusions: These data indicate that non-classical monocytes accumulate at the CLS and contribute to myocardial salvage, potentially via effective clearance of cell debris and NETs. CX3CR1 appears to be highly important in this process.

12-3

Fibrin-derived Bß¬15–42 peptide is a gatekeeper of thrombus resolution

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Background: Thrombus resolution is driven by leukocyte recruitment and thrombus angiogenesis.

A naturally occurring peptide Bß¬15–42, part of the beta chain of the fibrinogen molecule is an effective inhibition of leukocyte transmigration in vitro. Bß¬15–42 peptide is a competitive inhibitor of the interaction between the N-terminus of the fibrin beta chain and vascular endothelial cell cadherin (VE-cadherin). We investigated the effect of Bß¬15–42 on thrombus resolution in two murine stagnant flow venous thrombosis models, and studied Bß¬15–42 levels in thrombus tissues from humans.

Methods and Results: We have studied two mouse models of inferior vena cava (IVC) ligation. In the first model we have ligated only the inferior vena cava. In the second model we ligated the IVC and all visible side and back branches.

Study groups of 8–12 weeks old BALB/c mice were injected i. p. over various time periods with Bß¬15–42, random peptide or saline after thrombus had been induced by subtotal inferior vena cava (IVC) ligation.

Bß¬15–42 delayed thrombus resolution after IVC ligation. Thrombi of the treated groups were significantly larger on day 7 and day 14 than controls. We saw a significant change in the area and volume of the treated thrombi. Moreover, we observed decrease of thrombus macrophages and diminished microvessel density.

Additionally, we have demonstrated that Bß¬15–42 blocks leukocyte transmigration through endothelial cell monolayer. Measurements of Bß¬15–42 in red clot of human cases of chronic thrombosis indicated higher concentrations compared with controls.

Conclusions: Our data suggest that an excess of the fibrin fragment Bß¬15–42 misguides thrombus resolution, presumably by inhibiting VE-cadherin mediated leukocyte migration during early organization. The presence of the N-terminal fragments entailing an inhibition of leukocyte recruitment may be a mechanism for thrombus non-resolution in CTEPH.

12-4

Protein tyrosine phosphatase non receptor type 22 (PTPN22) function impacts neutrophil extracellular trap formation

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Background: Neutrophils undergo NETosis via peptidylarginine deiminase 4 (PAD 4) activation and release extracellular traps (NETs) into the extracellular space to combat pathogens. NETs also have a significant role in thrombotic disease. Coronary NET burden correlates positively with infarct size in ST-elevation myocardial infarction (STEMI) patients. It was reported that a missense mutation (R620 W) in the protein tyrosine phosphatase non receptor type 22 (PTPN22) results in abrogated PAD4 inhibition and consecutively leads to enhanced NETosis. Deoxyribonuclease (DNase) is a natural counter mechanism against NETs.

Purpose: We analyzed the effect of PTPN22 deficiency on NET formation in a murine model and studied the R620 W single nucleotide polymorphism (SNP) in coronary artery disease (CAD) patients with regard to outcomes.

Methods: Blood was drawn from PTPN22 knockout (KO) mice, NETosis was induced by ionomycin and compared to wildtype (WT) mice (each $n=10$). NETotic neutrophils were measured by flow cytometry. DNase activity in murine plasma samples was measured by an in-house built activity assay. Furthermore, we tested the R620 W SNP in 711 CAD patients who suffered from ST elevation myocardial infarction using allelic discrimination polymerase chain reaction (PCR).

Results: PTPN22 KO mice displayed significantly reduced NETosis compared to WT. Interestingly, PTPN22 mice had a significantly increased plasmatic DNase activity, which correlated with reduced NETosis. CAD patients carrying the R620 W showed no altered mortality compared to controls.

Conclusions: In contrast to present literature, we found decreased NETosis in PTPN22 KO mice. In this ongoing project, we will further evaluate NETosis and DNase in connection to PTPN22.

12-5

Release of danger associated molecular patterns activates innate immunity and initiates calcific aortic valve disease after mediastinal radiation

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Background: Cardiovascular disease after adjuvant thoracic radiation has become the leading nonmalignant cause of death in cancer survivors. Up to 40% develop calcific aortic valve disease (CAVD) after thoracic radiation. CAVD is caused by an osteoblastic phenotype switch of valvular interstitial cells (VICs). However, the trigger for the phenotype switch after radiation remains unknown. Danger associated molecular patterns (DAMPs) are released from stressed cells and are known to activate Toll-like receptor 3 (TLR3), a receptor of the innate immune system. We hypothesized that radiation causes release of DAMPs with subsequent activation of TLR3. TLR3 activation leads to an osteoblastic phenotype switch of VICs with subsequent initiation of CAVD.

Methods: Valvular interstitial cells (VICs) were isolated from aortic valves of healthy donors undergoing heart transplantation and treated with radiation therapy (10 Gy). Expression levels of TLR3, inflammatory cytokines and osteoblastic markers were compared with cells treated either with TLR3 agonist poly(I:C) or a TLR3/dsRNA complex inhibitor. Osteoblastic activity of radiated cells was assessed via alkaline phosphatase assay and Alizarin Red staining. ApoE-/- and ApoE-/-/TLR3-/- mice underwent mediastinal radiation (15 Gy). Cardiac function and aortic valve morphology was assessed via transthoracic echocardiography and histological analyses.

Results: Radiation of VICs resulted in TLR3 activation with increased expression of TNF-a, IL-6, IFN-y and IL-10. In parallel, radiated VICs showed enhanced osteoblastic activity with increased Runx2 and BMP2 expression, alkaline phosphatase activity and calcific nodule formation. TLR3 inihibition resulted in prevention of osteogenic phenotype switch. Aortic valves from patients with history of thoracic radiation showed clearly increased TLR3 expression. In vivo, thoracic radiation of ApoE-/- mice resulted in increased TLR3 expression and osteoblastic activity on aortic valves. However, we found no osteoblastic activity after radiation in ApoE-/-/TLR3-/- mice. In addition, ApoE-/-/TLR3-/- mice showed improved functional outcome after radiation regarding LV ejection fraction (%: 45 ± 1.7 vs. 50 ± 1.5, $p = 0.04$), aortic valve opening (mm: 0.81 ± 0.05 vs. 0.95 ± 0.03, $p = 0.04$) and leaflet thickness (mm: 0.09 ± 0.01 vs. 0.07 ± 0.004, $p = 0.03$).

Conclusions: Radiation activates TLR3 and leads to an osteoblastic phenotype switch of VICs. Inhibition of TLR3 prevents from calcification after radiation. ApoE-/-/TLR3-/- mice show no signs of CAVD after radiation. We show major involvement of TLR3 in the pathogenesis of CAVD after radiation. TLR3 could become an effective target for the pharmacological prevention of radiation induced CAVD.

12-6

Role of B cells in venous thrombus resolution

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Background: Venous thromboembolism (VTE) is a major health problem with an annual incidence of 0.75 to 2.69 per 1000 individuals in the general population. Recurrence or non-resolution occurs in up to 25% of cases. Thrombus persistence can lead to chronic thromboembolic pulmonary hypertension (CTEPH) or post-thrombotic syndrome (PTS). It is unclear which mechanisms underlie thrombus non-resolution.

One risk factor for CTEPH is splenectomy. The spleen plays an important role in B cell maturation and is required for the maintenance of peritoneal B1 cells, which secrete natural IgM antibodies that fulfill important housekeeping functions. We therefore hypothesized that B cells and IgM might be involved in the natural resolution of venous thrombi, and studied venous thrombus resolution in different mouse models characterized by alterations of B cell function.

Methods: We splenectomized female Balb/c mice and after 4 weeks subjected them to partial ligation of the inferior vena cava (IVC) to induce thrombus formation. After the surgery, we injected isolated splenic B cells intraperitoneally, a control group received PBS. We monitored thrombus resolution over a period of 28 days using the Vevo 2100 high-frequency ultrasound system.

In addition, we used two transgenic mouse strains with different modifications of B cell function: sIgM-/- mice are unable to secrete IgM, but normally express membrane-bound immu-

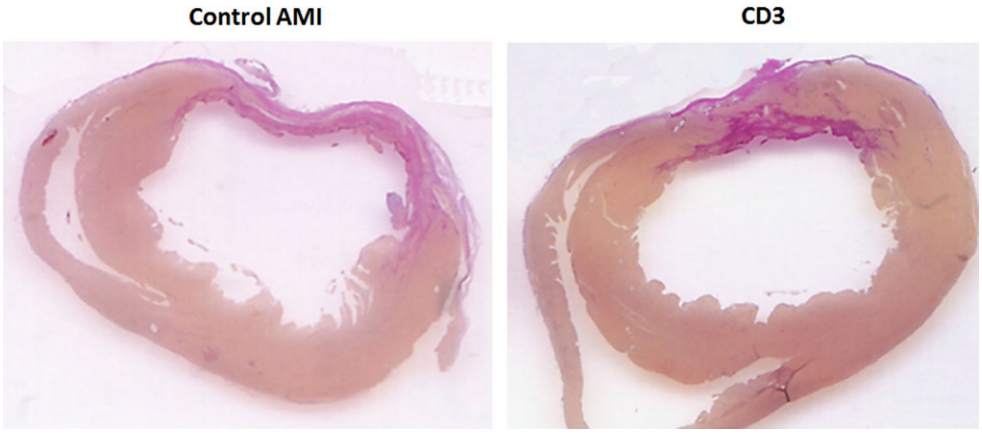

Fig. 1 | 12-7

noglobulins. SiglecG-/- mice are characterized by increased B1 cell numbers as well as increased plasma IgM levels. These mice as well as wildtype controls were subjected to IVC stenosis, and resulting thrombi were harvested at different time points and processed for histological analyses.

Results and Conclusions: Treating splenectomized mice with a single injection of purified splenic B cells after IVC ligation resulted in significantly reduced thrombus size at day 1 and day 3 after thrombus induction, while we observed no effect in the later course of thrombus resolution. sIgM-/- mice were characterized by smaller thrombi than wildtype mice 3 days after IVC ligation, while after 7 days, thrombi harvested from sIgM-/- mice were bigger than those from wildtype controls. In SiglecG-/- mice, only a small reduction in thrombus length was observed 7 days after vena cava ligation. Taken together, these results point towards a role of B cells in thrombus resolution, which needs to be further elucidated by future experiments.

12-7

T-cell stimulation via CD3 epitope directed antibodies leads to the release of pro-angiogenic chemokines and mircoRNAs and preserves ventricular geometry after experimental myocardial infarction

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Background: Ischaemic cardiomyopathy after acute myocardial infarction (AMI) leads to high morbidity and mortality in the western world. Paracrine effects of secretomes of stem cells have been shown to induce cardioprotective and pro-angiogenic mechanism within the ischaemic myocardium. Comparable effects elicited by paracrine factors secreted by "stressed" cells have also been found when cells where subjected to irradiation or stimulation with T-cell antibodies (Anti-thymocyte globulin (ATG)). These paracrine therapies have shown potential to induce cardioprotection and angiogenesis after AMI. Possible candidate factor transducing these cardioprotective effects were speculated to be pro-angiogenic factors such as Interleukin-8 and also mircoRNAs.

Objective: To evaluate which single anti-T-cell-epitope antibody alters IL-8 expression, a cytokine associated with angiogenesis, at a similar or superior level compared to ATG and to assess treatment with this single antibody.

Methods and Results: We quantified in vitro IL-8 expression in human peripheral blood mononuclear cell cultures (PBMCs) using a commercially available ELISA after treatment with 20 µg of anti-IgG2a, IgG1, CD4, CD8, CD11a, CD3, CD28, CD2, HLA-DR and different doses of ATG. Only addition of anti-CD3 antibodies led to a pronounced IL-8 expression compared with other epitopes and also ATG (21.438 + 4740 pg/ml vs 4005 + 1378 pg/ml; $p < 0.01$). Both CD3 and ATG stimulation led a significant and dose dependent rise of IL-8.

We assessed anti-CD3-treatment in a rat model of AMI in which ischaemia was induced by ligation of the left anterior descending artery. After induction of AMI, anti-CD3 antibodies were injected intravenously via the femoral vein. Treatment with CD3 antibodies led to less pronounced infarct sizes (10 + 13% vs 26 + 9%; $p < 0.001$). Moreover, we performed a quantification of microRNA expression with next-generation sequencing. Here, we found an increase in cardioprotective and pro-angiogenic microRNAs (such as miR146a).

Conclusions: Secretomes of (stem) cells treated with a stimulating agent such as an anti-CD3 antibody might further optimize cell processing with special regards to paracrine factors leading to cardioprotection after AMI.

12-8

Inhibition of microRNA-494 halts atherosclerotic plaque progression and stabilizes advanced atherosclerotic lesions

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Background: Previously we showed that inhibition of miR-494 reduced early atherosclerotic lesion development in the carotid artery. Patients at risk of atherosclerotic complications however, generally present themselves in the clinic with advanced and unstable atherosclerosis. Therefore, in this study, we investigated the in vivo effect of miR-494 inhibition on advanced atherosclerotic plaques in the aortic root and carotid artery.

Purpose: Investigating the in vivo effects of miR-494 inhibition on progression and stability of advanced atherosclerotic lesions.

Methods: LDLr-/- mice were fed a Western Type Diet (WTD) for 10 weeks to induce atherosclerosis. Semi-constrictive collars were placed around both carotid arteries 4 weeks after start of WTD and 6 weeks after collar placement, a subset of mice (N = 10) was sacrificed to analyze baseline plaque size and composition. For the remaining mice, WTD was replaced by normal chow and 3rd Generation Antisense (3GA) against miR-494 (3GA-494; N = 10) or negative control (3GA-ctrl; N = 10) were administered (i. v., 1 mg/mouse) immediately after and at 2 and 4 weeks after diet switch. Mice were sacrificed one week after final injection.

Results: 3GA-ctrl mice showed increased carotid artery plaque size compared to baseline, indicating continued atherogenesis, even after lowering plasma cholesterol levels by diet-replacement (before: 863 ± 115 mg/dL vs. after: 214 ± 13 mg/dL). 3GA-494 mice however, showed a significant decrease in carotid artery plaque size compared to control; in fact, 3GA-494 mice had similar plaque sizes to baseline mice (baseline: 30 ± 8*103 µm2, 3GA-ctrl: 56 ± 16*103 μm^2 vs. 3GA-494: 23 ± 9*103 μm^2, $P < 0.05$). Relative intra-plaque collagen content and macrophage infiltration remained unaltered after treatment. In the aortic root, we did not observe differences in plaque size between the 3GA-treated groups, however, plaque stability was significantly increased upon 3GA-494 treatment. Intra-plaque collagen content was increased in 3GA-494 mice (3GA-ctrl: 37 ± 3% vs. 3GA-

494: 52 ± 4%, P < 0.05), whereas necrotic core size remained similar (3GA-ctrl: 20 ± 2 vs. %3GA-494: 16 ± 3%). Blood analysis revealed a significant decrease in platelet count in the 3GA-494 group (3GA-ctrl: 1097 ± 109*109/L vs. 3GA-494: 288 ± 64*109/L, P < 0.05), as well as a further reduction in plasma cholesterol (3GA-ctrl: 214 ± 13 mg/dL vs. 3GA-494: 154 ± 6 mg/dL, P < 0.05).

Conclusions: These results show that treatment with 3GA-494 halts plaque progression in the carotid artery and increases plaque stability in aortic root plaques. Furthermore, 3GA-494 treatment reduces the platelet count, as well as plasma cholesterol levels, which is an additional improvement of cardiovascular risk factors.

POSTERSITZUNG 13 – Diverse 2

13-1

Growth differentiation factor 15 (GDF-15) is an early predictor of mortality after cardiac arrest

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Background: Early prognostication in post-cardiac arrest (CA) patients remains challenging and biomarkers have evolved as helpful tools in risk assessment. Growth differentiation factor 15 (GDF-15) is dramatically up-regulated during various kinds of tissue injury and predicts outcome in many pathological conditions. We aimed to assess the predictive value of GDF-15 in post-CA patients.

Methods: This study included 53 consecutive post-CA patients who were transferred to a tertiary intensive care unit (ICU) after return of spontaneous circulation. GDF-15 serum levels were determined at ICU admission.

Results: A total of 27 patients (50.9%) died during the 6-month follow-up. Median GDF-15 levels were significantly lower in survivors (2257 ng/L (interquartile range (IQR): 1392–3757 ng/L) than in non-survivors (6124 ng/L (IQR: 2317–9605 ng/L), $p = 0.006$). GDF-15 levels were also significantly lower in patients with favourable neurological 6-month outcome (cerebral performance category (CPC) 1–2) than in those with poor neurological outcome (CPC 3–5; $p = 0.03$). GDF-15 significantly predicted 6-month all-cause mortality in univariate Cox regression analysis ($p = 0.003$) with a 5-fold higher risk (95% confidence interval (CI) 1.7–14.3; $p = 0.003$) in the third tertile as compared to the first tertile (Fig. 1). The association remained significant after multivariable adjustment. GDF-15 had a Harrell's c-statistic of 0.73 (95%CI 0.63–0.83; $p < 0.001$) for 6-month mortality.

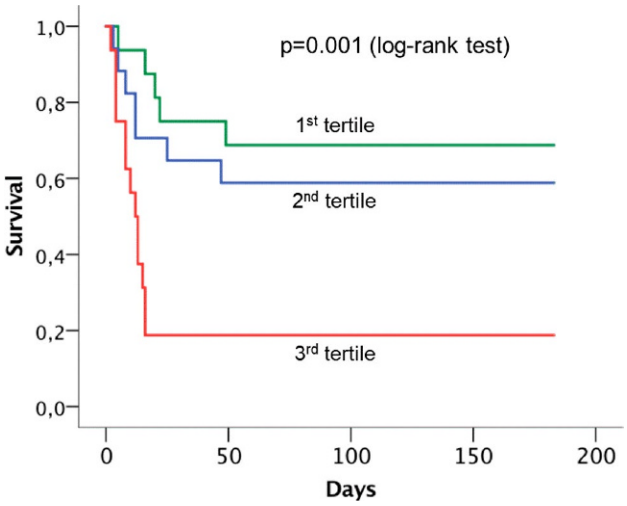

Fig. 1 | 13-1 Kaplan-Meier plot showing the probability of survival after cardiac arrest with initially successful resuscitation according to tertiles of growth differentiation factor 15 (GDF-15)

Conclusions: The stress-response cytokine GDF-15 predicts poor outcome in post-CA patients. GDF-15 may reflect the extent of hypoxic injury to the brain and other organs and might help to improve early risk stratification after CA.

13-2

Komplikationen kardiologischer Interventionen unter NOAC Therapie

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Grundlagen: Nicht-Vitamin-K-abhängige orale Antikoagulantien (NOACs) werden immer häufiger zur Prophylaxe ischämischer Ereignisse bei Patienten mit Vorhofflimmern und erhöhtem Risiko für einen Schlaganfall eingesetzt. Laut aktuellen Leitlinien sollen NOACs vor und während einer elektiven kardiologischen Intervention vorübergehend abgesetzt werden, um das periprozedurale Blutungsrisiko zu minimieren. Wir haben ein prospektives Register der Eingriffe an unserer Abteilung erstellt, um die aktuelle Vorgehensweise des Absetzens der NOACs vor einem kardiologischen Eingriff und das Auftreten von ischämischen und hämorrhagischen Komplikationen in einem nationalen Referenzzentrum zu analysieren.

Methodik: Die Analyse umfasste 100 kardiologische Interventionen an 98 Patienten (Durchschnittsalter 68,4 Jahre) und erstreckte sich von Dezember 2016 bis Juni 2017. Die häufigste Indikation für die Antikoagulation war Vorhofflimmern (91 %). Der durchschnittliche CHA2DS2-VASc-Score betrug 3,5 ± 1,6 und der durchschnittliche HASBLED-Score lag bei 2,3 ± 1,1. Bei ihrer stationären Aufnahme wurde bei jedem der Patienten im Rahmen der standardmäßigen Blutentnahme Faktor II- und Faktor Xa-Aktivität bestimmt. Der genaue Zeitpunkt des Eingriffs sowie die Zeit zwischen der letzten Einnahme des NOACs vor und der ersten Einnahme nach der Intervention wurde ebenfalls erfasst und dokumentiert. Zusätzlich wurde eine kurze Patientenanamnese erstellt, welche eventuelle zusätzliche Medikation wie Thrombozytenaggregationshemmer oder Heparin, sowie Details zur Intervention oder im Rahmen des stat. Aufenthalts aufgetretene ischämische oder hämorrhagische Komplikationen (Herzinfarkt, Schlaganfall, TIA oder Systemische Embolien), enthielt.

Ergebnisse: Bei 65 % der Patienten wurde eine Koronarangiographie mit oder ohne PCI vorgenommen, bei 12 % eine elektrophysiologische Studie oder Ablation, bei 11 % die Implantation eines Herzschrittmachers und bei 5 % ein anderer Eingriff. 48 Patienten waren in Behandlung mit Rivaroxaban, 40 mit Apixaban und 10 mit Dabigatran (je ca. 30 % in reduzierter Dosierung). 30 % hatten eine Kreatinin-Clearance von <50 ml/min/m² und 57 % hatten eine erhöhten Faktor II- oder Xa-Spiegel (>30 ng/ml) bei ihrer Aufnahme. Im Durchschnitt wurden NOACs 2,6 ± 1,4

Tage vor dem Eingriff abgesetzt. Die Wiederaufnahme der oralen Antikoagulation erfolgte im Mittel 1,3±0,8 Tage nach der Intervention. Bei keinem der inkludierten Patienten kam es zu einem thromboembolischen Ereignis. Bei 3 Patienten kam es allerdings zu femoralen Komplikationen (2 Hämatome und 1 Pseudoaneurysma) und ein Patient litt während seines Aufenthaltes an einer selbstlimitierenden Epistaxis. Bei allen Patienten mit Komplikationen erfolgte das Absetzten der NOACs entsprechend der aktuellen Leitlinien. Bei einem der Patienten mit Leistenhämatom fand sich ein signifikant erhöhter NOAC-Spiegel. Es wurde eine schwache Korrelation zwischen Faktor II- und Xa-Spiegeln, anderen Gerinnungsparametern und Nierenfunktion festgestellt.

Schlussfolgerungen: In der von uns untersuchten Kohorte wurden NOACs früher als empfohlen abgesetzt. Die Wiederaufnahme erfolgte entsprechend der aktuellen Leitlinien. Trotzdem wurden bis jetzt keine ischämischen Komplikationen beobachtet und Blutungskomplikationen waren rar. Blutungskomplikationen nach den Interventionen ließen sich weder durch erhöhte NOAC-Spiegel (>30 ng/ml) noch durch erhöhte Gerinnungsparameter vorhersagen.

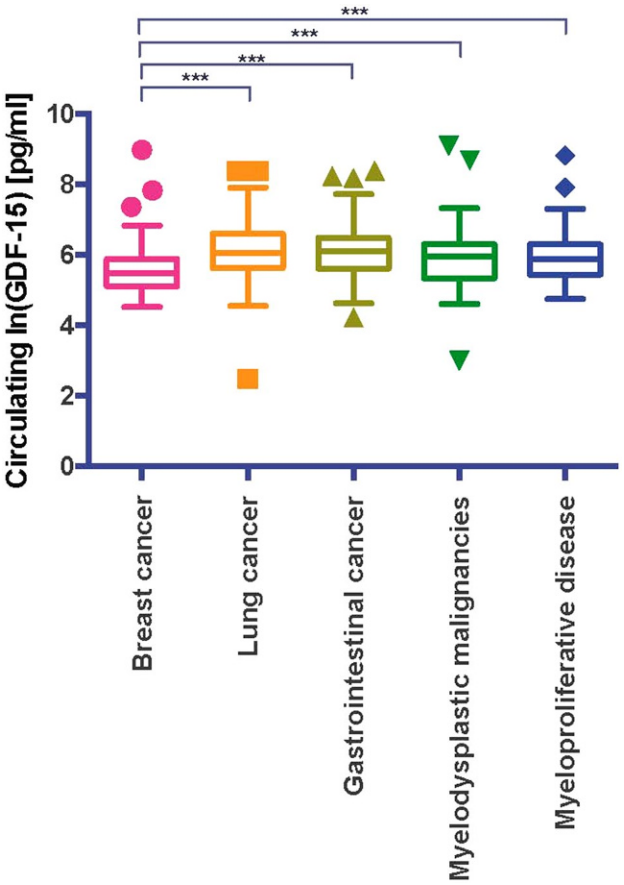

Fig. 1 | 13-3

13-3

Cardiac fibrosis marker GDF-15 is associated with prognosis in treatment naïve cancer patients

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Background: The prognostic importance of growth differentiating factor-15 (GDF-15) has been investigated in numerous pathologic cardiac processes as myocardial infarction or heart failure. Elevated levels of GDF-15, which is equally implicated in cell growth and survival, have also been observed in distinct tumor entities. However, its general impact on prognosis in cancer has not been investigated yet. This study aimed to explore whether cardiac fibrosis marker GDF-15 has ability to predict long-term mortality also in an unselected cohort of cancer patients without prior anti-cancer therapy.

Methods: We prospectively enrolled 555 consecutive treatment naïve patients with primary diagnosis of cancer. GDF-15 as well as other cardiac and routine laboratory markers were determined. All-cause mortality was defined as the primary endpoint.

Results: GDF-15 levels were 338 pg/ml (IQR 205–534) for the total cohort and values were comparable in different tumor entities except for lower concentrations in breast cancer

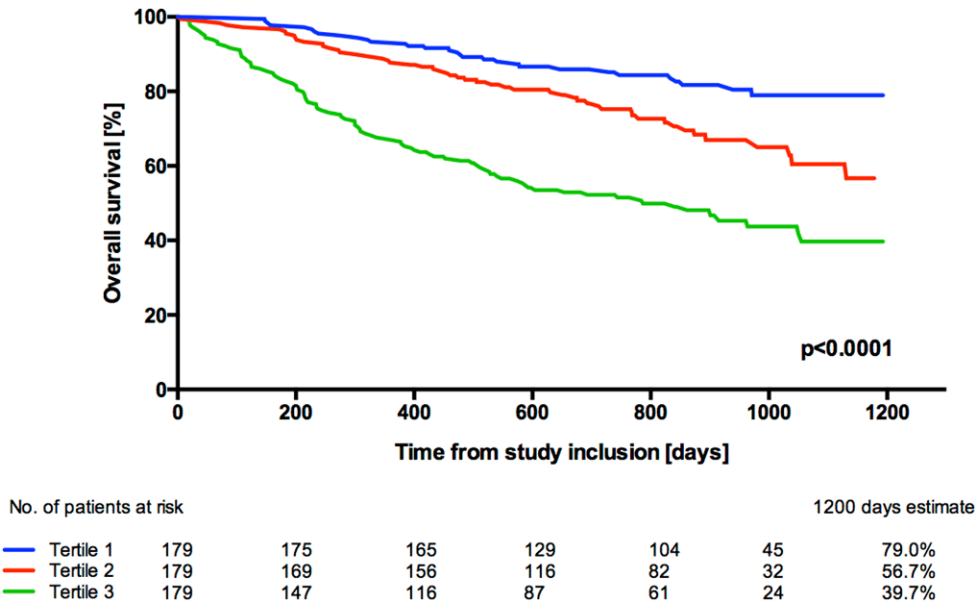

Fig. 2 | 13-3

patients (Fig. 1). Metastatic disease was characterized by higher circulating GDF-15 [266 (IQR 175–427) vs 435 (IQR 279–614), $p<0.001$]. GDF-15 was significantly associated with all-cause mortality in the univariate analysis [crude HR for ln(GDF-15) 2.08, 95%CI:1.77–2.43, $p<0.001$] and this effect was persistent after multivariate adjustment. Kaplan-Meier analysis revealed the high discriminatory power of GDF-15 ($p<0.001$ between all groups according to tertiles) (Fig. 2). There was a significant interaction of solid and liquid malignancies with loss of association of GDF-15 with outcome in myelodysplastic and myeloproliferative disease. GDF-15 correlated positively with the inflammatory status reflected by CRP, SAA and IL-6 (r = 0.31, $p<0.001$, r = 0.23, $p<0.001$ and r = r = 0.14, $p=0.002$) and cardiac biomarkers as NT-proBNP, hsTnT or MR-proADM and CT-proET1 (r = 0.46; r = 0.46; r = 0.59; r = 0.50, $p<0.001$ for all).

Conclusions: Increased plasma GDF-15 levels are associated with disease severity and all-cause mortality in solid tumors of treatment-naïve cancer patients. This association accompanies progressing systemic inflammation with subclinical involvement of other organ systems including the heart. GDF-15 represents a further molecule in the field of cardiooncology linking pathophysiologic conditions of both cardiac and neoplastic disease.

13-4

Normobaric hypoxia-induced responses in heart rate and blood pressure correlate with symptoms of acute mountain sickness

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Background: Acute Mountain sickness (AMS) is the most common disease in high altitude and since the number of tourists who venture out into respective heights is on the rise, its incidence is increasing world-wide. Obviously, it would be of interest to identify those at risk, however, no reliable predictors have been identified so far. Interestingly, easy to measure blood pressure and heart rate have received little attention in this setting, even though remarkable effects have been reported. It was therefore the purpose of this study to focus on the acute effects of hypoxia on these parameters.

Methods: In this double-blind, placebo controlled trial, 80 healthy and physically fit participants (age 24 (22–28)) spent 12 hours in a normobaric hypoxia chamber. This simulated an altitude of 4500 m with an FiO2 of 12.6%. This analysis concentrated on blood pressure and heart rate measurements which were obtained after 30 min, 3, 6, 9 and 12 hours as well as the AMS score.

Results: Systolic, diastolic and mean arterial pressure (MAP) all took a similar course: during the first 30 min a highly significant fall was observed (all $p < .001$) with the lowest values after 3 hours, followed by a highly significant increase back to baseline values (all $p < .001$). The fall of the systolic pressure was more pronounced in the AMS positive group resulting in significantly different values after the first 30 min ($p = .011$) which was not the case for the other parameters. Heart rate increased significantly after 30 min ($p < .001$). Neither blood pressure nor heart rate correlated with the occurrence of AMS. The incidence of symptoms of AMS amounted to 73%, affected mainly women and those with a more pronounced variation in blood pressure and heart rate recordings.

Conclusions: Not the absolute values but the courses of the blood pressure and heart rate response were correlated with the occurrence of AMS, with the course of systolic blood pressure measurements being the most reliable predictor. Our results suggest that monitoring blood pressure and heart rate more closely during ascent as well as at altitude might help identify susceptible subjects and thus prevent AMS.

13-5

Complications in endomyocardial biopsy—A single center experience

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Background: According to current literature endomyocardial biopsy (EMB) is a relatively safe procedure when performed by experienced physicians. Previous studies investigating EMB-related complications have included relatively young and healthy patient populations. However, EMB is often necessary in clinically compromised patients in order to establish a correct diagnosis (e. g. cardiac amyloidosis versus heart failure with preserved ejection fraction). Whether EMB is safe in an elderly, clinically compromised patient population is not known.

Methods: The present study aimed to assess the frequency and severity of EMB-associated complications in an elderly, clinically compromised patient population. Consecutive patients who underwent EMB at the Division of Cardiology at the Medical University of Vienna were analyzed for the present study. Clinical as well as invasive hemodynamic parameters were assessed at the time of EMB.

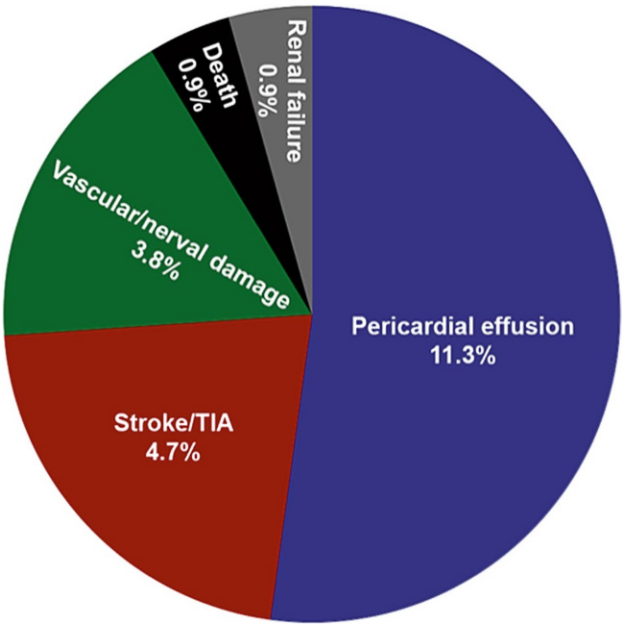

Fig. 1 | 13-5

		VKA Medication courses	NOAC Medication courses
SSRI	Medication courses (n/person years)	31162/27225	15101/10179
	Bleeding events (n)	684	285
	Bleeding events per person-year (%)	0.025	0.028
AD	Medication courses (n/person years)	29995/20233	15274/8251
	Bleeding events (n)	621	250
	Bleeding events per person-year (%)	0.031	0.030

Fig. 1 | 13-6

Results: Between May 2010 and September 2017, 106 patients were analyzed for our study. The study population consisted of 44 (41.5%) female and 62 (58.5%) male patients. Median age was 67.0 years [Interquartile range (IQR): 55.0–74.0] and median N-terminal prohormone of brain natriuretic peptide (NT-proBNP) was 1725 pg/mL (IQR: 572–4239). Mean pulmonary arterial pressure was 30.5 mmHg (IQR: 24.0–38.0). The vast majority of EMBs were performed with left heart catheterization via femoral access [$n=96$ (90.6%)]. Further EMBs were acquired during surgery [$n=8$ (7.5%)] or right heart catheterization using a jugular access [$n=2$ (1.9%)].

In total, 23 (21.7%) EMB-associated complications occurred. The most common complication was pericardial effusion [$n=12$ (11.3%)] followed by stroke/transient ischemic attack [$n=5$ (4.7%)], vascular or nerval damage at site of puncture [$n=4$ (3.8%)], death [$n=1$ (0.9%)], and contrast agent induced renal failure [$n=1$ (0.9%)] (Fig. 1).

Patients who experienced complications had higher NT-proBNP levels as compared to patients without [2838 pg/mL (IQR: 783–9065) versus 1473 pg/mL (IQR: 433–4049)]. However, this was only borderline significant ($p=0.065$). No further differences regarding clinical or invasive hemodynamic parameters were detected between patients with and without complications.

Conclusions: A significant number of patients experienced EMB-related complications in our patient cohort. Patients with complications showed a trend towards higher NT-proBNP levels. Therefore, we should be aware of a possibly greater rate of complications and question the necessity for EMB in clinically compromised patients.

13-6

SSRI co-medication with NOAC or vitamin K antagonist does not increase hospitalization for bleeding events

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Background: Selective serotonin receptor inhibitors (SSRI) are prescribed for depression and associated with increased bleeding risk. We have studied if hospitalisation for bleeding events is increased in patients with SSRI and co-medication of vitamin K antagonists (VKA) or new oral anticoagulants (NOAC).

Methods: Prescription and demographic data and information on hospital discharge diagnoses from 13 Austrian health insurance funds between 2014 and 2016 were analysed. 81.523 patients (62% female, 38% male) were identified who had treatment with VKA or NOAC with co-medication of SSRI or other antidepressant medicine (AD). Bleeding events during treatment or within 30 days were summarized as a composite of the hospital discharge diagnosis intracerebral haemorrhage, gastrointestinal bleedings, or bleeding anaemia.

Results: In total, 91,523 patient treatment courses with a maximum of one switch between oral anticoagulant or antidepressant therapy were analysed. 1840 hospitalisations for bleeding events were recorded. Patients with SSRI had significantly lower bleeding events compared to patients with other antidepressant drugs ($p=0.0021$) when adjusted for effects of anticoagulant medication with estimated bleeding events per person year of 0.025 for SSRI and 0.031 for AD.

Conclusions: Co-medication of SSRI with VKA or NOAC has little if any impact on hospital discharge diagnosis for bleeding events compared to co-treatment with other antidepressant medicine. This argues against a clinically relevant increase in risk for major bleeds associated with SSRI and oral anticoagulation.

POSTERSITZUNG 14 – Herzinsuffizienz 2

14-1

Disease management programs in Austrian heart failure patients

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Background: Nowadays there are multiple ways to improve the prognosis of heart failure including pharmaco- and device therapy. Nevertheless, decompensated heart failure is still frequent and hospitalization rates in patients with heart failure are

high. To better control patients' well-being as well as their daily drug intake, Disease Management Programs (DMPs) have been developed and are recommended as class IA in the European Society of Cardiology heart failure guidelines. In Austria, discrepancies in the acceptance of DMPs have been observed which are, so far, not clarified. We hypothesized that patients in rural and urban regions may have different attitudes toward DMPs.

Methods: In a prospective study, patients hospitalized because of heart failure were asked by using a preset questionnaire comprising 40 questions about their opinion on DMPs and their knowledge and attitude about heart failure management. Two different groups were defined: one consisted of patients hospitalized in a rural area, the other comprised patients hospitalized in a big city. The survey results between the rural and urban patients were compared.

Results: Sixty patients (females $n=26$, mean age 76 years, range 40–94) were included, 30 each in a hospital in a rural area and in a big city. Significant differences between rural and urban patients were found regarding the acceptance of nurse-based DMPs (p-value = 0.029) which was higher among rural patients. The level of willingness to be included into a telenursing-based program was the same for both groups ($p=0.441$). Patients from rural areas tended to accept nurses more likely in their private surroundings than patients living in an urban environment ($p=0.114$). While the patients' knowledge of heart failure was similar in both population groups and overall adequate, their views on the current medical care varied: Only 22% of the rural patients would consult a specialist for the follow-up, whereas 37% of the urban patients would consult a specialist ($p=0.005$).

Conclusions: Nurse-based DMPs seem to be more accepted by patients from a rural area than by patients living in a big city. DMPs for urban patients have to be developed according to their special needs.

14-2

Edge-to-edge mitral valve repair as a bridge to heart transplantation

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Background: Heart transplantation (HTx) is well established in end-stage heart failure (HF). Successful transplantation is substantially related to disease stability while on the waiting list and pulmonary artery pressure before transplantation. Percutaneous edge-to-edge mitral valve repair using the MitraClip system has been shown to improve mitral regurgitation (MR) and secondary pulmonary hypertension. We here present our initial experience with MitraClip implantation as bridge-to-transplant in a series of patients with end-stage HF and severe functional MR.

Methods: We retrospectively analysed six patients with end-stage HF (mean age 45 ± 18, five males) who underwent MitraClip implantation for severe functional MR at our center between May 2015 and November 2017 immediately before or while on the waiting list for HTx. Laboratory, echocardiographic, and hemodynamic findings were evaluated pre-MitraClip implantation and at follow-up.

Results: MitraClip implantation was uncomplicated in all patients. Substantial improvement in MR was achieved in five patients. At 107 ± 38 days following clip implantation all but one patient improved in NYHA functional class (NYHA 2.5 to 1.9, $p=0.033$). NT-proBNP decreased from 4815 ± 1883 to 3141 ± 1020 ng/l ($p=0.04$) and systolic pulmonary artery pressure decreased from 54 ± 7 to 44 ± 9 mmHg ($p=0.034$). So far, three patients were successfully transplanted, one patient died from sepsis before HTx, and two patients are still on the waiting list 485 and 66 days, respectively, after MitraClip implantation.

Conclusions: MitraClip implantation is feasible, safe and is associated with functional and hemodynamic improvement in high-risk end-stage HF patients with functional MR while on the waiting list for HTx. This strategy appears effective as bridge-to-transplant in selected patients.

14-3

Angiotensin converting enzyme 2 activity predicts outcome in heart failure with preserved ejection fraction

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Attoquant Diagnostics, Vienna, Austria

Background: The importance of the renin-angiotensin system (RAS) for the development and progression of heart failure (HF) has been studied extensively. In patients with HF with reduced ejection fraction (HFrEF), inhibition of angiotensin-converting enzyme (ACE) is an effective treatment strategy, not only by preventing the formation of detrimental Angiotensin II (Ang II) but also by increasing its metabolites Ang 1–7 and Ang 1–5, which are produced via ACE2 action and mediate cardioprotective effects. Little is known about the importance of the RAS and its metabolites in the pathophysiology of HFpEF and no data exist on the importance of Angiotensin concentrations on outcome in these patients.

Purpose: A detailed understanding of RAS profiles and their response to cardio-protective therapies could be helpful in understanding the pathogenesis and prognosis of HFpEF. Our aim was to investigate the impact of novel angiotensin based parameters on outcome in HFpEF

Methods: Consecutive patients were included into a prospective registry at our dedicated HFpEF outpatient clinic. Clinical, laboratory and imaging parameters were assessed and serum samples were taken at baseline and analyzed by RAS fingerprint (Attoquant, Vienna Austria) using mass spectroscopy to quantify equilibrium angiotensin levels. The sum of Ang 1–7 and Ang 1–5 was calculated as a surrogate for ACE2 activity and separated by median values into high-and-low ACE2 activity groups.

Results: RAS-Fingerprint analysis was performed in 155 HFpEF patients. Fifty patients (32.3%) were on ACE inhibitors (ACEi), 69 patients (44.5%) were treated with Angiotensin receptor blockers (ARB) and 34 patients (21.9%) received neither ACEi nor ARB treatment. Notably, baseline parameters associated with advanced disease progression were associated with higher Ang 1–7 levels. During a mean follow- up time of 40.0 ± 27.7 months, 22 patients (14.2%) died. Of these, 11 (50.0%) patients died of cardiac causes. Univariable Cox regres-

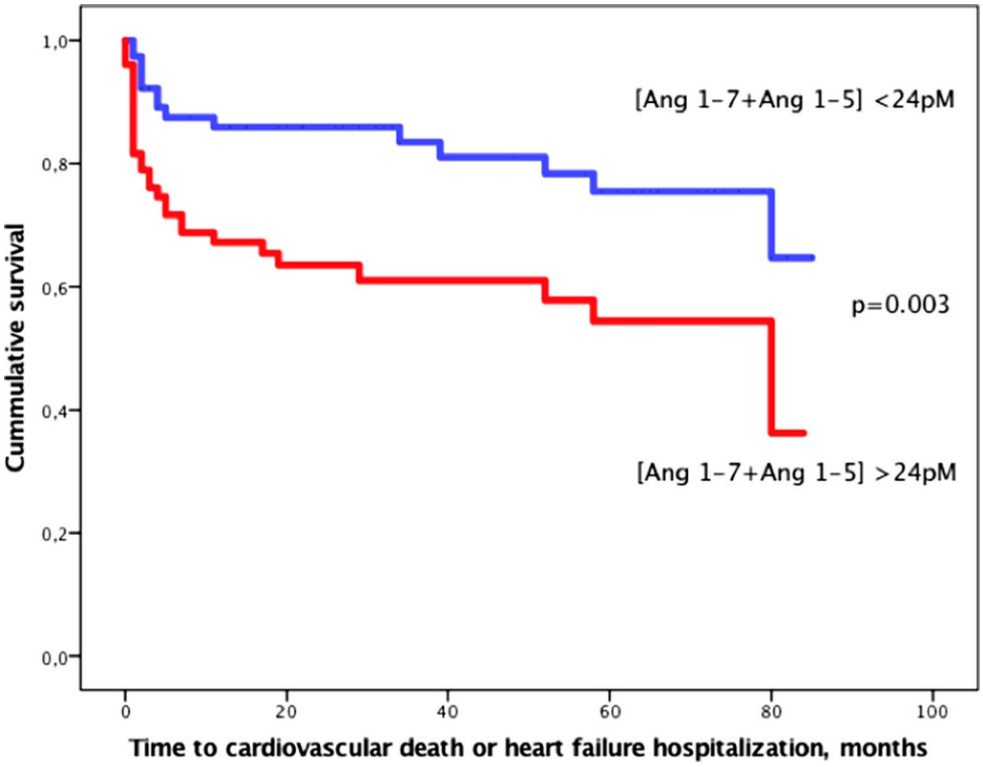

Fig. 1 | 14-3

sion analysis identified the ACE2 surrogate marker [Ang 1–7 + Ang 1–5] as a predictor for all-cause death with a hazard ratio of 1.006 (95% CI 1.003–1.009, $p<0.001$), and remained predictive even after adjusting for common risk factors including age, N-terminal pro-brain natriuretic peptide and glomerular filtration rate and systolic pulmonary artery pressure, with an adjusted hazard ratios of 1.006 (95% CI 1.003–1.009, $p<0.001$).

Conclusions: We hypothesize, that ACE2 activity is enhanced in progressive HFto counteract the detrimental effects of Ang II. Angiotensin based biomarkers not only serve as predictors of outcome in patients with HFpEF but also give valuable insight into the individual state of the RAS, which in turn could potentially identify patients who would benefit from RAS inhibiting therapies. However, additional research is needed to validate our findings and further characterize HFpEF patients according to their RAS profiles.

14-4

Renin activity is an independent predictor of outcome in patients with heart failure and preserved ejection fraction independent of RAAS blocker therapy

C. Binder, M. Poglitsch, F. Duca, C. Zotter-Tufaro, C. Nitsche, S. Aschauer, A. Kammerlander, B. Öztürk, C. Donà, L. Schachner, J. Mascherbauer, D. Bonderman

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Background: Drugs which interact with the renin-angiotensin aldosterone system (RAAS) aim to reduce the negative effects of Angiotensin (Ang) II. This can be achieved by either decreasing its production or inhibiting its binding to the Ang II receptor Type 1 (AT1R) using angiotensin-converting enzyme inhibitors (ACEi) or Ang receptor blockers (ARB), respectively. While both therapies anticipate a compensatory up-regulation of renin secretion, there is a large variability in circulating plasma renin even in patients with optimal medical therapy in patients with heart failure (HF) with reduced ejection fraction (HFrEF). However, no such data exist in HF with preserved ejection fraction (HFpEF).

Study aim: To demonstrate the effects of plasma renin activity (PRA) on outcome in patients with HFpEF.

Methods: Consecutive patients were included in a prospective registry at our HFpEF outpatient clinic. Clinical, laboratory and imaging parameters were assessed at baseline. Equilibrium Ang (eqAng) concentrations were measured from serum samples using mass spectroscopy. The sum of equal I and equal II was calculated as a surrogate for plasma renin activity (PRA-S). Patients were divided into PRA-based tertiles and compared with respect to the primary endpoint defined as all-cause death.

Results: Ang profiling was performed in 155 HFpEF patients. Fifty patients (35.4%) were on ACEi, 69 patients (44.5%) were treated with ARB and 36 patients (23.2%) received neither ACEi nor ARB treatment. PRA-S of patients with RASi therapy was not significantly higher than in patients without RASi (243 pM (IQR 99–1001) versus 412 pM (IQR 167–1467, $p=0.221$). Cox regression analysis showed that PRA-S was predictive for all-cause death with a crude hazard ratio of 2.51 (95%CI 1.25–5.03, $p=0.010$). Even after adjusting for established risk factors including age, NT-pro BNP, GFR and systolic pulmonary artery pressure, only PRA-S and NT-pro BNP remained predictive in the multivariable model with a hazard ratio of 2.54 (95%CI 1.28–5.06, $p=0.008$) and 3.37 (95%CI 1.06–10.70, $p=0.039$), respectively. Furthermore, Kaplan Meier analysis showed that patients with high PRA-S had markedly worse outcomes when compared to patients with lower PRA-S.

Conclusions: We conclude that a large subset of HFpEF shows a strongly elevated PRA-S that is predictive for poor outcome. We hypothesize that the pharmacologic efficacy of RAAS

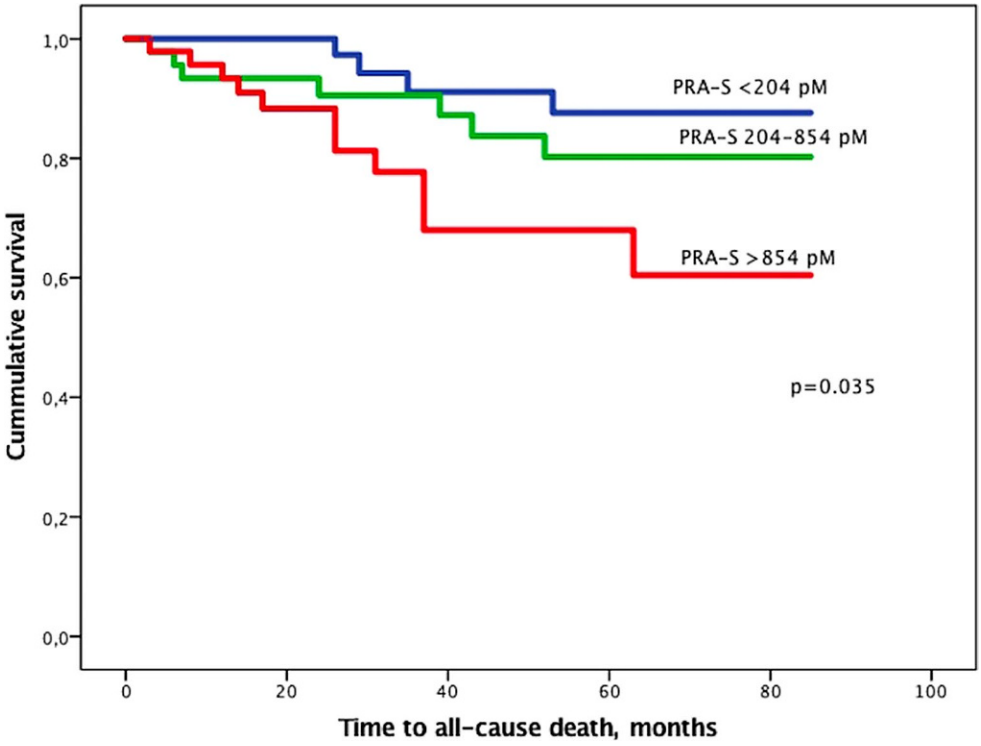

Fig. 1 | 14-4

blockers might be insufficient at high renin activity. Especially in patients with a strong compensatory up-regulation of renin in response to RAAS blockers, Ang II formation or receptor binding could be restored, rendering standard RAAS blocker therapy and dosing less effective or even harmful in this subgroup of patients, as during the drug elimination phase, Ang II signaling could overshoot baseline levels. Further studies are required to investigate the potential benefits of a more stringent RAAS blocker treatment regime for high PRA-S patients in HFpEF.

14-5

Serum potassium levels and outcome in patients with heart failure and preserved ejection fraction

B. Öztürk, F. Duca, C. Binder, C. Zotter-Tufaro, C. Nitsche, A. A. Kammerlander, S. Aschauer, L. Schachner, C. Dona, C. D. J. Capelle, J. Mascherbauer, D. Bonderman

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Background: Previous studies could demonstrate the prognostic significance of serum potassium levels in heart failure (HF) patients. However, studies investigating the association of

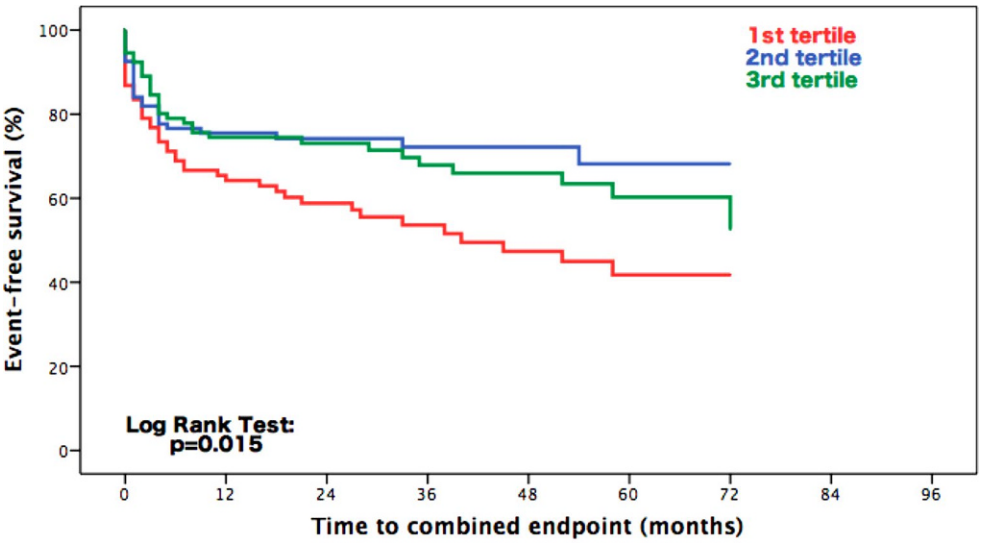

Fig. 1 | 14-5

serum potassium levels with prognosis or clinical parameters in patients with HF and preserved ejection fraction (HFpEF) have not been examined thus far. In the present study, we aimed to investigate the prognostic significance of baseline potassium levels and its correlation with clinical parameters in patients with HFpEF.

Methods: Consequtive HFpEF patients from a prospective registry were included into our study. Patients underwent clinical as well as laboratory assessment, 6-minute walk test, right heart catheterization, and cardiac magnetic resonance imaging. Patients were prospectively followed in 6-month invervals. The primary endpoint was a composite of cardiac death or HF hospitalization.

Results: Between December 2010 and May 2017, 280 HFpEF patients were included into our study. Median age of the study population was 72.0 years [Interquartile range (IQR): 67.0–77.0], 196 (70.0%) were female, median N-terminal prohormone of brain natriuretic peptide levels were 1115 pg/mL (IQR: 455–2062) and 182 (65.0%) were in New York Heart Association class ≥III. Median level potassium was 4.2 mmol/L (IQR: 3.9–4.6). 13 (4.6%) patients had hypokalemia (<3.5 mmol/L), 26 (9.3%) had hyperkalemia (≥5.0 mmol/L) and 241 (86.1%) were normokalemic (≥3.5—<5.0 mmol/L). 102 (36.4%) patients experienced the combined endpoint.

Patients were grouped according to potassium tertiles (<4.0 mmol/L, ≥4.0 mmol/L—<4.4 mmol/L and, ≥4.4 mmol/L). Significant differences between the groups were detected with regards to the combined endpoint [$n=44$ (48.4%) versus $n=26$ (27.4%) versus $n=32$ (34.0%) $p=0.005$)] and right ventricular EF (RVEF) [49.0% (IQR: 44.0–55.5) versus 53.5% (IQR: 45.0–64.0) versus 52.0% (IQR: 44.0–60.5), ($p=0.033$)]. No differences with regards to concomitant medication were found between the groups.

The lowest potassium tertile was significantly associated with adverse outcome in univariable [hazard ratio (HR): 1.843, 95% confidence interval (CI): 1.195–2.842, $p=0.006$] (Fig. 1) as well as in multivariable analyses (HR: 1.601, 95% CI: 1.044–2.456, $p=0.031$).

Conclusions: Low potassium levels (<4.0 mmol/L) are independently associated with adverse outcome in HFpEF patients.

14-6

Functional, haemodynamic and prognostic impact of mitral regurgitation in patients with heart failure and preserved ejection fraction

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Background: Functional mitral regurgitation (FMR) is a common finding in various heart failure entities. However, its prevalence, pathophysiologic and prognostic role in heart failure and preserved ejection fraction (HFpEF) is fairly unknown. In the light of currently emerging techniques of trans-catheter mitral valve repair, the present study was undertaken to clarify mechanisms underlying the evolution of FMR and its impact on functional status and prognosis in HFpEF patients.

Methods and Results: Between December 2010 and January 2017, 261 consecutively enrolled HFpEF patients were studied in a prospective manner. At baseline, patients were stratified into three groups: no or mild FMR (51%), moderate FMR (42%) and greater than moderate FMR (7%). With increasing FMR severity, patients were older ($P<0.001$), had higher rates of atrial fibrillation ($P=0.04$), had a reduced right ventricular ejection fraction ($P=0.005$) and showed higher NT- pro BNP serum levels ($P=0.002$). Multivariable binary logistic regression analysis revealed mitral annulus dilatation ($P=0.048$), the degree of mitral valve degeneration ($P=0.046$) and elevated left ventricular filling pressures ($P=0.025$) as independent determinants of FMR. During a follow-up period of 33 ± 22 months, 39 (15.2%) patients had died and FMR was independently associated with mortality ($P=0.024$).

Conclusions: Relevant FMR is a common finding in HFpEF patients with a clear negative impact on their clinical status and outcome. Further studies are warranted to confirm our findings and may pave the way for interventional therapies targeting the mitral valve.

14-7

Cell therapy for patients with heart failure and reduced ejection fraction—an individual patient data meta-analysis

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Background: On the basic research level, cell therapy is a promising approach for the treatment of chronic heart failure (HF). Due to relatively high costs and complicated procedures, clinical trials in the field of cardiac regeneration of chronic HF patients are commonly small-sized and discrepancies exist between the different study's results.

Aim: We aimed to pool and meta-analyze individual patient data (IPD) of clinical randomized controlled trials (RCT) investigating any cell therapy in patients with HF and reduced ejection fraction.

Methods: RCTs are prospectively identified by a systematic search strategy and the respective primary investigators were invited to participate in the international and collaborative "meta-Analysis of Cell-based CaRdiac study" (ACCRUE, NCT01098591) database. The present study represents an analysis from the ACCRUE database and was restricted to RCTs investigating cell therapy by percutaneous intra-myocardial injections of cells in patients with HF. Primary efficacy end-point was end-systolic volume (ESV) at study follow-up. Secondary efficacy endpoints were end-diastolic volume (EDV) and left ventricular ejection fraction (LVEF) at follow-up. Primary safety end-point was all-cause death 180 days following cell therapy. Secondary safety end-point was a combined end-point of major adverse cardiovascular events (including death, acute myocardial infarction, stroke and target vessel revascularization).

Results: We report pooled IPD of eight RCTs including 447 patients (272 cell therapy, 175 control). The mean age of patients was 61.2 ± 10.1 and 60.6 ± 9.7 years for the cell therapy and control group, respectively. There were no baseline differences with respect to classic cardiovascular risk factors and co-morbidities. Parameters of left ventricular function at baseline were balanced with one exception; ESV 158.7 ± 75.1 vs. 166.5 ± 73.6 ($P=0.30$); EDV 230.3 ± 83.9 vs. 235.1 ± 81.6 ($P=0.57$) and LVEF 33.4 ± 9.7 vs. 31.4 ± 9.5 ($P=0.04$) comparing cell therapy and

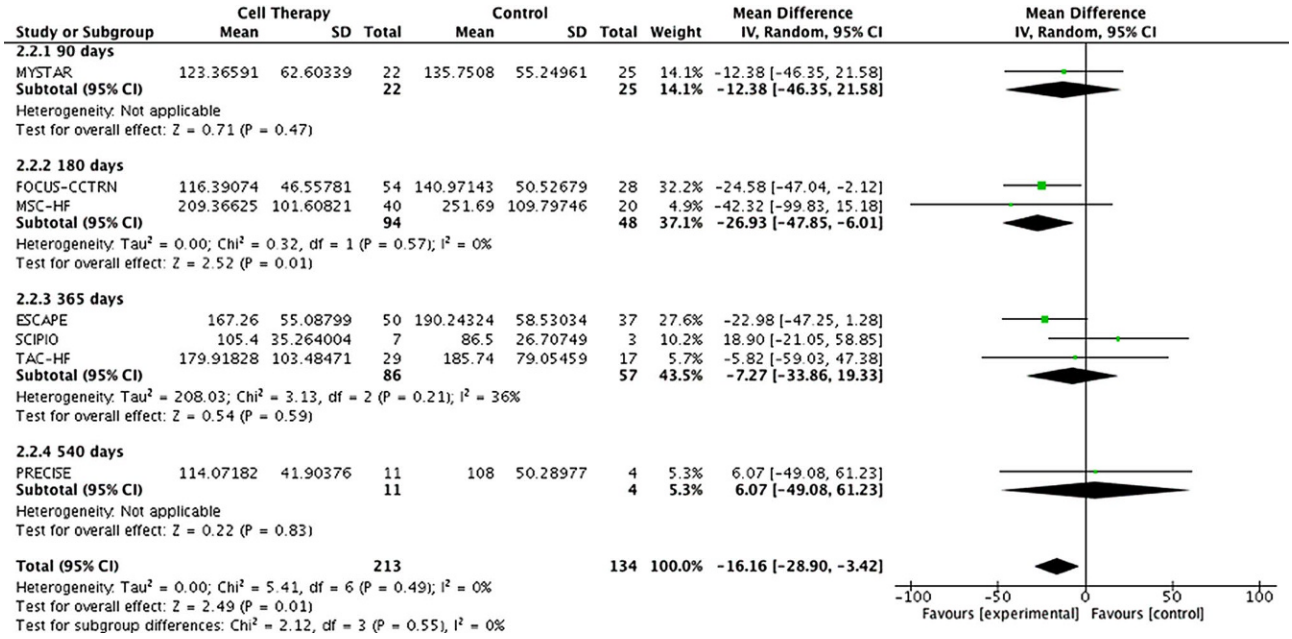

Fig. 1 | 14-7

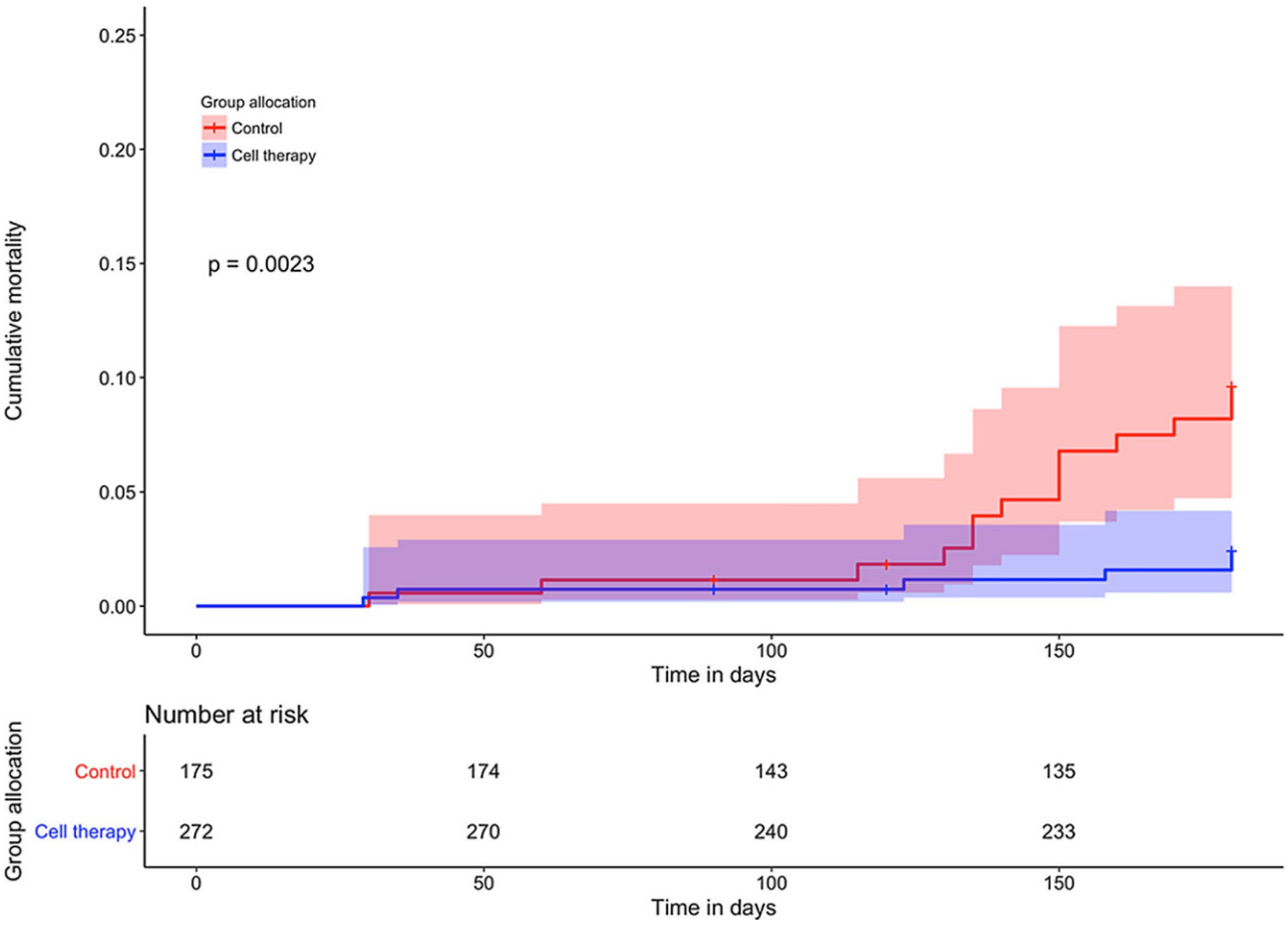

Fig. 2 | 14-7

control, respectively. With respect to the primary efficacy endpoint, cell therapy was associated with a significant smaller ESV (Fig. 1). Similarly, LVEF was significantly higher (mean difference 5.21, 95% CI 2.98 to 7.43, P < 0.001), whereas there was no significant difference with respect to the EDV (mean difference –10.56, 95% CI –25.31 to 4.19, P = 0.16). Within the first 180 days of follow-up, 20 patients deceased in total. The chance of survival was in favor for the cell therapy treated cohort (log-rank

0.0023, Fig. 2), as was the occurrence of MACCE (log-rank 0.004). Cox-regression analysis was performed including the group allocation and baseline LVEF. Both had independent influence on death (Cell treatment: exp(B) 0.255, 95% CI 0.091 to 0.712, P = 0.009; baseline LVEF: exp(B) 0.918, 95% CI 0.868 to 0.971, P = 0.003). Sensitivity analysis revealed that those results in favor for cell-therapy were triggered by one particular study. Upon its exclusion, there was no significant difference between groups, regarding mortality or MACCE.

Conclusions: Cell therapy by a percutaneous intra-myocardial administration of cells is associated with better cardiac function at follow-up. Both, baseline LVEF and cell therapy were associated with a reduction of death and MACCE during 180 days of follow up. Due to different follow-ups and significant heterogeneity between the studies, these finding should be interpreted with a certain degree of caution.

14-8

Die RAS-Blockade mit Sacubitril/Valsartan bei HFrEF und renaler Insuffizienz ist sicher und effektiv: ein Single-Center Experience

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Grundlagen: Die chronische Herzinsuffizienz (CHI) ist eine sehr häufige Ursache für Morbidität und Mortalität in den industrialisierten Ländern. Viele Patienten mit CHI haben auch ein hohes Risiko für eine chronische Niereninsuffizienz und vice versa. Der optimierte Einsatz von Blockern des Renin-Angiotensin Systems (RAS) wie ACE-Hemmer (ACEH) oder Angiotensin Rezeptor Blocker (ARB) sind laut Guidelines zwingend indiziert, können aber bekanntermaßen zu einer Verschlechterung der Nierenfunktionsparameter führen, woraufhin manchmal eine Reduktion der RAS-Hemmer notwendig ist.

Es gibt für die neue Substanz Sacubitril/Valsartan nur sehr begrenzte Daten im Setting von chronischer Niereninsuffizienz und chronischer Herzinsuffizienz.

Methodik: Wir untersuchten retrospektiv den Einfluss von Sacubitril/Valsartan auf die Nierenfunktionsparameter in einem Patientenkollektiv mit chronischer symptomatischer Herzinsuffizienz (NYHA II-IV) und reduzierter Auswurfleistung (HFrEF). Alle Patienten ($n = 36$) hatten eine neurohumorale Therapie mit einem ACEH oder ARB, in wenn möglich optimierter Dosis. Wir verglichen die Entwicklung der Nierenfunktionsparameter bei Umstellung und nach 3 Monaten. Es wurde für die Subgruppe der Patienten im KDIGO-Stadium 2–4 ($n = 29$) eine gesonderte Analyse durchgeführt. Als Surrogat-Parameter für das klinische Ansprechen auf Sacubitril/Valsartan wurden die NYHA-Klassen sowie der NT-proBNP-Wert im Verlauf herangezogen.

Ergebnisse: Insgesamt konnte in unserem Kollektiv eine signifikante klinische Verbesserung nach 3-monatiger Therapiedauer nachgewiesen werden. Sowohl im Gesamtkollektiv als auch in der Gruppe mit eingeschränkter Nierenfunktion konnte gezeigt werden, dass die Nierenfunktion, gemessen an den Parametern Serum-Kreatinin und eGFR (CKD-EPI-Formel), unter Sacubtril/Valsartan im Beobachtungszeitraum von 3 Monaten stabil waren. Im Mittel lag bei Patienten im KDIGO-Stadium 2–4 der Serum-Kreatinin-Wert zu Beginn bei 1,35 mg/dl, nach 3 Monaten bei 1,40 mg/dl. Auch bei der eGFR zeigte sich keine signifikante Änderung nach 3 Monaten (56,7 vs.55,8 ml/min/1,73 m^2). Unter Vorbehalt der sehr kleinen Fallzahl ($n = 8$) zeigte sich auch im KDIGO-Stadium 3b-4 keine Verschlechterung der Serum-Kreatinin-Werte (1,85 mg/dl vs. 1,96 mg/dl) bzw. der eGFR (34,8 vs 34,8 ml/min/1,73 m^2).

Schlussfolgerungen: Auch bei Herzinsuffizienz-Patienten mit eingeschränkter Nierenfunktion kann eine klinische Verbesserung mittels Sacubitril/Valsartan erzielt werden, während in dem vorliegenden Kollektiv mit kleiner Fallzahl die Anwendung bei Patienten auch mit höhergradig eingeschränkter Nierenfunktion sicher scheint.

14-9

Left atrial function and atrial fibrillation in heart failure with preserved ejection fraction

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Background: Left atrial (LA) size and function have been shown to be associated with adverse events in heart failure with preserved ejection fraction (HFpEF).

Objectives: To study LA size and function and its impact on outcome in HFpEF patients in sinus rhythm versus atrial fibrillation (AF).

Methods and Results: 189 HFpEF patients were prospectively enrolled and underwent baseline clinical and echocardiographic assessment, cardiac magnetic resonance imaging (CMR) and invasive hemodynamic assessment. Coronary artery

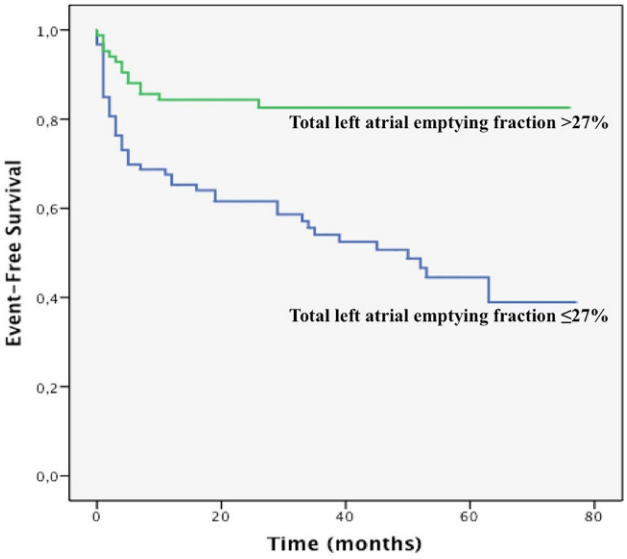

Fig.1 | 14-9

disease was ruled out by coronary angiography. 90 patients were in persistent AF, 24 in paroxysmal AF and 71 in sinus rhythm. LA size and function were assessed by CMR including LA strain imaging by myocardial feature tracking.

Patients in AF had significantly larger endsystolic LA volume indices (LAVI) (81 ± 27 vs. 55 ± 18 ml/m^2, $p < 0.001$), larger enddiastolic LAVI (68 ± 25 vs. 35 ± 17 ml/m^2, $p < 0.001$), lower total LA emptying volume (24 ± 11 vs. 41 ± 14 ml, $p < 0.001$) and fraction (16 ± 7 vs. 39 ± 11%, $p < 0.001$) as well as lower fraction of longitudinal shortening (5 ± 4 vs. 14 ± 7%, $p < 0.001$). Total LA strain was significantly lower (7 ± 4 vs. 20 ± 10%, $p < 0.001$), as well as total LA strain rate (58 ± 36 vs. 119 ± 67%/sec, $p < 0.001$) and LA passive emptying strain rate (63 ± 34 vs. 107 ± 64%/sec, $p < 0.001$).

Among patients in sinus rhythm passive LA emptying volume and fraction were 21 ± 10 ml and 20 ± 7%. Active LA emptying volume and fraction were 21 ± 13 ml and 20 ± 11%, respectively.

After 31 ± 24 months, 64 patients reached the combined endpoint defined as hospitalization for heart failure or cardiac death. By multivariate cox regression analysis including all LA parameters, only reduced total LA emptying fraction was significantly associated with adverse outcome ($p < 0.001$, HR 0.962, 95% CI 0.944–0.981). After adjustment for sex, age, presence of persistent AF, NTproBNP, right ventricular ejection fraction by CMR and pulmonary capillary wedge only elevated NTproBNP ($p = 0.022$, HR 1.078, 95% CI 1.011–1.150) and reduced total LA emptying fraction ($p = 0.004$, HR 0.969, 95% CI 0.949–0.990) were predictive for adverse events.

Conclusions: Impaired LA function plays a key role in HFpEF. Reduced total LA emptying fraction outperforms LA size and presence of persistent AF in prediction of adverse events in HFpEF.

POSTERSITZUNG 15 – Koronare Herzkrankheit (chronisch)

15-1

Functional capacity and quality of life in patients with stable angina in Austria

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Background: Many patients (pts) with stable angina pectoris (SA) are still limited by their disease in daily life activities even after successful revascularization. The cross-sectional survey LENA (Lebensqualität von Angina pectoris Patienten in Österreich) aimed to assess the functional capacity and quality of life of pts with SA in Austria under real-life conditions.

Methods: Patients across Austria managed by general practitioners (GP's), internists or in cardiologic outpatient clinics were included. Inclusion criteria were: documented myocardial infarction >3 months ago, coronary stenosis >50% based on coronary angiogram, symptoms of myocardial ischemia based on stress-test, bypass-surgery or other invasive coronary procedures >3 months. Pts with hospitalisation for CV disease <3 months as well as pts with planned revascularisation were excluded. Demographic data and SA functionality were assessed by a questionnaire assessing the patient-rated Seattle Angina Questionnaire© (SAQ) with 5 domains (physical limitation, angina stability, angina frequency, treatment satisfaction, quality of life), each subscale rated between 0 and 100 with higher values indicating better outcome. The study was approved by the ethic committee of the Medical University of Graz EK 29-563 ex 16/17.

Domain	SAQ subscales (0-100)
Physical limitation	67
Angina stability	65
Angina frequency	79
Treatment satisfaction	86
Quality of life	64

Fig. 1 | 15-1 Results of the SAQ

Results: Between September and December 2017 659 pts. across Austria were included. 70% were male, the mean age was 69 (+/– 10) years (55% of patients >70 years, 16% were >80 years), 64% had a history of PCI, 22% had bypass-surgery, 46% had a history of myocardial infarction. 187 pts were managed by GP's, 429 pts by internists and 43 in cardiology outpatient clinics. The results of the SAQ are shown in Fig. 1. In addition, 36% of pts reported to experience specific limitations in their desired daily life activities such as gardening, hiking, sexual activities and others.

Conclusions: In LENA—for the first time in Austria—functional capacity and quality of life of 659 pts with SA managed in different medical settings were assessed using a standardized and specific questionnaire. Although treatment satisfaction was excellent, a substantial number of pts still experience frequent angina episodes and significant limitations in daily life activities. The observed numbers are in accordance with other studies and underline the importance of an ongoing and comprehensive care in this important group of pts.

15-2

Cardiovascular and non-cardiovascular mortality in type 2 diabetes patients with established coronary artery disease: a prospective cohort study

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Background: Type 2 diabetes (T2 DM) in the general population is a strong risk factor for cardiovascular as well as for total mortality. Here, we aimed at investigating the association of T2 DM with cardiovascular as well as with non-cardiovascular mortality in patients with established coronary artery disease (CAD).

Methods: We prospectively recorded dates and causes of deaths over a mean follow-up period of 7.5 ± 2.9 years in a cohort of 1472 patients with angiographically proven CAD. Data were retrieved from a national registry and verified using patient records.

Results: Overall, 355 patients died during follow-up, i. e. 24.1% of the total study cohort. From all deaths, 170 (47.9%) were caused by cardiovascular disease, and 184 (52.1%) were non-cardiovascular deaths. T2 DM at baseline was present in 454 patients (30.8% of the total study population). During follow-up, both cardiovascular (18.5 vs. 8.4%; $p < 0.001$) and non-cardiovascular mortality (15.0 vs. 11.5%; $p = 0.023$) were significantly higher in patients with T2 DM than in nondiabetic individuals.

Conclusions: We conclude that in patients with angiographically proven CAD, T2 DM significantly increases both cardiovascular and non-cardiovascular mortality.

15-3

Pro-B-type natriuretic peptide strongly predicts future cardiovascular events in cardiovascular disease patients with type 2 diabetes as well as in those without type 2 diabetes

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Background: Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker in various patient populations. Its power to predict cardiovascular events in the extremely high risk group of patients with the combination of established cardiovascular disease (CVD) and type 2 diabetes (T2 DM) is unclear and is addressed in the present study.

Methods: We measured serum proBNP in 900 patients with established CVD including 591 patients with angiographically verified coronary artery disease and 309 patients with sonographically proven peripheral artery disease. Prospectively, we recorded vascular events over 6.3 ± 2.0 years.

Results: At baseline, proBNP was significantly higher in patients with ($n = 317$) than in those without T2 DM (990 ± 2556 vs. 742 ± 2328 pg/ml; $p = 0.003$). The cardiovascular event rate was significantly higher among CVD patients with than among those without T2 DM (50.5 vs. 35.1%; $p < 0.001$). ProBNP significantly predicted the incidence of cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol and the eGFR both in patients with T2 DM (standardized adjusted HR 1.48 [1.28–1.73]; $p < 0.001$) and in subjects without T2 DM (HR 1.33 [1.20–1.47]; $p < 0.001$).

Conclusions: We conclude that serum proBNP in patients with established CVD predicts future cardiovascular events independently of established cardiovascular risk factors both among those with as well as among those without T2 DM.

15-4

Sex differences in coronary artery disease patients with and in those without type 2 diabetes

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Background: Life-term cardiovascular risk is high also in women, and women with coronary artery disease (CAD) or with type 2 diabetes (T2 DM) are at a particularly high risk. In this prospective cohort study, we addressed sex differences in CAD patients with as well in those without T2 DM.

Methods: We recorded cardiovascular events in an unselected consecutive series of 1472 patients with angiographically proven CAD over 7.5 ± 2.9 years.

Results: T2 DM prevelance was similar in men ($n = 1060$) and women (27.3 vs. 30.1%; $p = 0.277$). Among non-diabetic CAD patients women were older than men (68 ± 9 vs. 63 ± 11 years; $p < 0.001$), had higher LDL cholesterol (138 ± 42 vs. 130 ± 38 mg/dl; $p = 0.022$) and HDL cholesterol (63 ± 16 vs. 51 ± 14 mg/dl; $p < 0.001$) and a lower prevelance of smoking (35.5 vs. 69.6%; $p < 0.001$) and of prior myocardial infarction (20.6 vs. 31.2%; $p = 0.001$). Among those with T2 DM, women also were older (69 ± 9 vs. 64 ± 10 years; $p < 0.001$), had higher HDL cholesterol (53 ± 14 vs. 46 ± 13 mg/dl; $p < 0.001$) and a lower prevalence of smoking (28.6 vs. 80.1%; $p < 0.001$); further among those with T2 DM the prevelance of hypertension (79.9 vs. 70.7%; $p = 0.049$) and of statin use (66.9 vs. 48.3%; $p < 0.001$) was higher in women. Prospectively, sex did not predict cardiovascular events in CAD patients without nor in those with T2 DM, with adjusted hazard ratios of 0.96 [0.73–1.26]; $p = 0.757$ and 0.82 [0.55–1.22]; $p = 0.329$, respectively.

Conclusions: We conclude that baseline risk factors both among CAD patients without and among those with T2 DM differ between women and men, whereas irrespective of diabetes status sex does not affect the incidence of future cardiovascular events in this population.

15-5

The novel adipokine C1QTNF1 significantly predicts the incidence of future major cardiovascular events in patients with type 2 diabetes

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Background: Increased serum levels of the novel adipokine C1q and tumor necrosis factor related protein 1 (C1QTNF1)

have been linked with type 2 diabetes (T2 DM) and ischemic heart disease. The impact of circulating C1QTNF1 on the incidence of future major cardiovascular events (MACE) is unclear and is addressed in the present study.

Methods: We measured C1QTNF1 serum levels in 542 patients undergoing coronary angiography for the evaluation of established or suspected coronary artery disease (CAD) using an enzyme-linked immunosorbent assay. Prospectively, MACE were recorded over a mean follow-up period of 6.3 years.

Results: C1QTNF1 serum levels at baseline were significantly increased in patients with T2 DM ($n=160$) compared to those without diabetes (521.4 ± 224.8 vs. 429.5 ± 130.3 ng/ml; $p<0.001$). Prospectively, the incidence of MACE increased significantly through tertiles of C1QTNF1 (17.8%, 24.7%, and 29.7% in the 1st, 2nd and 3rd tertiles, respectively; ptrend = 0.010). Also after adjustment for age, sex, and T2 DM as well as after additional adjustment for body mass index, hypertension, LDL cholesterol, HDL cholesterol, triglycerides, and angiographically determined baseline CAD, C1QTNF1 significantly predicted MACE, with adjusted HRs of 1.30 [1.04–1.61]; $p=0.019$ and 1.36 [1.09–1.70]; $p=0.007$, respectively. Patients with T2 DM were at a significantly higher risk of MACE than those who did not have diabetes (48% vs. 26%; $p=0.003$). C1QTNF1 in subgroup analyses also in T2 DM patients proved to be a strong predictor of MACE (adjusted HR 1.57 [1.10–2.24]; $p=0.013$).

Conclusions: We conclude that high serum levels of C1QTNF1 significantly predict MACE, in particular in patients with T2 DM.

15-6

Influence of outpatient cardiac rehabilitation on quality of life and wellbeing

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Background: Cardiac rehabilitation (CR) is a key component of the treatment of cardiac diseases and a class IA indication in guidelines of professional medical associations. Cardiopsychological interventions are part of the treatment next to other risk factor modifications. In this analysis, we present data of all consecutive patients who have completed outpatient CR Phase II (OUT-II) and/or Phase III (OUT-III) as well as outpatient Phase III after inpatient phase II (IN-II/OUT-III) until the end of 2015, focusing on quality of life and wellbeing.

Methods: The "Hospital Anxiety and Depression Scale" (HADS), Heart-Specific-Health-Related Quality of Life (HRQL) and the Visual Analog Scale (EQ-VAS, as part of the EuroQol (EQ-5-D)) were assessed for all eligible patients at the beginning of OUT-II, end of OUT-II/beginning of OUT-III and end of OUT-III.

Results: For OUT-II complete questionnaires from 3506 patients were available for analyses. The median EQ-VAS score improved from 70 (0–100) to 80 (0–100) ($r=-0.2$; $p<0.001$), indicating an improved overall health status. Also, global HRQL score improved from (5.5 (1–7) to 6.2 (1.2–7) ($r=-0.5$; $p<0.001$)), as well as anxiety (4.0 (0–21) to 3.0 (0–20) ($r=-0.2$; $p<0.001$)) and depression scores (3.0 to 2.0 (0–21) ($r=-0.2$; $p<0.001$).

For OUT-II/OUT-III complete questionnaires were available from 1338 patients for analyses. EQ-VAS ($r=-0.1$; $p<0.001$), and global HRQL score significantly improved ($r=-0.1$; $p<0.001$), indicating a small but further gain in overall health status and health related quality of live. Scores for anxiety and depression remained essentially unchanged ($r=0.0$, $p=0.517$; $r=0.0$, $p=0.346$, respectively).

Finally, for IN-II/OUT-III complete questionnaires from 1642 patients were available for analyses. Median EQ-VAS ($r=-0.3$; $p<0.001$), global HRQL ($r=-0.3$; $p<0.001$), anxiety ($r=-0.1$; $p<0.000$), and depression scores ($r=-0.1$; $p<0.001$) indicated a significantly improved overall health status, quality of life and wellbeing.

Conclusions: Outpatient cardiac rehabilitation effectively improved quality of life and wellbeing. Beneficial results were sustained for up to one year.

POSTERSITZUNG 16 – Risikofaktoren/ Stoffwechsel/Lipide 2

16-1

Influence of ticagrelor on cardiovascular risk factors in patients after PCI

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Background: Cardiovascular disease is still the leading cause of death in Austria. Additional to traditional risk factors, there is evidence for a new emerging risk factor, the elevation of serum uric acid. Ticagrelor is a drug frequently used after PCI for the prevention of a stent thrombosis or atherothrombosis. It has been associated with elevated uric acid levels in previous studies. This study is going to analyse to which extent the use of ticagrelor is able to influence metabolic cardiovascular risk factors including uric acid.

Methods: The analyzed patient population consisted of the former participants of the international multicenter Global Leaders study, who were included at the Medical University Graz (1). In this all-comers PCI-study, a new antithrombotic regimen after PCI has been investigated. In an open-label design one group was treated by ticagrelor 90 mg bid monotherapy for two years, with the addition of ASS 100 mg od only during the first month. As a comparator served standard of care therapy with

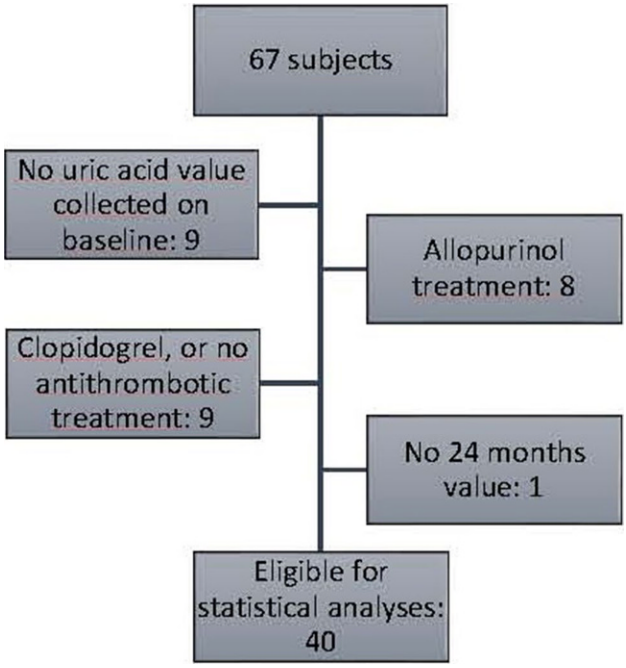

Fig. 1 | 16-1 Extended exclusion criteria

ticagrelor in patients with acute coronary syndromes or clopidogrel in stable patients for one year and acetylsalicylacid as lifelong therapy. In this paper, patient's metabolic parameters after the two year study period were investigated. Baseline laboratory values and 24-months follow-up values were collected out of the medical recording system. An ethical approval was obtained (28–228 ex 15/16).

Out of the 84 patients of the Global Leaders study, 3 died before follow-up after 2 years, 13 did not complete the study and one did not want to give informed consent. Further exclusion criteria are listed in the Fig. 1. A total of 40 patients, 20 in ticagrelor treatment and 20 in acetylsalicylacid treatment were analysed for the first analysis concerning uric acid (Mean age 64 +/– 8.95 years, 12.5% female, 87.5% male, 62.5% ACS, 37.5% stable CAD). In the second analysis concerning lipids 8 baseline lipid values were missing, 7 subjects were not in standard of care group anymore and 3 LDL-levels after 24 months were missing. Overall data of 59 samples could be analysed.

Results: No significant difference in uric acid levels between baseline and 24 months was observed in the ticagrelor group and in the standard of care group, respectively ($p=1.04$ for ticagrelor and $p=0.432$ for acetylsalicylacid). Having a closer look at the values, the means rose slightly by 0.33 mg/dl in ticagrelor and 0.04 mg/dl in the standard of care group and the medians by 0.45 mg/dl in ticagrelor group, whereas there was no difference in standard of care group. This elevation was independent of kidney function (GFR in ml/min) and not statistically significant (Fig. 2).

Remarkable issue was a significantly lower LDL cholesterol level in the ticagrelor group compared with standard of care ($p=0.020$), while both groups were under current statin treatment (Fig. 3).

Conclusions: The real impact of uric acid on cardiovascular risk has to be investigated in the future via randomized trials with uric acid lowering therapy. Ticagrelor seems to elevate uric acid slightly and not significantly. On the other hand ticagrelor improved LDL cholesterol levels, which might have a positive impact on cardiovascular risk.

16-2

Effects of monacolin K on serum parameters of nonalcoholic fatty liver disease (NAFLD)

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Background: There is compelling evidence of an increase in cardiovascular risk in patients with NAFLD due to the underlying metabolic disorders. Statin therapy has shown beneficial effects on cardiovascular risk as well as on NAFLD progression. Little is known about the effects of monacolin K (a phytotherapeutical statin equivalent) on indirect parameters of NAFLD.

Aim: We evaluated the effects of monacolin K 10 mg on serum total cholesterol (TC) and triglyzerides (TG) as well as aspartate aminotransferase (AST), alanine aminotransferase (ALT), AST/ALT ratio (<1.5), g-glutamyl transferase (GGT) and alcaline phosphatase (AP).

Methods: Fifty-two dyslipidemic subjects (25 F, age 58+ 11 yrs) were treated for 4 weeks with monacolin K. Plasma lipids and liver enzymes were measured using an enzyme-linked immunosorbent assay at baseline and after 4 weeks.

Results: Monacolin K supplementation resulted in a decrease in TC (– 39%; $p<0.01$) and in TG (–19%; $p<0.05$). Moreover, it significantly decreased GGT from baseline 38 + 35 to 30 + 20 U/l ($p<0.01$). There were no significant changes in AST (25 + 9 vs 29 + 8 U/l), ALT (27 + 18 vs 31 + 15 U/l) and AP (95 + 22 vs 90 + 23 U/l) as well as in AST/ALT ratio (1.10 + 0.3 vs 1.09 + 0.3).

Uric acid levels in ticagrelor and standard of care group at baseline and after 24 months.

	Uric acid mean Baseline	Uric acid median Baseline	Uric acid mean 24 months	Uric acid mean 24 months
Ticagrelor	5.6 ±1.38 mg/dl	5.6mg/dl	6.12 ±1.34mg/dl	6.3mg/dl
Standard of care	6.32 ±1.22mg/dl	6.25mg/dl	6.21 ±1.17mg/dl	6.15mg/dl

Fig. 2 | 16-1

LDL levels in ticagrelor and standard of care group at baseline and after 24 months.

	LDL mean 24 months	LDL median 24 months
Ticagrelor	63.42 ± 19.98mg/dl	59.0mg/dl
Standard of care	82.83 ±33.11mg/dl	73.0mg/dl

Fig. 3 | 16-1

Conclusions: The decrease in GGT may reflect the possible beneficial effects of monacolin K supplementation on NAFLD in dyslipidemic patients.

16-3

Effects of monacolin K supplementation on serum lipoprotein levels in dyslipidemic subjects

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Background: The benefit of lipid-lowering therapies on cardiovascular risk has strong evidence. Nevertheless, not all patients are compliant with a statin therapy due to different reasons. Monacolin K is a phytotherapeutical derived from fermented red yeast rice which acts comparable to lovastatin.

Aim: We evaluated the effects of monacolin K 10 mg on serum total cholesterol (TC), high-density lipoprotein (HDL), low-density (LDL) and triglyzerides (TG) levels as well as CHOL/HDL ratio in statin-naive hypercholesterolemia subjects with low-moderate cardiovascular risk (SCORE).

Methods: Fifty-two dyslipidemic subjects (25 F, age 58+ 11 yrs) were treated for 4 weeks with monacolin K. Plasma lipids were measured using an enzyme-linked immunosorbent assay.

Results: Monacolin K intake significantly reduced plasma level of TC from 332+34 to 203+30 mg/dl (–39%; $p<0.01$), LDL from 234+30 to 127+25 mg (– 45%; $p<0.01$) and TG from 158+78 to 128+28 (–19%; $p<0.05$). No significant changes in HDL levels were observed. There were no adverse events (myopathy, CK/GOT elevation) during FU.

Conclusions: Monacolin K intake improves the serum lipoprotein profil without servere clinical adverse events. Monacolin K may act as alternative for initiation of a lipid-lowering therapy in patients refusing conventional statin therapy.

16-4

Influence of inpatient cardiac rehabilitation on advanced glycation endproducts (AGEs)

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Background: Advanced glycation end products (AGEs) are a heterogenous group of molecules that are generated through non-enzymatic glycation and oxidation of proteins, lipids and nucleic acids. They affect nearly every type of cell and molecule in the body and are thought to play a key role in developing age-related chronic diseases, such as neurodegeneration, arteriosclerosis and cardiovascular disease. Therefore AGEs represent a novel marker of vascular complications in high-risk patients for cardiovascular disease. There are different forms of receptors for interaction with AGEs. The soluble form of the AGEs receptor (sRAGE) can bind the ligand. However, because of lacking the cytoplasmic domain it works as decoy receptor with protective effects.

Objective: There is no evidence about the effects of a structured cardiovascular rehabilitation program on AGEs and sRAGE levels up to now.

Aim: In this pilotstudy we studied the impact of a multimodal 3-week inpatient rehabilitation program including physical exercise on AGEs and oxidative stress in patients with coronary heart disease (CHD).

Methods: In 62 patients with CHD, aged from 33–75 years blood serum was collected at the beginning (baseline) and the end of the rehabilitation (discharge). Mainly ELISA technique was used: Myeloperoxidase (MPO) as a marker for oxidative stress, AGEs and also the soluble receptor (sRAGE). Additionally, the AGEs were measured on the skin with a special non-invasive method by an AGE-reader using autofluorescence properties. To get a more reliable marker the quotient AGE/sRAGE was estimated.

Results: The study showed that a multidisciplinary rehabilitation program (including passive and active physical therapies, nutritional regimen and education) can decrease oxidative stress in a significant manner by reducing MPO levels from 255.5 to 216.2 ng/ml ($p<0.05$). Furthermore the AGE-level was slightly reduced in serum from 10.9 to 10.2 ng/ml and the protective receptor increased simultaneously from 893 to 938 pg/ml. Therefore we can observe a significant decline in the calculated quotient AGE/sRAGE from 0.014 to 0.011 ratio ($p<0.01$). Interestingly if the cohort is divided into two groups (with/without physical activity before rehabilitation) an already higher basic AGE value can be seen in the group without activity.

Conclusions: A structured cardiovascular rehabilitation program is a well-established and powerful instrument to improve cardiovascular risk. Moreover, it results in a reduction of oxidative stress and an improvement of the AGE/sRAGE quotient.

16-5

Long-term physical activity leads to a significant decrease of serum H-FABP and increase of sST2 levels: a prospective clinical trail

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Background: Regular physical activity was shown to have several beneficial effects on the heart. It was the aim of this prospective study to investigate the influence of long-term physical activity on biomarkers for myocyte ischemia (heart-type fatty acid-binding protein—H-FABP), matrix remodelling/vascular stress (soluble isoform of suppression of tumorigenicity 2—sST2) and inflammation (soluble urokinase-type plasminogen activator receptor—suPAR).

Methods and Results: 109 subjects were recruited, 98 completed the study. Participants were asked to perform exercise within the calculated training pulse for 8 months. Training diaries were kept by the participants and the performance gain was measured/quantified by bicycle stress tests at the beginning and

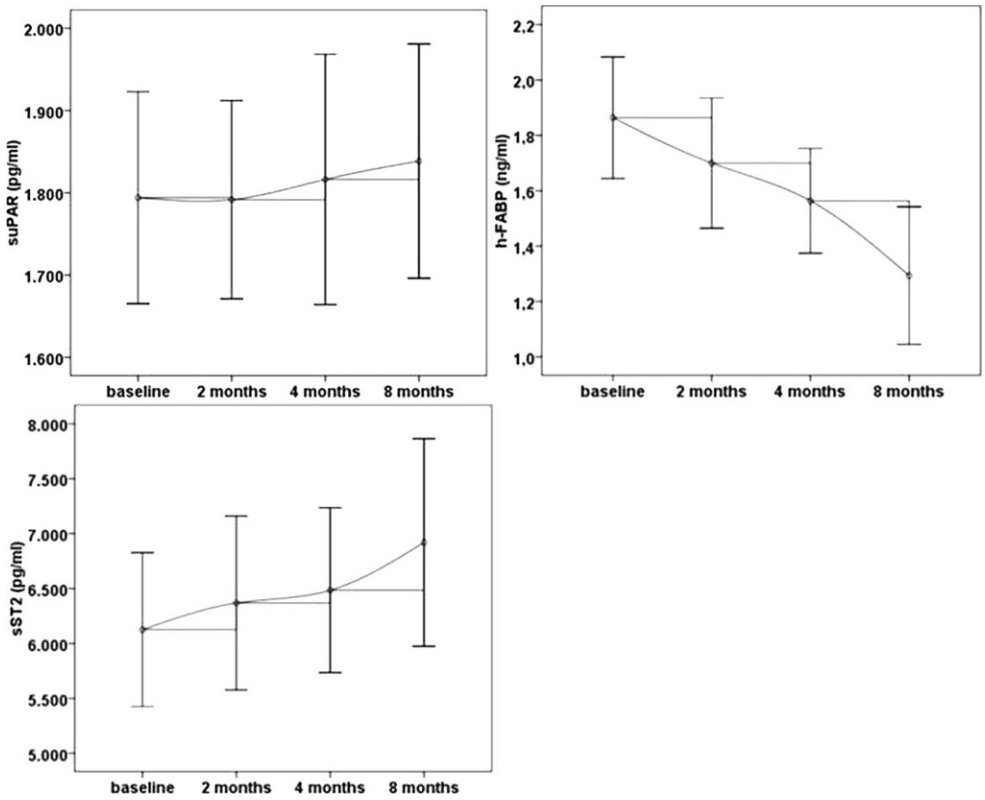

Fig. 1 | 16-5

end of the study. 27 participants with a performance gain <2.9% were excluded. suPAR, H-FABP and sST2 were measured in serum at baseline and after 2, 4 and 8 months by ELISA. We found a significant decrease of H-FABP (1.86 ± 0.86 to 1.29 ± 0.98 ng•ml; $p < 0.001$) and a significant increase in sST2-levels (6126 ± 2759 to 6919 ± 3720 pg•ml; $p = 0.045$) during the observation period of 8 months while there was no remarkable change in suPAR-levels.

Conclusions: We interpret the activity-induced decrease of H-FABP as sign of lower sub-clinical myocardial ischemia and better perfusion, probably due to a more economic metabolization and electrolyte balance. The increase of sST2 might reflect physiological sports-induced vascular stress. As H-FABP and sST2 play an important role in the pathomechanism of ischemic cardiomyopathy (iCMP) further studies should investigate the influence of regular physical activity on these biomarkers in a population of iCMP-patients.

16-6

The a Body Shape Index and type 2 diabetes are mutually independent predictors of cardiovascular events in patients with peripheral artery disease

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Background: The A Body Shape index (ABSI) is calculated based on waist circumference, height and BMI and is a validated measure of visceral adiposity. In the general population, the ABSI has been shown to be an independent risk factor for premature mortality. Its power to predict cardiovascular events in patients with peripheral artery disease (PAD) is not known and is addressed in the present study.

Methods: We prospectively recorded cardiovascular events in 319 patients with sonographically verified PAD over a mean follow-up time of 7.2 ± 2.1 years.

Results: At baseline, the ABSI was significantly higher in patients with type 2 diabetes (T2 DM) than in those who did not have diabetes (19.5 ± 1.9 vs. 14.0 ± 1.1; $p < 0.001$). Prospectively, the ABSI significantly predicted the incidence of cardiovascular events ($n = 57$) both univariately (standardized HR 1.36 [1.20–1.52]; $p < 0.001$) and after adjustment for age, gender, smoking, LDL cholesterol, HDL cholesterol, hypertension and T2 DM (standardized adjusted HR 1.17 [1.08–1.29]; $p = 0.010$); also T2 DM significantly predicted cardiovascular events in this fully adjusted model (adjusted HR 1.48 [1.25–1.74]; $p < 0.001$).

Conclusions: We conclude that the ABSI and T2 DM are mutually independent predictors of cardiovascular events in patients with PAD.

16–7

Neutrophil gelatinase-associated lipocalin as novel biomarker for atherosclerotic risk stratification in patients with high carotid plaque burden

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Background: Neutrophil gelatinase-associated lipocalin (NGAL) was initially described as biomarker for acute and chronic renal failure. Recent clinical trials reported an elevated NGAL plasma levels also in coronary artery disease, myocardial infarction and heart failure. Moreover, this acute phase protein is elevated in inflammatory disease. However, only low numbers of patients were analysed in most studies and so far no data exist on peripheral plaque quantification and NGAL levels. The current standard biomarker for atherosclerosis, high-sensitivity C-reactive protein (hs-CRP), has several limitations. Therefore additional biomarkers are needed to identify early patients at elevated cardiovascular risk. Sonographic 3D plaque volumetry is a promising new approach to exactly quantify atherosclerotic plaque burden in peripheral arteries. In a recently published study the authors could show that peripheral arteriosclerotic plaque burden determined by this method strongly correlates with coronary artery calcium score.

Methods: In this prospective, single centre study, we included 361 asymptomatic patients with at least one cardiovascular risk factor or an established cardiovascular disease. The level of NGAL was measured in peripheral blood plasma samples using a commercially available ELISA. Carotid atherosclerotic plaque burden (3D plaque volume) was measured using an automated software on a Philips iU22 system equipped with a VL 13-5 probe. Statistical analyses were performed using SPSS 24.

Results: Patients with no—or low carotid plaque burden ($n=297$) and those with high carotid plaque burden ($n=64$) were separated in two groups. In our baseline measurements NGAL was significantly higher in patients with high carotid plaque burden versus patients with no-or low carotid plaque burden (65 [median, IQ 50–81] versus 82 [median, IQ 70–103] ng/ml, $p<0.001$), whereas hs-CRP did not differ significantly (0.17 [median, IQ 0.08–0.36] versus 0.25 [median, IQ 0.1–0.42] ng/ml, $p=0.084$) in our study. The value of the NGAL amplitude for the prediction of high carotid plaque burden (AUC: 0.727, 95%CI 0.67–0.79; $p=<0.001$) was significantly higher when compared with hs-CRP (AUC: 0.568, 95%CI 0.49–0.64; $p=0.093$). In patients without established cardiovascular disease, NGAL levels for the prediction of high carotid plaque burden (AUC: 0.734, 95% CI 0.63–0.84; $p=<0.001$) were also significantly higher when compared to hs-CRP (AUC: 0.463, 95%CI 0.34–0.59; $p=0.58$) and to the Framingham-Risk-Score (AUC: 0.703, 95%CI 0.59–0.82; $p=0.002$).

Conclusions: NGAL seems to be a promising biomarker for the identification of patients with atherosclerotic disease. In our study NGAL was a better predictor for high atherosclerotic plaque burden than hs-CRP, the current standard biomarker for atherosclerosis.

Registered as ClincalTrials.gov Identifier NCT01895725.

16-8

Impact of platelet turnover on long-term adverse cardiovascular outcomes in patients undergoing percutaneous coronary intervention

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Background: Reticulated platelet count (RPC), a marker of platelet turnover, has been shown to be a strong independent predictor of platelet response during dual antiplatelet therapy (DAPT). Besides RPC, mean platelet volume (MPV) is used as a surrogate parameter of platelet turnover and has been linked with myocardial infarction and cardiovascular death in patients with coronary artery disease. Increased platelet turnover and high platelet reactivity are associated with short-term major adverse cardiovascular events (MACE) after percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS) or stable coronary artery disease (SCAD).

Purpose: We investigated the impact of platelet turnover on long-term MACE.

Methods: Consecutive patients presenting with ACS or SCAD undergoing PCI between 2009 and 2011 were included for this analysis. All patients received clopidogrel and acetyl-

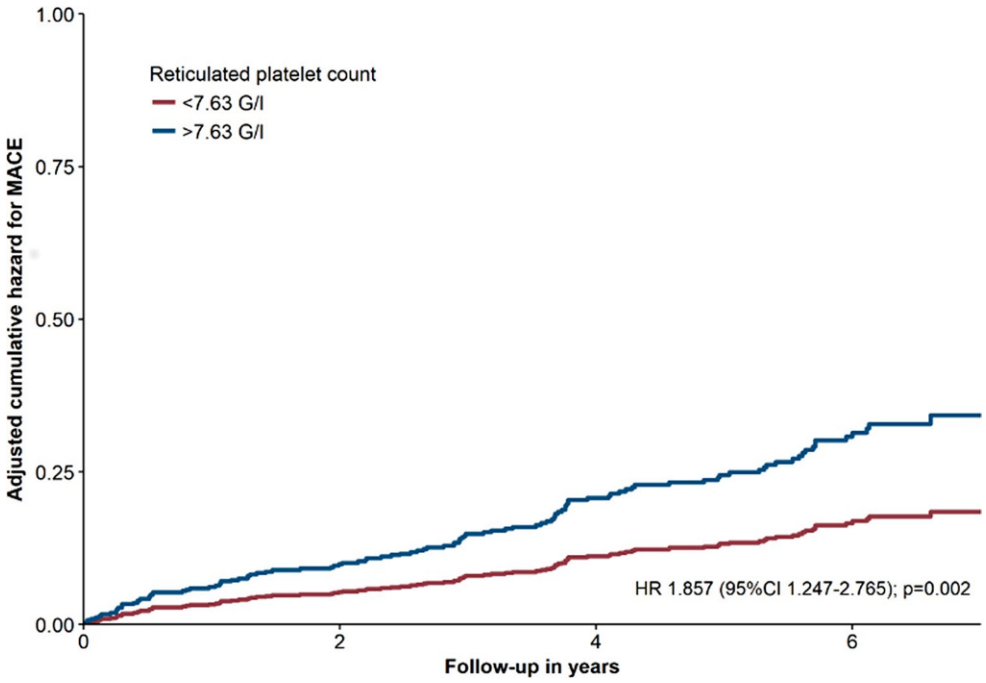

Fig. 1 | 16-8

salicylic acid as dual antithrombotic therapy regimen for 12 months. Multivariable Cox proportional hazard models were applied to assess the prognostic impact of platelet turnover (RPC, MPV) on long-term MACE, a composite of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

Results: In total 477 patients were eligible for analysis. Mean age was 64.3 ± 12.7 years, 68.8% were male and the long-term follow-up was 5.1 ± 1.9 years. Mean RPC was 8.26 ± 3.70 G/l and mean MPV was 10.73 ± 0.86 fl.

In univariate analysis, RPC was associated with long-term MACE, both as continuous (HR 1.064 [95%CI 1.021–1.111]; $p = 0.006$) and dichotomized (HR 1.693 [95%CI 1.156–2.481]; $p = 0.006$) variable. After adjustment for significant confounders, continuous RPC (HR 1.064 [95%CI 1.021–1.111]; $p = 0.003$) and dichotomized RPC (HR 1.857 [95%CI 1.247–2.765]; $p = 0.002$) remained significantly associated with MACE (Fig. 1). MPV was not associated with adverse outcomes, both in univariate and multivariable analysis.

Conclusions: Our data show an independent association of RPC with long-term adverse outcome in patients with ACS or SCAD undergoing PCI on aspirin and clopidogrel. RPC might function as potential new marker of elevated atherothrombotic risk and may guide antiplatelet therapy.

POSTERSITZUNG 17 – Kardiologisches Assistenz- und Pflegepersonal

17-1

Spezielle Pflege bei CTO/PCI im Herzkatheterlabor

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Fallbeispiel: 74jähriger männlicher Patient, Z. n. Myokardinfarkt mit kardiopulmonaler Reanimation und RCA-PCI (11/2016), KHK III mit Hauptstammbeteiligung.

Vorbereitung: Bei der Übernahme des Patienten ins Herzkatheterlabor werden alle pflegerelevanten und medizinischen Befunde von der DGKP ausgehoben und überprüft. Während der Monitorisierung des Patienten wird eine Gesprächsbasis aufgebaut, um dem Patienten Sicherheit zu geben und ihm die Angst zu nehmen. Da es sich um einen langwierigen Eingriff handelt, ist die optimale Lagerung wichtig, um Hautveränderungen, sowie lagerungsbedingte Schmerzen zu vermeiden. Auch das professionelle Vorbereiten der gesamten Materialien muss genau und zügig durchgeführt werden, um eine Verlängerung der Prozedur und somit eine längere Liegedauer zu vermeiden. Eventuell notwendiges Notfallequipment sowie geschultes Pflegepersonal gehören bei jeder Untersuchung zum Standard.

Durchführung der Intervention: Über die A. radialis wird die RCA retrograd über die LAD dargestellt und der arterielle Druck gemessen. Über den femoralen Zugang wird der Führungskatheter ans Ostium des LM gebracht und der Dilatationsdraht unter retrograder Darstellung über die Engstelle positioniert. Über diesen Dilatationsdraht wird mit diversen Ballonen die Engstelle dilatiert. Im Verlauf wird das Gefäß rekanalisiert und zwei Engstellen mit DES Stents versorgt.

Pflege während der Intervention: Nicht nur die Überwachung der Vitalparameter über den Monitor ist während der Behandlung essentiell, sondern auch die direkte Beobachtung und Kommunikation durch eine Pflegeperson mit dem Patienten. Im Zuge dieser Beobachtungen fällt eine allgemeine Unruhe des Patienten auf, die auf lagerungsbedingte Schmerzen zurückzuführen ist und durch zeitnahe Umlagerung behoben werden kann. Nach erfolgreicher Intervention, werden die Punktionsstellen von der DGKP im Nachsorgeraum versorgt, um ihn dann mit den pflegerelevanten Informationen und gutem Allgemeinzustand auf die Bettenstation zu verlegen.

Ergebnisse: Zusammenfassend kann gesagt werden, dass durch optimale Versorgung und geschultes Pflegepersonal dem Patienten Sicherheit vermittelt wird und sich so die Situation bei langwierigen Interventionen angenehmer gestaltet.

17-2

Zielgerichtete Einarbeitung neuer Mitarbeiter im Herzkatheterlabor

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Die Tätigkeiten des kardiologischen Pflege- und Assistenzpersonals werden aufgrund des medizinischen Fortschrittes immer vielfältiger und anspruchsvoller. Daher war es unser Ziel, ein zielorientiertes und strukturiertes Einarbeitungskonzept zu erstellen.

Im Rahmen der Weiterbildung zum Praxisanleiter hat DGKP Omer das Thema Einarbeitung neuer Mitarbeiter behandelt. Im Oktober 2016 wurde damit begonnen das bestehende Konzept zu evaluieren. Es wurde zusammen mit dem Team der Ist-Zustand erhoben. Gemeinsam mit den bestehenden Mentoren für neue Mitarbeiter wurde das Tätigkeitsprofil überarbeitet und ein effizientes Einarbeitungskonzept erstellt.

„Nicht alles auf einmal“: zuviel Information, viele verschiedene Mentoren und daraus resultierend unterschiedliche Anleitungen in der Einarbeitungsphase führen zu Verwirrung und Unzufriedenheit.

Das Einarbeitungskonzept beinhaltet, dass jeder neue Mitarbeiter eine Ansprechperson zugewiesen bekommt und anhand eines Einarbeitungskatalogs ein transparenter Einschulungsprozess gegeben ist.

In diesem Einarbeitungskatalog wird mit Hilfe einer Checkliste der aktuelle Wissenstand dokumentiert und die vereinbarten Lernziele evaluiert. Neben der Kontrollfunktion haben Lernziele auch eine Motivationsfunktion und geben Orientierung.

Zusätzlich finden wöchentliche Feedbackgespräche statt. Es ist ein wichtiges Instrument, da durch Lob und Anerkennung die Motivation gesteigert und durch konstruktive Kritik Missverständnisse geklärt werden.

Es wird auch auf das breite fachliche Wissen anderer Kollegen zurückgegriffen: z. B.: Notfallmanagement durch einen ALS Provider im Team oder Information über Hygiene – Fachrichtlinien und Hygienepläne durch die Hygienefachkraft

Dieses Projekt soll die Bedeutsamkeit eines strukturierten und zielorientierten Einarbeitungsprozesses hervorheben. Mentoren, der Einarbeitungskatalog und Feedbackgespräche ermöglichen diesen Prozess transparent zu gestalten. Sobald der neue Kollege seine auszuführenden Tätigkeiten sicher beherrscht, eine bestmögliche Patientenversorgung gewährleistet ist und er sich gut in das Team integriert hat, kann der Einarbeitungsprozess als abgeschlossen gesehen werden.

17-3

Case report: misdiagnosis of epilepsy uncovered by an implantable loop recorder

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Background: Misdiagnosis of epilepsy is a known problem (1.) The actual magnitude of the problem remains unclear. Studies show that up to 20%–30% of epileptics may have been misdiagnosed (2, 3).

Case Report: We report about a 76-year-old male patient. Since summer 2016 the patient suffered from recurrent seizures. The patient's wife described the seizure as a sudden pause with a gaze, shortly followed by a fall and a short unconsciousness, each with a rapid recovery. A contraction of the limbs has been observed once. An EEG conducted in August 2016 was inconspicuous, as well as a skull MRI carried out in October 2016. A 24 h Holter in November 2016 showed normal sinus rhythm.

The "gold standard" in the diagnosis of epileptic seizures is a recording of a typical event during video-EEG monitoring. During this procedure, the EEG is recorded for a prolonged period, accompanied by continuous closed-circuit video observation. In February 2017 a five days video-EEG monitoring has been recorded with a negative result. Nevertheless, in May 2017 the neurology department made the diagnosis of a "generalized myoclonic epilepsy syndrome" and initiated an anti-epileptic medication with valproic acid. Another cardiological examination showed an inconspicuous ECG with a left bundle branch block (LBBB). The corresponding echo showed a good systolic LV function with a diastolic dysfunction and septal asynchrony. Under anti-epileptic medication a further seizure event occurred, with the same potential cause as described above. The anti-epileptic medication was increased, and the patient was introduced for a cardiologic assessment. On the 29.08.2017 an implantable loop recorder (ILR) was implanted without complications. On 30.09.2017 the patient suffered again a "seizure" with a fall on the back of his head. The FUP of the implantable loop recorder on 04.10.2017 showed an asystole with 12 seconds as the cause of the fall. On the 05.10.2017 the patient receives a DDDR pacemaker.

Conclusions: This case illustrates again the clinical challenge to distinguish between seizure and syncope and reinforces the importance of implantable loop recorders (ILRs) in these patients.

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17-4

Multidisciplinary patient management for complex CRT-D extraction after system infection

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A patient with chronic ischemic cardiomyopathy and with an implanted Medtronic CRT-D system was admitted for elective replacement indication in March 2017. This has been the sixth surgical procedure at the same implantation site. The patient was discharged free from complications on the first postoperative day. Eight weeks after the operation the patient complained about sudden swelling at the pectoral wound as well as fever. Ultrasound imaging and blood work indicated a massive systemic infection. In addition, the oral anticoagulation with phenoprocoumon was highly overdosed (INR 6.83) probably due to acute renal failure. On the first day of readmission the patient presented at the outpatient clinic for cardiac pacemakers for deactivation of defibrillation mode and evaluation of pacemaker dependency. Afterwards the patient underwent surgical supracutaneous externalization of the device to allow infection healing and avoid reinfection after reimplantation. After 10 days of continuous parenteral antibiotic therapy and hemodynamic surveillance, the patient underwent successful CRT-D system extraction on the left pectoral side and reimplantation of a new CRT-D system on the right side. In order to maintain cardiac pacing during the operation, a pacemaker lead (Medtronic CapSureFix 4076 85 cm) was inserted temporarily via the left femoral vein. Parenteral Antibiotics were continued for 10 postoperative days, the postoperative course was uneventful and the patient was discharged on the 5th postoperative day after reimplantation. Due to the high risk procedure case discussions were held on a regular basis in a multi-professional environment. Patients and his relatives were provided repeatedly with detailed procedure related explantations.

Conclusions: Next to a thoroughly planned extraction program, close multidisciplinary collaboration between cardiologists, nurses and surgeons is of highest importance. Since in addition to a successful operation, rational patient evaluation, bridge-pacing concepts and postoperative examinations demand an effective team approach with participation of all professions. Furthermore, quality standards constantly rise so that not only medical doctors but also nurses are an integral part of an cardiac pacing outpatient clinic and should undergo special training. They manage personal and social needs of our patients, are in regular contact with patients' relatives and intensely involved in procedural management.

17-5

Role of standardized patient evaluation by nurses in caring for CRT patients

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Background: Despite recent guidelines, technical innovations and the increasing experience of implanting physicians, there is a need for optimization in the area of cardiac resynchronization therapy (CRT), especially in follow-up care. Nurses can contribute to the success of the therapy through documentation and communication between physician-patient and technical support.

Aim: Does standardized patient evaluation before and after CRT implantation improve patient quality of life?

Methods: A standardized patient evaluation was performed before implantation and 6 months later for 30 patients who had an indication for a CRT system according to the ESC guidelines. In addition to diagnostic data and symptoms, the quality of life of these patients were recorded by means of questionnaires.

Results and Conclusions: Through the standardized evaluation of the patients, not only measurable improvements, but also different and controversial perceptions of the patient regarding their state of health could be made visible. Thus, data made a valuable contribution to the optimization of drug and device therapy.

17-6

Aufbau und Entwicklung der Weiterbildung kardiologische Fachassistenz

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Die Entwicklung neuer und innovativer Therapieverfahren in der Kardiologie erfordert auch im Bereich des kardiologischen Assistenzpersonals eine weitere Spezialisierung und Professionalisierung.

Viele unterschiedliche Berufsgruppen arbeiten im Bereich der kardiologischen Funktion bzw. in Bereichen der Vor- und Nachsorge von kardiologischen Patienten.

Nach der allgemeinen Berufsausbildung haben nur wenige Berufsgruppen die Möglichkeit Ihr Arbeitsgebiet aufzuwerten bzw. eine offizielle Anerkennung Ihrer Qualifikation zu erhalten.

Das Angebot für Weiterbildungsmöglichkeiten für kardiologisches Assistenzpersonal ist sehr begrenzt.

Aus diesem Grund entstand in Kooperation mit dem Universitätsklinikum München eine berufsbegleitende Weiterbildung zur kardiologischen Fachassistenz. Anhand der Daten der Evaluation, die zu Beginn der Weiterbildung erhoben wurden, konnte festgestellt werden, welch hohen Stellenwert bei den Teilnehmern der Erwerb einer Zusatzqualifikation im Rahmen der Fachweiterbildung hat.

Entscheidende Punkte für die Planung der Weiterbildung sind die Evaluation des Arbeitsspektrums, die persönlichen Erwartungen, der aktuelle Wissensstand und die praktischen Erfahrungen der Teilnehmer zu Beginn der Weiterbildung.

Es ermöglicht ein Abschätzen des individuellen Wissensstandes der Teilnehmer, um gezielt die Absolventen auf ein höheres fachspezifisches Wissen bringen zu können.

Zudem können mit Hilfe der Evaluationsergebnisse punktuelle Fokussierungen der Weiterbildungsthemen von Beginn an festgelegt werden.

In der ersten Selbsteinschätzung stuften die Teilnehmer Ihr Wissen bezüglich der intravaskulären Bildgebung auf ein niedriges Niveau ein.

Um die Wissenserweiterung in diesem Fachgebiet unterstützen zu können, erhöhten wir den Anteil der Unterrichtseinheiten für die intravasculäre Bildgebung, zogen die Hilfe von Fachfirmen für ein Simulationstraining und eine Geräteeinweisung hinzu.

In der Abschlussevaluation konnte ein Anstieg des Wissensniveaus im Teilbereich der intravaskulären Bildgebung um das Doppelte verzeichnet werden.

Auch in den übrigen Teilbereichen der Weiterbildung kam es überwiegend zu einem deutlichen Anstieg der Fachkenntnisse.

Schlussfolgerungen: Zusammenfassend konnte gezeigt werden, dass eine modular aufgebaute und berufsbegleitende Weiterbildung zur kardiologischen Fachassistenz, unter der Berücksichtigung von bereits bestehendem Fachwissen durch langjährige Berufserfahrung und die Integration von Teilnehmererwartungen ein erfolgversprechendes Konzept ist, das den Ansprüchen an ein immer komplexer werdendes Arbeitsumfeld Rechnung trägt.

17-7

Das Erleben von Patientinnen und Patienten mit einem akuten Hebungsinfarkt während einer PCI in einem Herzkatheterlabor

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Grundlagen: In dieser Literaturanalyse wird versucht anhand von vier qualitativen Studien einen Einblick in die Situation von Patientinnen und Patienten mit einem akuten Hebungsinfarkt (STEMI) während einer Koronarangiographie mit einer perkutanen koronaren Intervention (PCI) in einem Herzkatheterlabor, zu geben. Es wird untersucht wie die Patientinnen und Patienten diese Akutsituation subjektiv erleben und welche Faktoren dieses positiv oder negativ beeinflussen. Ein Herzinfarkt ist für die meisten Patientinnen und Patienten ein sehr einschneidendes Erlebnis und sie befinden sich in einer Ausnahmesituation. Da sie um ihr Leben bangen, werden die Betroffenen von vielen Gefühlen bewältigt. Durch den Eingriff in einem Herzkatheterlabor mittels PCI können sie durch eine wenig invasive Maßnahme in kürzester Zeit behandelt werden.

Fragestellung: Es stellt sich die Frage, welche Auswirkungen diese außergewöhnliche Situation auf die Betroffenen hat und wie am besten damit umgegangen wird. Abgeleitet aus dieser Problembeschreibung ergeben sich folgende Fragestellungen: „Wie erleben Patientinnen und Patienten die Behandlung eines akuten Myokardinfarktes in einem Herzkatheterlabor?“ und „Welche Faktoren beeinflussen eine PCI positiv oder negativ für die Betroffenen?“

Methodik: Bei der systematischen Literatursuche wurden Onlinedatenbanken, wie PubMed und Cinhal verwendet. Die Suche wurde auf deutsch- und englischsprachige Literatur eingegrenzt. Insgesamt wurden sechs Publikationen als relevant identifiziert. Nach einer systematischen Analyse der Texte wurden schlussendlich vier Studien eingeschlossen.

Ergebnisse: Es werden verschiedene, subjektive Faktoren dargestellt, welche das Patientenerleben positiv sowie negativ beeinflussen. Die Hauptaussage aus den Studien ist, dass die schnelle und effektive Behandlung eines STEMI sich zwar positiv auf den Genesungsverlauf auswirkt jedoch den Patientinnen und Patienten meist nicht bewusst ist, in welcher kritischen Lebenslage sie sich befinden. Kritisch zu betrachten ist allerdings, dass

die Betroffenen nach dem Nachlassen der Symptomatik nicht glauben können, dass sie einen Herzinfarkt erlitten haben und sie sich in einem sehr kritischen Zustand befanden. Zudem zeigt sich, dass sich die Kommunikation während der PCI äußerst positiv auf den psychischen Zustand der Betroffenen auswirkt. Die Patientinnen und Patienten empfinden den reibungslosen Ablauf als sehr professionell und haben deshalb großes Vertrauen in das Behandlungsteam. Kritische Notfallsituationen werden meist gar nicht wahrgenommen. Gefühle wie Angst, Schockempfinden oder Zweifel werden nur in der Anfangsphase des Geschehens wahrgenommen. Ein wichtiger Faktor ist die Kommunikation mit den Patientinnen und den Patienten. Hier kann man zwischen nonverbaler und verbaler Kommunikation unterscheiden. Bei der nonverbalen Kommunikation kann es sich um die Mimik der Betroffenen handeln aber auch um die Untersuchung selbst. Mittels verbaler Kommunikation kann man den Patientinnen und Patienten sehr viel Sicherheit geben.

Schlussfolgerungen: Zur Beantwortung der Forschungsfragen stehen zwar Studien zur Verfügung jedoch ist die Anzahl solcher limitiert. Die Entwicklung der demografischen Daten der letzten Jahre weist darauf hin, dass die Anzahl der Herzkranken Patientinnen und Patienten stetig zunimmt. Daraus ergibt sich ein dringender Forschungsbedarf zu dieser Thematik.

17-8

Notfallmanagement an der Universitätsklinik für Innere Medizin Graz

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An der UKIM Graz wurde im Jahr 2016 schrittweise ein neues Notfallkonzept implementiert. Das eingereichte Poster beschreibt die Umsetzung.

Im Oktober 2016 gab es eine Kickoff-Veranstaltung zur Implementierung des neuen Notfallkonzepts. Um zu verstehen welche Vorteile diese Neuerung bringt, wird zunächst verdeutlicht wie der Ist-Zustand davor ausgesehen hat:

- keine einheitliche Notfallausrüstung
- kein einheitliches Notfallteam
- kein Einsatzprotokoll
- keine einheitliche Notfallschulung
- verschiedene Defibrillatoren

Eine Expertengruppe, bestehend aus Ärzten und Pflegepersonal, erstellte ein neues Notfallkonzept. Seit 2016 gibt es:

- ein fixes Notfallteam
- einheitliches Equipment
- einheitliche Defibrillatoren und Protokolle

Zusätzlich wird nach jedem Einsatz ein Debriefing durchgeführt. Notfallschulungen werden nun, durch die Pflegeleitung, zentral koordiniert. Die Schulungen werden von ALS Providern des Notfallschulungsteams interdiziplinär und einheitlich abgehalten.

Zusammenfassend kann man sagen, dass das neue Notfallkonzept einen großen Beitrag zur Erhöhung der Patientensicherheit liefert. Abgesehen davon ist auch der Nutzen für die Mitarbeiter sehr groß, da sie nun regelmäßig an Notfallschulungen teilnehmen und so Notfälle im Team sicher abarbeiten können. Ein weiterer großer Benefit für die Stationen liegt darin, dass sich die Mitarbeiter auf das Backup des neuen Notfallteams verlassen können, was wiederum die Selbstsicherheit der Mitarbeiter auf den Stationen stärkt.

POSTERSITZUNG 18 – Basic Science 4

18-1

The impact of remote ischemic conditioning on hemodynamic function in reperfused myocardium in rats

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Background: Remote ischemic preconditioning (RIC) is considered as a potential clinical approach to reduce myocardial infarct size (MI). However, lacking evidence that RIC beyond MI size reduction that acts, on inflammation and LV remodelling. Furthermore, the activation of Neuregulin-1 (NRG-1)/ErbB3 signalling provides significant anti-inflammatory effects. The aim of the study was to clarify the impact of RIC on NRG-1/ErbB3 axis in association with expression of pro-inflammatory cytokines, ECM components as well as LV function.

Methods: Male Sprague-Dawley rats were subjected to a 30 min left anterior descending artery (LAD) occlusion followed by 2 weeks reperfusion (IR) in three groups: (1) sham operated (SOP, without occlusion; $n=6$); (2) IR ($n=10$) and (3) IR+RIC, ($n=10$; three cycles of 5 minutes of IR on hindlimb performed during myocardial ischemia). Cardiac function was evaluated by transthoracic echocardiography and on an isolated erythrocyte-perfused working heart model (WH). Plasma levels of NRG-1 was measured by ELISA. mRNA expression of pro-inflammatory cytokines, ECM components and ErbB receptors were assessed by RT-qPCR.

Results: IR resulted in a marked decline in cardiac output (CO), external heart work (EHW) ($P<0.01$, respectively) obtained from WH as well as ejection fraction (EF). ($P<0.01$, respectively). Preserved cardiac function by RIC was associated with higher NRG-1 levels ($P<0.05$) and a decline in mRNA expression of IL-1β and TNF-α, TNC, MMP2 and MMP9 ($P<0.05$, respectively) on reperfused myocardium. ErbB3 mRNA expression significantly increased by RIC ($P<0.01$).

Conclusions: Our data first time demonstrated that preserved LV function by RIC was associated with a marked reduction in inflammation via a possible mechanism involving NRG-1/ErbB3 signalling in reperfused myocardium

18-2

Tenascin-C deficiency attenuates abdominal aortic aneurysm progression in mice

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Background: Tenascin-C (TNC) is a matricellular protein produced mainly by vascular smooth muscle cells (VSMC) as well as fibroblasts and plays a role in various pathological remodeling processes, including abdominal aortic aneurysms (AAA). The aims of this study are to evaluate 1) whether TNC deficiency could attenuate AAA formation and 2) whether TNC influence VSMC phenotypes.

Methods: Male A/J TNC -/- and A/J wildtype (WT) mice were used. After laparotomy and preparation of the infrarenal aorta, AAA were induced by periaortal CaCl2 at 0.5 M application for 15 minutes. The sham-operated groups were treated identically with saline solution. The external diameter of the infrarenal aorta was measured both prior to AAA induction and before organ harvesting at 3 and 10 weeks. Aortic samples were stained with Elastica Van Gieson for elastin structure evaluation and further qualitative scoring. Additionally, in vitro human VSMC were incubated with either TNF-α (5 ng/ml) or TNC (3 µg/ml) for 4 and 24 h. The relative expression of SM22-α and TNC were evaluated by quantitative real-time PCR.

Results: Mice with CaCl2 induced AAA showed significantly higher diameter ratios than the sham groups (3w: $p<0.0001$; 10w: $p<0.0001$). Whereas, no significant changes in diameter ratios were found in sham groups, TNC knockout (KO) mice with AAA showed significantly lower diameter ratio compared to the wildtype group 3 weeks (TNC KO: 1.39 ± 0.25, WT: 1.67 ± 0.22 $p<0.05$) and 10 weeks (TNC KO: 1.51 ± 0.47, WT: 1.98 ± 0.55 $p<0.05$) after AAA induction. Additionally, WT mice with AAA showed a more disrupted Elastin structure than TNC KO mice 10 weeks after AAA induction. VSMC exposed to TNF and TNC markedly reduced the expression of TNC and SM22-α, respectively. Although, after 24 h incubation, expression of TNC showed an upregulation tendency, while the expression of SM22-α was significantly upregulated (TNF-α:195.18 ± 43.79, TNC: 8.96 ± 1.91, Control: 0.22 ± 0.06 $p<0.001$).

Conclusions: Our results are a first evidence that TNC might play a role in the formation and progression of AAA as well as in changes of VSMC. These results might indicate that targeting TNC is a potential therapeutic approach in AAA.

18-3

Multi-biomarker risk stratification to identify patients with coronary artery disease at high risk for subsequent cardiac adverse events

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Background: Established mortality or morbidity risk scores are useful in prediction of cardiovascular adverse events (AE). Based on traditional atherosclerotic risk factors and biomarkers, these parameters are usually transformed into dichotomic variables. In contrast, discriminant analysis combining several continuous variables, such as laboratory measures, allows to use the absolute values of the measured parameters. Therefore, this type of analysis separates the groups with/without AE most accurately, by mathematically discarding parameters with less predictive values in the group classification. This type of multimarker approach may have a better sensitivity/specificity in the prediction of AE than the usual logistic regression or C-statistics.

Methods: We have included $n=81$ patients in our multi-biomarker Study. Our study was a prospective, non-randomized, single-center cohort study. We have chosen different classes of biomarkers, all of them reportedly associated with cardiovascular AE and combined them in a multimarker approach by using canonical discriminant analysis: S100-calcium-binding-protein-A12 (S100A1), interleukin-1-like-receptor-4 (IL1R4), adrenomedullin, copeptin, neutrophil-gelatinase-associated-lipocalin (NGAL), soluble-urokinase-plasminogen-activator receptor (suPAR) and ischemia-modified-albumin (IMA). The primary endpoint was to evaluate the combined discriminatory predictive value of the selected 7 biomarkers in prediction of AE (death, stroke, myocardial infarction, coronary revascularization, hospitalization and implantation of pacemaker or implantable cardioverter defibrillator). The secondary endpoints were the separated blood levels of the 7 biomarkers in the groups with/without AE and a comparison of the sensitivity and specificity of the calculated discriminant score of the biomarkers with that of the traditional logistic regression and C-statistics.

Results: During the 1-year follow-up, 24 AEs occurred. By stepwise exclusion of biomarkers exhibiting weak correlation with the other labor parameters, combination of NGAL, suPAR and IL1R4 had the strongest significant discriminant predictive power. The canonical correlation coefficient was 0.496, with a Wilk's lambda value of 0.001. By utilizing the calculated discriminant equation with the weighted mean discriminant score (centroid), the sensitivity and specificity of our model were 72.2% and 78.7% in prediction of AE. These values were better than those of the calculated C-statistics (70.0% and 35.0%) if traditional risk factors (male gender, older age, diabetes, hypertension, hyperlipidaemia, smoking) with/without biomarkers (mandatory transformed to categorical variables) were used for AE prediction. Plasma levels of the separate biomarkers were not predictive for AE, emphasizing the necessity of multi-biomarker analysis.

Conclusions: Canonical discriminant analysis of multimarker approach is able to define risk threshold in individual patient level for personalized medicine.

18-4

Spatiotemporal differences of the myocardial phospholipid fatty acid compositions induced by ischemia-reperfusion injury in pigs

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Background: Myocardial energy metabolism is based on the beta-oxidation of fatty acids (FA), which requires continuous and high oxygen supply. Myocardial Ischemia is characterized by dramatic decrease of tissue oxygen concentration. The aim of our study was to characterize the cell membrane phospholipid (one of the three major classes of cell membrane lipids, beside glycolipids and cholesterol) integrity after myocardial ischemia/reperfusion (I/R). Phospholipids (PL) are rich in polyunsaturated fatty acids (PUFA) fractions, and being extremely prone towards lipid peroxidation, mostly occurring during the reperfusion.

Methods: Domestic pigs underwent closed chest reperfused myocardial infarction. At the 3-day follow-up, the heart was explanted, and heart muscle samples (remote, border and infarcted areas) were washed in ice-cold physiological saline, homogenized, and total lipids (C14-C22) were extracted. PLs were separated and fatty acid profile was determined with gas chromatography. The individual myocardial fatty acid compositions were given as the % of the total PL fatty acid content. Antioxidant products, such as malondialdehyde (MDA), reduced glutathione (GSH) and the activity of glutathione peroxidase (GSHPx) were measured in blood samples, collected at the initial time point of the coronary occlusion, then after 90 minutes occlusion (the beginning of reperfusion), 30 minutes after reperfusion start and at 3 days follow-up.

Results: Infarcted myocardium contained significantly ($p<0.05$) higher PL compositions of saturated fats of C14:0 (myristic acid; 0.15±0.07% vs 0.12±0.05% and 0.08±0.02%), C18:1 (oleic acid; 15.7±4.03% vs 13.3±4.03% and 10.7±1.21%), and C20:3 (dihomo-gamma-linolenic acid; 1.06±0.19% vs 0.92±0.1% and 0.82±0.09%) as compared to the border and remote areas, respectively. In contrast, C18:2 (linoleic acid) was decreased ($p<0.05$) in the infarcted area, as compared to the border and the remote region (22.0±4.72% vs 26.8±3.27% and 26.9±2.73%). The total amount of polyunsaturated fatty acids decreased significantly ($p<0.05$) both in remote (53.5±5.8%) and infarcted area (47.0±7.5%) as compared to the remote myocardium (56.0±3.4%). 90 min coronary occlusion led to mild increase in plasma GSH and GSHPx level, but both GSH (3.17±0.73 vs 3.68±0.99 mM/g protein) and GSHPx (5.20±1.60 vs 6.08±1.38 IU/g) increased significantly 30 min after reperfusion as compared to baseline and 3-day values, while MDA concentration did not change.

Conclusions: Ischemia/reperfusion injury led to myocardial fatty acid profile modifications including depletion of polyunsaturated fatty acids, and increase in saturated lipids, suggesting cell membrane disruption, partially also in the border zone of ischemia. Increased level of plasma GSH and GSHPx during reperfusion post-infarction might be a sensitive acute reperfusion injury marker.

18-5

Toll-like receptor expression and mortality in critical Ill patients

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Background: Toll-like receptors (TLRs) play an important role in acute inflammatory processes in critical ill patients by binding to pathogen associated molecular patterns (PAMP) and danger associated molecular patterns (DAMP). However, it is not known whether the expression pattern of TLRs on neutrophils and monocytes are associated with outcome in critical illness. Therefore the aim of this prospective, observational study was to analyze whether expression of TLR-2, TLR-4 and TLR-9 on neutrophils and monocytes is associated with 30-day survival in critically ill patients.

Methods: We enrolled 215 consecutive patients admitted to a cardiac ICU at a tertiary care center. Blood was taken at admission and expression of TLR-2, TLR-4 and TLR-9 on neutrophils and monocytes was analyzed by flow cytometry.

Results: Median acute physiology and chronic health evaluation II (APACHE II) score was 20, and 30-day mortality was 26%. TLR-2 expression on neutrophils correlated with APACHE II and sequential organ failure assessment (SOFA) score. TLR-2 ($p<0.001$) and TLR-9 ($p<0.05$) expression on neutrophils was significantly higher in non-survivors as compared to survivors. In contrast, TLR-4 expression on neutrophils and TLR-expression on monocytes were not associated with survival, respectively. TLR-2 (OR 2.9, 95% CI 1.2–7.2; $p<0.001$) and TLR-9 (OR 2.6, 95% CI 1.3–5.0; $p<0.005$) expression in the third tertile predicted mortality independent from age, gender, diagnosis and APACHE II score.

Conclusions: Neutrophil expression of TLR-2 and TLR-9 predict mortality in patients admitted to a cardiac ICU. This suggests that activation of the innate immune system by TLR-binding of DAMPs may play a significant role in critical ill patients.

18-6

Toll-like receptor expression on monocytes and neutrophils after cardiac arrest

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Background: Successful resuscitation after cardiac arrest (CA) is associated with a systemic inflammatory response. Toll-like receptors (TLRs) may play an important role in this inflammatory process by binding to pathogen associated molecular patterns (PAMP) and danger associated molecular patterns (DAMP). The aim of this study was to examine the expression of TLRs on neutrophils and monocytes after CA.

Methods: This study included 50 consecutive post-CA patients who were transferred to a tertiary intensive care unit (ICU) after return of spontaneous circulation. TLR expression of monocytes and neutrophils were analysed by flow-cytometry. Monocyte subsets were defined according expression of CD14, CD16 and CCR2 as classical monocytes (CD14++CD16-; CM), intermediate monocytes (CD14++CD16+CCR2+; IM) and non-classical monocytes (CD14+CD16++CCR2-; NCM).

Results: 25 patients (50%) died during the 6-month follow-up. Patients that died during follow-up showed a significant higher expression of TLR-2 on neutrophils (MFI 3928 IQR 3174–4672 vs 2695 IQR 2519–3393; $p=0.004$) and TLR-4 on monocytes (MFI 843 IQR 766–947 vs. 704 IQR 651–777; $p=0.001$). In contrast, neutrophil-expression of TLR-4 and TLR-9 as well as monocyte-expression of TLR-2 and TLR-9 did not differ between survivors and non-survivors. Neutrophil-TLR-2 and monocyte-TLR-9-expression predicted survival independent from APACHE-II sore and time to ROSC. Interestingly, expression of TLRs was significantly higher on IM as compared to CM and NCM. In addition, subset-specific expression of TLR-4 on CM ($p<0.05$) and IM ($p<0.05$) but not on NCM ($p=0.1$) was associated with survival.

Conclusions: TLR-expression on neutrophils and monocytes differentially predict survival in patients after CA.

18-7

The role of TLR-9 in ischemia-reperfusion injury following acute myocardial infarction

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Background: Ischemia and subsequent reperfusion cause cell death within the reperfused tissue, followed by mitochondria leaking from the cells to the extracellular space. As recently demonstrated by experimental studies and clinical trials, circulating extracellular mitochondrial DNA (mtDNA) exhibits pro-inflammatory effects by binding to its corresponding receptor TLR-9. This activation causes chemotaxis and activation of neutrophils as well as monocytes which play a pivotal role in further damaging the infarcted tissue. Nonetheless, the exact role of TLR-9 in ischemia-reperfusion injury due to acute myocardial infarction remains to be unknown.

Methods: By ligation of the left coronary artery, ischemia was induced in male Wistar rats. After an ischemic period of 30 minutes, reperfusion was initiated by removal of the ligature. At this point, the animals were randomly divided into groups receiving TLR-9 antagonist ODN 2088 (bolus: 500 µg and subsequently 1500 µg over 24 h via subcutaneous pump) or ODN-control (bolus: 500 µg and subsequently 1500 µg over 24 h via subcutaneous pump). Circulating neutrophil count was determined by flow cytometry 24 h after the operation. Furthermore, hemodynamic measurements and histological analyses were performed 28 days thereafter.

Results: Rats receiving treatment with ODN 2088 showed significantly lower counts of circulating neutrophils after 24 h compared to animals receiving ODN-control (ODN 2088: 22.866 ± 7992/µl Vs. ODN-control: 35.651 ± 15.121/µl, $p = 0.02$). After 28 days, we analyzed for subsequent changes in cardiac repair in these animals. Though, hemodynamic parameters remained unchanged, left ventricular mass was significantly decreased accompanied by an enhanced aneurysm formation which was characterized by a 50% thinning of the left ventricular wall (ODN 2088: 0.93 ± 0.41 mm vs. ODN-control: 1.96 ± 0.75 mm, $p = 0.02$).

Conclusions: We used the TLR-9 antagonist ODN 2088 to inhibit TLR-9 signaling within the first 24 h following ischemia and reperfusion. This was in order to illuminate the involvement of TLR-9 in immune system activation and cardiac repair. Our presented data suggests that inhibiting TLR-9 results in a reduced activation profile of neutrophils 24 h after the ischemic event. Furthermore it leads to changes in myocardial structure including a dramatic reduction of wall thickness and ventricular muscle mass. We speculate that these structural changes could cause severe defects including rupture at later stages of the healing process.

18-8

Matrix metalloproteinase-2 impairs homing of intracoronary delivered mesenchymal stem cells in a porcine reperfused myocardial infarction: comparison with intramyocardial cell delivery

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Background: Intracoronary injection of mesenchymal stem cells (MSCs) resulted in a prompt decrease of absolute myocardial blood flow (AMF) with late and incomplete recovery of myocardial tissue perfusion. Here we investigated the effect of decreased AMF on oxidative stress marker matrix metalloproteinase-2 (MMP-2) and its influence on the fate and homing and paracrine character of MSCs after intracoronary or intramyocardial cell delivery in a closed-chest reperfused myocardial infarction model in pigs.

Methods: One week after myocardial infarction, porcine MSCs transiently transfected with green fluorescence protein and luciferase (GFP-Luc-MSCs) were injected either intracoronary (group IC) or intramyocardially (group IM). AMF was measured before, immediately after, and 24 h post cell delivery. In vitro bioluminescence signal was used to identify tissue samples containing GFP-Luc-MSCs.

Myocardial tissue matrix metalloproteinase 2 (MMP2) and CXCR4 receptor expression (index of homing signal) were measured in bioluminescence positive and negative myocardial areas one day post cell transfer.

At 7-day follow-up, myocardial homing (cadherin, CXCR4, SDF-1alpha) and angiogenic factors (FGF2, VEGF) were quantified by ELISA of homogenized myocardial tissues from the bioluminescence positive and negative infarcted, border, and non-ischemic myocardium.

Biodistribution of the implanted cells was quantified by using Luciferase assay and confirmed by fluorescence immunochemistry. Global left ventricular ejection fraction (LVEF) was measured at baseline and one month post cell therapy using MRI.

Results: AMF decreased immediately after intracoronary cell delivery, while no change in tissue perfusion was found in the IM group. Intracoronary delivery led to a significant increase in myocardial MMP2 (64 kD) expression with significantly exponentially decrease of CXCR4 expression. FGF2 and VEGF of the bioluminescence infarcted and border zone of homogenized tissues were significantly elevated in the IM group as compared to IC group. LVEF increase was significantly higher in IM group at the 1-month follow up.

Conclusions: Intracoronary stem cell delivery decreased AMF, with consequent increase in myocardial expression of MMP-2 and reduced CXCR4 expression with lower level of myocardial homing and angiogenic signals and less regenerative capacity of the heart.

POSTERSITZUNG 19 – Bildgebung 2

19-1

Artefacts in 1.5 Tesla and 3 Tesla cardiac magnetic resonance imaging in patients with leadless cardiac pacemakers

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Background: There is only limited data on patients with leadless cardiac pacemakers (LCP) undergoing magnetic resonance imaging. The aim of this prospective, single-center, observational study was to evaluate artefacts on cardiac magnetic resonance (CMR) images in patients with LCP.

Methods: Fifteen patients with MicraTM LCP, which were implanted at least six weeks prior to CMR scan, were enrolled and underwent either 1.5 Tesla or 3 Tesla CMR imaging. Artefacts were categorized into grade 1 (excellent image quality), grade 2 (good), grade 3 (poor) and grade 4 (non-diagnostic) for each myocardial segment. One patient was excluded because of an incomplete CMR investigation due to claustrophobia.

Results: LCP caused an arc-shaped artefact (1.14 ± 0.23 cm^2) at the apex of the right ventricle (RV). Out of 224 analyzed myocardial segments of the left ventricle (LV) 158 (70.5%) were affected by grade 1, 27 (12.1%) by grade 2, 17 (7.6%) by grade 3 and 22 (9.8%) by grade 4 artefacts. The artefact burden of grade 3 and 4 artefacts was significantly higher in the 3 Tesla group (3 Tesla vs 1.5 Tesla: 3.7 ± 1.6 vs 1.9 ± 1.4 myocardial segments per patient, $p = 0.03$). A high artefact burden was particularly observed in the mid anteroseptal, inferoseptal and apical septal myocardial segments of the LV and in the mid and apical segments of the RV. Quantification of LV function and assessment of valves was feasible in all patients. We did not observe any clinical or device-related adverse events.

Conclusions: CMR imaging in patients with LCP is feasible with excellent to good image quality in the majority of myocardial segments of the LV. The artefact burden is comparable small allowing an accurate evaluation of LV function, cardiac structures and valves. However, artefacts in the mid anteroseptal, inferoseptal and apical septal myocardial segments of the LV due to the LCP may impair or even exclude diagnostic evaluation of these segments. Artefacts on CMR images may be reduced by the use of 1.5 Tesla MRI scanners.

19-2

Biomarker assessment for early infarct size estimation in ST-elevation myocardial infarction

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Background: High-sensitivity cardiac troponin (hs-cTnT) represents the biomarker of choice for infarct size (IS) estimation in patients with acute ST-elevation myocardial infarction (STEMI). However, admission values of hs-cTnT are only weakly associated with IS. The aim of this study was to investigate the incremental value of different biomarkers measured on admission for IS estimation in STEMI patients.

Methods: In this prospective observational study, we included 161 consecutive STEMI patients treated with primary percutaneous coronary intervention (pPCI). The following biomarkers were assessed on admission: hs-cTnT, N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) and neutrophil/lymphocyte ratio (NLR). IS was determined by cardiac magnetic resonance (CMR) imaging 3 (Interquartile range [IQR] 2 to 4) days after the index event.

Results: Patients with large IS (>19% of left ventricular myocardium) showed significantly higher levels of admission hs-cTnT (399.6 vs. 53.4 ng/L, $p < 0.001$), NT-pro-BNP (140 vs. 86 ng/L, $p = 0.008$) and NLR (6.4 vs. 4.1, $p < 0.001$). The combination of hs-cTnT, NT-pro-BNP and NLR on admission resulted in a significantly higher area under the curve (0.78; 95% CI 0.704 to 0.838, ($p = 0.01$)) for the prediction of large IS than admission hs-cTnT alone (0.69; 95% CI 0.619 to 0.767).

Conclusions: In STEMI patients undergoing pPCI, a comprehensive biomarker approach on admission including hs-cTnT, NT-pro-BNP and NLR was significantly better for immediate infarct severity estimation as compared to hs-cTnT alone.

19-3

Impact of atrial fibrillation during ST-elevation myocardial infarction on infarct characteristics and prognosis

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Background: AF is frequently observed in patients with ST-elevation myocardial infarction (STEMI) and associated with worse clinical outcome. However, the mechanisms for this increased risk are not fully understood. The purpose of this study was to investigate the relationship of the presence of atrial fibrillation (AF) to cardiac magnetic resonance (CMR) derived myocardial salvage and damage as well as clinical outcomes.

Methods and Results: This multicenter CMR study enrolled 786 STEMI patients. CMR parameters (infarct size, myocardial salvage index, microvascular obstruction and myocardial function) were assessed 3 (interquartile range [IQR] 2–4) days post-STEMI and compared between patients with or without AF during hospitalization. Major adverse cardiac events (MACE) were assessed as a composite of all-cause death, re-infarction and new congestive heart failure at 12 months. AF was documented in 48 (6.1%) patients. There was no significant difference in infarct size (18 [IQR9-29] vs. 17 [IQR 9–25]% of left ventricular mass (%LV), $p = 0.340$), myocardial salvage index (51 [IQR 34–69] vs. 51 [IQR 33–69], $p = 0.830$), or microvascular obstruction (0.6 [IQR 0–2.0] vs. 0.0 [IQR 0–1.8]%LV, $p = 0.340$) between groups. Patients with AF had significantly lower left ventricular (47 [IQR 34–54] vs. 51 [IQR 44–58]%, $p = 0.003$) and left atrial (42 [IQR 17–57] vs. 53 [IQR 45–59]%, $p < 0.001$) ejection fraction. AF

was associated with MACE, even when adjusting for clinical risk factors (odds ratio = 2.48 [95% confidence interval:1.22–5.03], $p = 0.0120$) or CMR prognosis markers (odds ratio = 3.77 [95% confidence interval:1.83–7.79], $p = 0.001$).

Conclusions: This CMR study found no major differences in myocardial salvage, infarct size or microvascular damage in STEMI patients with or without AF. AF was, however, associated with cardiac dysfunction and independently related to MACE.

Clinical Trial Registration: https://clinicaltrials.gov/ct2/show/NCT00712101; NCT00712101

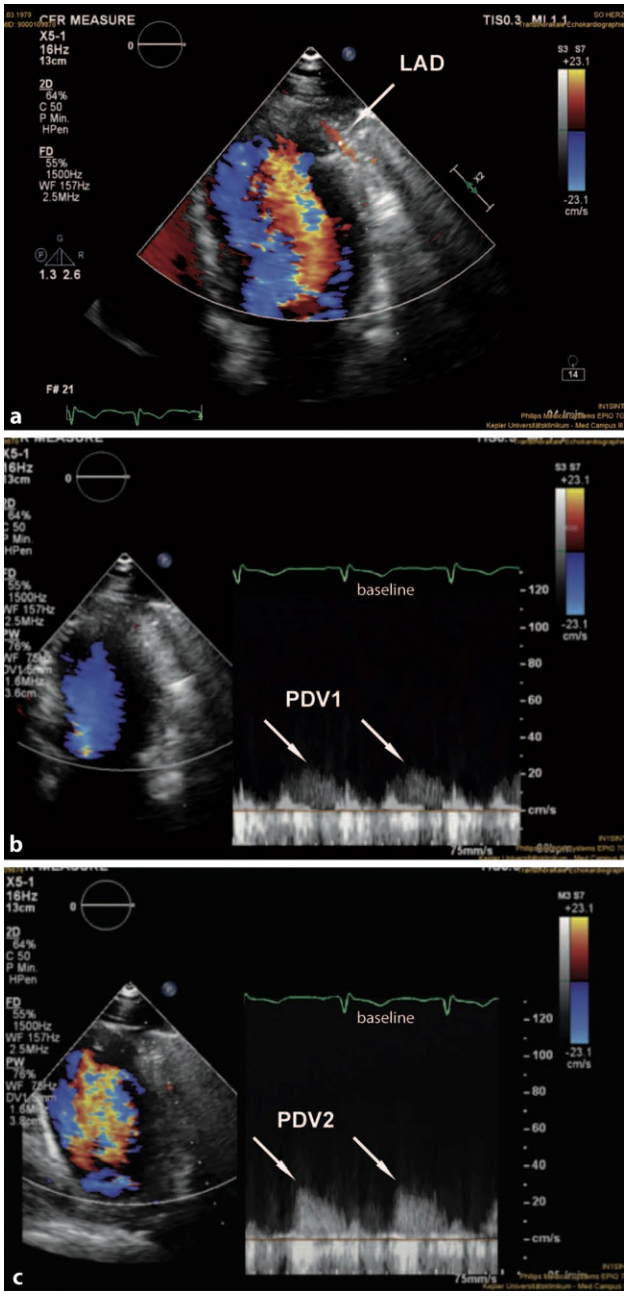

Fig. 1 | 19-4

19-4

Impaired coronary flow reserve (CFR) in clinically suspected acute myocarditis is associated with elevated markers of myocardial necrosis and larger areas of late gadolinium enhancement on cardiac magnetic resonance imaging

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Background: Acute myocarditis is accompanied by an impaired coronary microcirculation. These microcirculatory disturbances are not well defined and are derived from complex, invasive blood flow measurements. Therefore, this study aimed to evaluate coronary microcirculatory dysfunction including its association with markers of inflammatory severity (extend of late gadolinium enhancement [LGE] of cardiac magnetic resonance imaging [CMR] and laboratory markers of myocardial necrosis) using the non-invasive technique of echocardiographic coronary flow reserve (CFR) measurement.

Methods: Patients (N = 14) with clinically suspected acute myocarditis were prospectively recruited and echocardiographic CFR was determined at baseline (CFR was defined as the ratio of peak diastolic velocity measured in the left anterior descending artery at rest (PDV1) and after max. vasodilation during adenosine infusion (PDV2)). The extend of late gadolinium enhancement (LGE) in T1 weighted images on CMR was quantified using the AHA 17-segment model.

Results: 57% of all study patients showed an impaired baseline CFR. These patients were characterized by higher levels of cardiac troponin T (cTnT; 0.55 +/– 0.39 vs. 0.18 +/– 0.08; $p = 0.008$), creatinine-kinase (CK; 309 +/– 80 vs. 180 +/– 51; $p = 0.003$) and c-reactive protein (CRP; 5.8 +/– 2.8 vs. 3.5 +/– 1.4; $p = 0.087$) and larger areas of late gadolinium enhancement on CMR (total number of segments with LGE: 5.4 +/– 1.5 vs. 2.8 +/– 1.6; $p = 0.034$) in comparison to patients with normal baseline CFR.

Conclusions: An impaired coronary microcirculation is a frequent finding in clinically suspected acute myocarditis and is associated with elevated markers of inflammatory severity.

19-5

Mitral annular plane systolic excursion assessed by cardiac magnetic resonance predicts MACE after STEMI independently of EF

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Background: Following reperfused acute ST-elevation myocardial infarction (STEMI) the left ventricle (LV) undergoes structural adaptations contributing to contractile dysfunction, referred to as LV remodelling. Mitral annular plane systolic

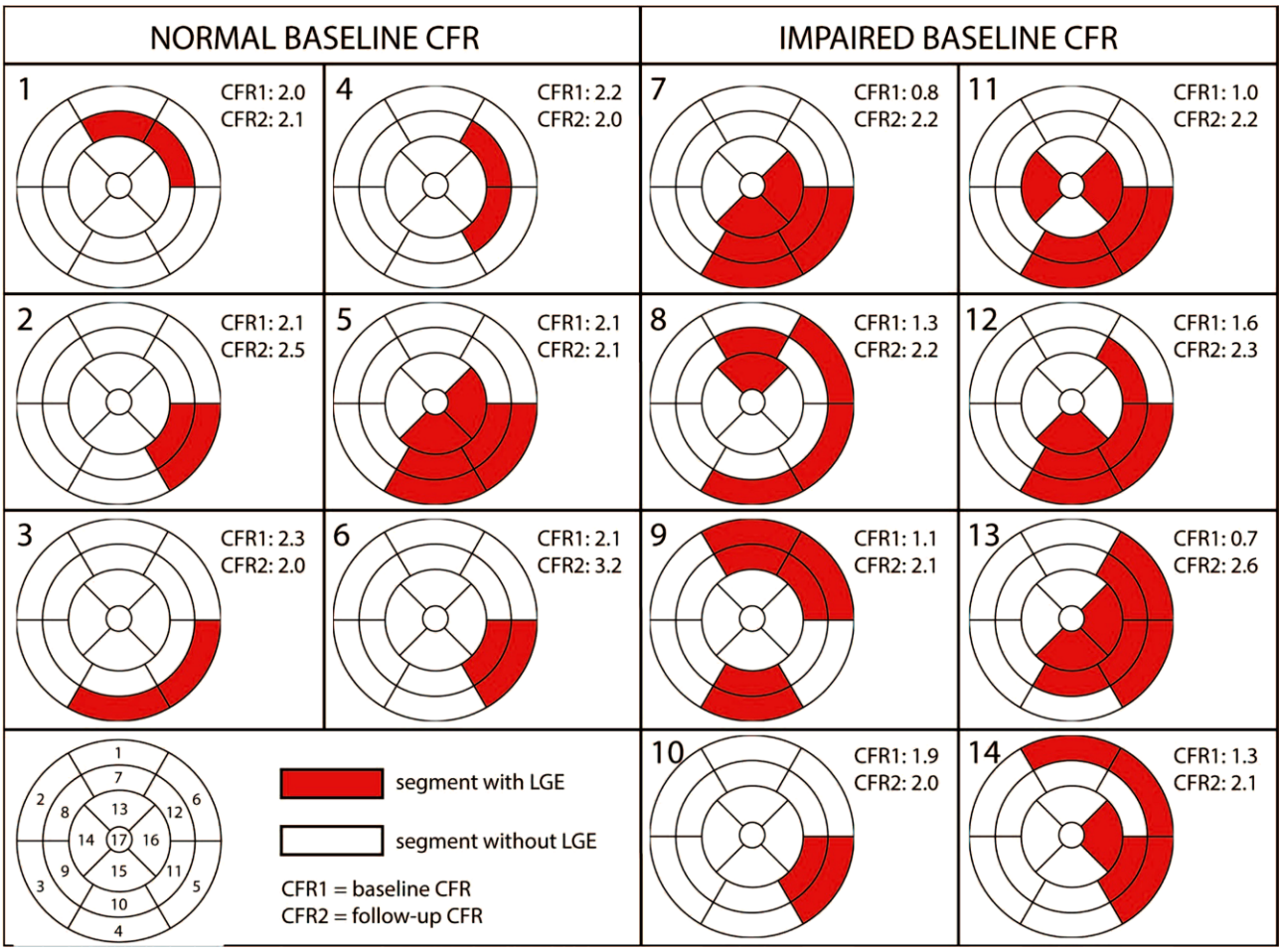

Fig. 2 | 19-4

excursion (MAPSE) measured by CINE Cardiac Magnetic Resonance (CMR) imaging has been suggested as a parameter for longitudinal left ventricular (LV) function. The aim of our study was therefore to assess whether MAPSE, as a surrogate for long axis function, is a predictor of major adverse cardiac events (MACE).

Methods: CMR was performed in 255 consecutive patients within 2 days (IQR 2–4 days) after successful interventional reperfused first acute ST-elevation myocardial infarction (STEMI). MAPSE was extracted at 4-chamber CINE SSFP view by measuring from atrioventricular plane corresponding to the septal wall at end-diastole to aortic valve closure. Patients were followed for major adverse cardiovascular events (MACE)—death, non-fatal myocardial re-infarction, stroke and congestive heart failure. Cox proportional hazards regression modeling was used to identify factors independently associated with MACE.

Results: Thirty-five MACE events (14%) occurred during a median follow-up of 3 years [IQR 1–4 years]. In ROC analysis, the AUC of MAPSE for the prediction of MACE was 0.74 [95% confidence interval (CI) 0.65–0.82] with an optimal cut-off value of 9 mm and was significantly higher than AUC of LVEF (0.61 [95%CI 0.50–0.71]; $p<0.001$). In multivariable analysis, including all significant clinical and imaging determinants of MACE, MAPSE <9 mm emerged as an independent predictor of MACE (hazard ratios >5.03 [CI 95% 2.11–12.01]; all $p<0.001$). By Kaplan-Meier analysis, patients with MAPSE <9 mm experienced significantly higher incidence of MACE than patients with a MAPSE ≥9 mm ($p<0.001$).

Conclusions: After acute STEMI, reduced long axis function assessed with MAPSE during cine-CMR is an independent long term predictor of MACE. Moreover, the evaluation of MAPSE provides significantly higher prognostic implication in comparison to routine LVEF measurement.

19-6

Relation of low-density lipoprotein cholesterol with microvascular injury and clinical outcome in revascularized ST-elevation myocardial infarction

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Background: Microvascular injury (MVI) after primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) is a major determinant of adverse clinical outcome. Experimental data indicate an impact of hypercholesterolemia on MVI, however, there is a lack of clinical studies confirming this relation. We aimed to investigate the

association of cholesterol concentrations on admission with MVI visualized by cardiac magnetic resonance (CMR) imaging and clinical outcome in STEMI patients treated by PPCI.

Methods: In this prospective observational study, we included 235 consecutive revascularized STEMI patients. Cholesterol (total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol) and triglyceride concentrations were determined at presentation. CMR scans were performed 2 [2–4] days after infarction to assess infarct characteristics including MVI. Clinical endpoint was the occurrence of major adverse cardiac events (MACE) comprising all-cause mortality, non-fatal re-infarction and new congestive heart failure.

Results: Patients with MVI ($n=129$, 55%) showed higher levels of total cholesterol (204 [172–226] vs. 185 [168–212] mg/dl; $p=0.01$) and LDL cholesterol (142 [113–166] vs. 118 [103–149] mg/dl; $p=0.001$), whereas HDL cholesterol and triglycerides did not differ significantly. In multivariable analysis including all significant clinical and CMR determinants of MVI, LDL concentration emerged as independent predictor of MVI (odds ratio 1.02 (95% confidence interval (CI): 1.01–1.02; $p=0.002$). Furthermore, increased LDL cholesterol (>150 mg/dl) significantly predicted the occurrence of MACE (hazard ratio 3.09 (95% CI: 1.22–7.87); $p=0.01$).

Conclusions: In STEMI patients undergoing PPCI, baseline LDL cholesterol concentrations were independently associated with MVI, revealing a clinically relevant link between LDL metabolism and MVI in acute STEMI.

	SR (n=122)	AFib (n=89)	P
Death	32 (23.9%)	24 (27%)	0.93
Stroke 30d	2 (1.5%)	2 (2.2%)	0.44
Stroke	5 (3.7%)	5 (5.6%)	0.14
Major Vascular Compl	4 (3.1%)	4 (4.5%)	0.25
MCI	2 (1.5%)	17 (19.1%)	0.02 *

Fig. 1 | 20-1

	APT (n=17)	OAK (n=17)	OAK+APT (n=46)	p
Age	80.4 ± 7.4	81.2 ± 7.8	82.3 ± 4.5	n.s.
Gender female	9 (52.9%)	8 (47.1%)	27 (58.7%)	n.s.
Death	8 (47.1%)	4 (23.5%)	4 (8.7%)	<0.05
Stroke 30d	1 (5.9%)	0	0	n.s.
Stroke	2 (11.8%)	2 (11.8%)	1 (2.2%)	n.s.
Major Vascular Complication	2 (11.8%)	0	2 (4.4%)	n.s.

Fig. 2 | 20-1

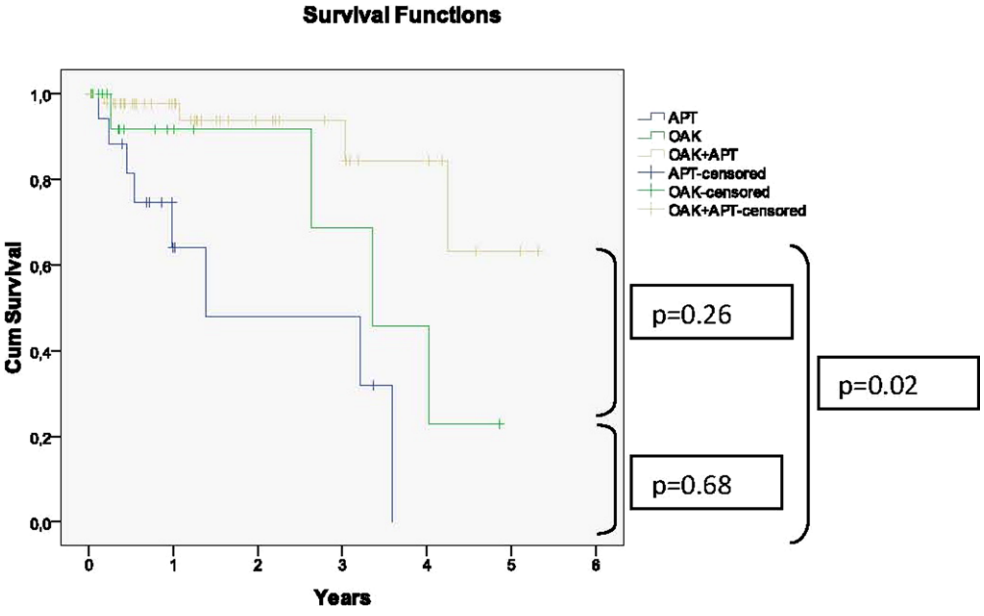

Fig. 3 | 20-1

POSTERSITZUNG 20 – Interventionelle Kardiologie 2

20-1

Antithrombotic treatment in patients undergoing transcatheter aortic valve implantation (TAVI): a single center experience

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Background: Transcatheter aortic valve implantation (TAVI) is an established treatment for high-risk and inoperable patients with symptomatic aortic stenosis (AS). Despite large-number reports of vascular complications (including major bleeding and thromboembolic events), no definite guidelines exist regarding the antithrombotic therapy after implantation in patients with indication for oral anticoagulation.

Methods: Eighty-seven patients underwent TAVI between 2008 and 2015 with atrial fibrillation (51.7% persistent), of which 47 (54%) were under oral anticoagulation prior to intervention. Endpoints were defined as all-cause and cardiac mortality, stroke and major vascular complications (VARC criteria). Baseline and follow-up medication was documented, follow-up was performed up to 6.2 years (mean 2y). Nine patients with periprocedural complications were excluded.

Three groups were defined as APT (mono or dual), OAK (vitamin K antagonists or new oral anticoagulants) and OAK+APT (mono or dual).

Results: Of 87 patients (81.6 ± 6 years, 49.4% female) with atrial fibrillation after TAVI, 20 were under antiplatelet therapy, 20 under oral anticoagulation and 46 under OAK and APT. There was no difference in age, gender or procedural mortality scores (EuroScore, STS) among the three groups. Overall mortality was 26.4%.

The mortality rate after up to 6.2 years was significantly higher in the patients with APT as compared to OAK+APT (55% vs. 10.9%, $p < 0.01$). Similarly, cardiac deaths were significantly increased in patients on APT compared to OAK alone. Stroke rate was not significantly different after 30 days ($n = 1$ (5.9%) vs. 1 vs. 0, $p = 0.5$) orafter a minimum of 3 months (10% vs. 9.5% vs. 2.2%, resp., $p = 0.6$). Similarly, overall vascular complications were not different.

Four patients under APT alone (20%) had contraindication for OAK and therefore may have been more comorbid relative to the patient cohort.

Conclusions: Patients with atrial fibrillation after TAVI may benefit from OAK+APT in regards to survival as compared to APT, while stroke rates were equal and low among patients under APT, OAK and OAK+APT.

20-2

Development of Late Lumen Loss in second generation Everolimus- versus Zotarolimus-eluting dtents at 12 and 24 month—a prospective, randomized comparison using optical coherence tomography

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Background: Large clinical outcome studies comparing ZES and EES suggested differences in the incidence of subacute stent thrombosis. The amount of intimal hyperplasia may be a better indicator of subacute endothelialization failure than endothelial coverage after one year. This study evaluates differences in Late Lumen Loss (LLL) comparing Zotarolimus- (ZES) and Everolimus-eluting (EES) second generation drug eluting stents 12 and 24 month after implantation measured with optical coherence tomography (OCT).

Methods and Results: In this study, 46 patients with 56 lesions were randomised to elective treatment with either Zotarolimus eluting stents (ZES, 23 patients with 29 lesions) or Everolimus eluting stents (EES, 23 patients with 27 lesions) and underwent OCT direct after implantation, after 12 and 24 month respectively. In a follow up of 36 patients (EES = 19 patients with 20 lesions, ZES = 17 patients with 19 lesions) after one year, stents with Zotarolimus eluting coatings showed less LLL compared to Everolimus coated stents (0.73 mm^2 vs. 1.16 mm^2 per frame, $p = 0.019$; respectively 10.8% vs. 15.7% relatively to the stent diameter, $p = 0.036$). This phaenomenon could again be observed in a follow up of 18 patients with 23 lesions (ZES = 10, EES = 13) after 24 month (0.91 vs. 1.47 mm^2 per frame, $p = 0.035$; respectively 13.6 vs. 23% relatively to the stent diameter, $p = 0.045$). In addition, stents with ZES showed a higher strut count compared to EES (1.161.2 vs. 841.2 struts, $p = 0.026$; respectively 11.5 vs. 8.6 struts per OCT frame, $p < 0.001$).

Conclusions: We conclude that ZES have lower LLL which might be related to a denser stent strut design observed. These finding may explain a higher risk for subacute ZES-thrombosis.

20-3

Discriminatory power of intensive care unit scoring systems for outcome prediction in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery

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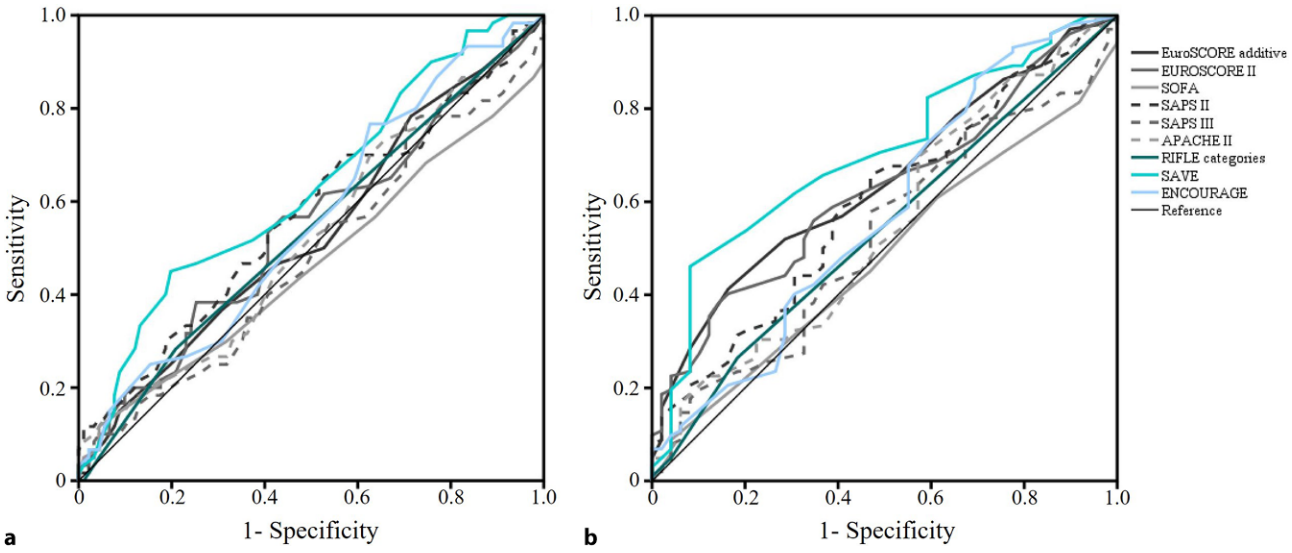

Fig. 1 | 20-3

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Background: Although extracorporeal membrane oxygenation (ECMO) represents a rapidly evolving treatment option in patients with refractory heart or lung failure, survival remains poor and appropriate risk stratification challenging, since established risk prediction models have not been validated for this specific population.

Methods: This observational single-center registry included a total of 240 patients treated with veno-arterial ECMO therapy following CV surgery and analyzed the discriminatory power of the EuroSCORE additive, EuroSCORE II, SOFA, SAPS II, SAPS III, APACHE II, the RIFLE classification, SAVE-score and ENCOURAGE score for outcome prediction.

Results: During a median follow-up time of 37 months (IQR 19–67), 65% of patients died. Only the SAVE-score and the SAPS II were significantly associated with 30-day mortality with a HR per 1-SD of 0.69 (95%CI 0.54–0.87;P = 0.002) for the SAVE-score and of 1.37 (95%CI 1.11–1.69;P = 0.004) for the SAPS II with a modest discriminatory power displayed by a C-index of 0.61 and 0.57, respectively. Six out of nine scoring systems revealed significant association with long-term mortality, with SAVE-score and SAPS II remaining the strongest predictors of long-term mortality with a HR per 1-SD of 0.70 (95%CI 0.58–0.84; P < 0.001, C-index: 0.61) for the SAVE-score and a HR per 1-SD of 1.43 (95%CI 1.20–1.70; P < 0.001, C-index: 0.58) for the SAPS II.

Conclusions: Risk assessment based on established risk models in ECMO patients remains deceptive. Only the SAPS II and SAVE-score were exclusively found suitable for short and long-term outcome prediction in this specific vulnerable patient population.

20-4

Is there an impact of left atrial appendage morphology on the incidence of peri device leaks?

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Background: In patients with atrial fibrillation and elevated stroke risk, percutaneous left atrial appendage closure (LAAC) is, according to recent ESC guidelines, an established treatment option in case of severe bleeding, ischemic stroke despite anticoagulation, incompliance with anticoagulation, or in patients with increased bleeding risk.

As the normal shape of an appendage is elliptical, there may be incomplete sealing with the LAA occluder. Residual flow into the atrial appendage may increase the risk of embolic events. We investigated the impact of LAA morphology on LAAC peri-device leaks leading to residual LAA flow despite LAAC implantation.

Methods: Our aim was to investigate a potential association between the morphology, size of the left atrial appendage or LAA device oversizing (the recommended device diameter is 10–20% bigger than the LAA ostium) and the rate of residual flows exists.

Results: Data of LAA morphology was available in 29 out of 42 patients, who underwent LAA occlusion in Graz between April 2012 and December 2017 (45% female; age 73 years; CHA2DS2VASc 4.5 ± 1.5; HAS-BLED score 3.8 ± 1.2).

There were 11 patients with chicken wing form, 7 with cauliflower form and 11 patients with wind sock form. Median ostium sizes were 20 ± 3 mm in chicken wing form, 23 ± 4 mm in cauliflower form and 18 ± 3 mm windsock form (p = ns).

21 patients received a Watchman Occluder, 5 patients had an Amplatzer Cardiac Plug and 2 patients had an Amplatzer Amulet device implanted. There were no significant differences between LAA morphology or sizes. As sole difference in the device groups, patients of the AMULET group had significant more device oversizing. Median Oversizing was 1.2 mm (range 1.0–1.8 mm).

At Follow up (153 ± 160 days), no patient had a major residual flow greater 5 mm, but in 8 patients (27.6%) a minor residual flow (<5 mm) could be found in at least one TEE. 6 of these residual flows (75%) closed spontaneously during the Follow Up period.

Minor residual flow appeared significantly more often in chicken wing form (6 patients, 54%) compared to cauliflower (n = 1, 14%) and windsock group (n = 1, 9%; chicken wing vs. others: p = 0.028).

Furthermore, LAA ostium was not significantly larger in patients in which residual flow appeared (p = ns). Lastly, the absence of LAA occluder oversizing was not significantly associated with residual flow (p = ns).

During follow up, one patient with a minimal residual flow experienced an embolic stroke.

Conclusions: These data show that the morphology but not sizeof the LAA or LAAO oversizingcontributes to the rate of residual flows. Residual flow is more common in appendages with chicken wing form. In this cohort, the only embolic event occurred in a patient with residual flow. Larger trials are needed to evaluate, whether residual flow truly predisposes for embolic events.

20-5

Primär PCI über die Arteria radialis führt zu keiner Verlängerung des Delays und ist mit verbessertem Outcome assoziiert

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Grundlagen: Während einer primären PCI (PPCI) ist der radiale im Vergleich zum femoralen Zugang mit weniger Blutungskomplikationen assoziiert, wobei eine mögliche Zeitverzögerung bis zur Wiedereröffnung des Zielgefäßes diskutiert wird.

Ziel der vorliegenden Studie war es, einen möglichen Einfluss des Zuganges auf die Dauer bis zur Reperfusion oder das intra-hospitale Outcome in der klinischen Praxis zu evaluieren.

Methodik: Für die gegenwärtige Analyse wurden Patienten aus einem multi-zentrischen Register zur Akutintervention, die zwischen Jänner 2012 und Dezember 2016 eine PPCI im Rahmen eines STEMI erhielten, herangezogen. Die in Bezug auf den Zugangsweg relevanten Zeitintervalle wie die Zeitdauer von Eintreffen im PCI-Zentrum bis zur Balloninflation („door to balloon time") als auch die Zeitdauer von Eintreffen im Katheterlabor bis zur Balloninflation („cathlab to balloon time") wurden analysiert. Ebenso wurden die in-hospitale Mortalität sowie die kombinierten Endpunkte MACE (Tod, Myokardinfarkt und Schlaganfall) und NACE (MACE und schwere Blutungen) in Abhängigkeit vom Zugang untersucht.

Ergebnisse: Insgesamt wurden 7412 Patienten eingeschlossen, wobei 2765 (37,3 %) einen radialen und 4647 Patienten (62,7 %) einen femoralen Zugang erhielten. Die „door to balloon time" betrug bei Patienten mit radialem Zugang im Median 48 min (IQR 35–75 min) und war damit etwas länger als bei Patienten mit femoralem Zugang (Median 45 min, IQR 30–67 min). Die „cathlab to balloon time" war unabhängig vom Zugang und betrug von radial im Median 23 min (IQR 18–30 min) von femoral im Median 22 min (IQR 17–30 min). In der multivariaten Regressions-Analyse unter Berücksichtigung von Alter, Geschlecht, Wiederbelebung, Diabetes und stattgehabtem Myokardinfarkt oder PCI war der radiale Zugang mit keiner zusätzlichen Zeitverzögerung assoziiert (OR 0,91, 95 % CI = 0,82–1,01, $p = 0,08$). Hingegen waren MACE (OR 0,73, 95 % CI = 0,55–0,96, $p = 0,03$) und NACE (OR 0,71, 95 % CI = 0,54–0,93, $p = 0,01$) bei diesen Patienten niedriger. Hinsichtlich der intrahospitalen Mortalität zeigte sich ebenfalls eine tendenzielle Reduktion bei Patienten die einen radialen Zugang erhielten (OR 0,74, 95 % CI = 0,54–1,01, $p = 0,06$).

Schlussfolgerungen: Der radiale Zugang beeinflusst die Zeitdauer bis zur Wiedereröffnung des Zielgefäßes nicht und führt zu einem verbesserten intra-hospitalen Outcome bei Patienten mit PPCI.

20-6

Percutaneous coronary intervention of unprotected left main stenosis and personalization of dual antiplatelet therapy: short-, mid- and long-term outcome in a real world all-comer population

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Aim: To evaluate the impact of personalization of dual antiplatelet therapy (DAPT) on short, mid- and long-term clinical outcome in all-comer patients with unprotected left main percutaneous coronary intervention (LM-PCI).

Methods and Results: Single-center cohort observation of 311 consecutive LM-PCI patients from November 2008 to January 2018 and personalization of DAPT by Multiplate Analyzer. Clinical end points (cardiovascular death, myocardial infarction, stroke, stent thrombosis of any definition, ischemia driven revascularization) were evaluated at 30 days, 1 year, and up to 9 years.

Demographics: 50% of patients presented with acute coronary syndrome (ACS) (9% STEMI, 91% NSTEMI), 5% in cardiogenic shock. Patients with stable coronary artery disease (SCAD) were treated with PCI according to the decision of the local heart team. 25% of patients were females, 33% diabetics, mean age 67 ± 12 years, (range 31–93).

Interventional details: Radial access site for LM-PCI changed over time from 4% (11/2008–6/2012) to 88% (7/2012–1/2018) ($p < 0.001$). Multivessel PCI was performed in 97% of patients with rotablation in 6%. The provisional one-stent bifurcation-PCI strategy was chosen in 68% of patients [with final kissing balloon dilatation (FKB) in 77%]. A two (or three) stent-strategy was applied in 32% (79% Crush, 11% Culotte, 5% Combinations, 3% V-Stenting, 2% T-and Protrusion) with mandatory FKB. 2nd or 3rd generation DES were used in 97%, and intravascular imaging was performed in 91% of patients.

Platelet reactivity: High on-treatment platelet reactivity (ADP ≥50 U) to clopidogrel occurred in 33%, to prasugrel in 8%, to ticagrelor in 11% of patients, and was successfully treated by either reloading or switching to prasugrel/ticagrelor (ADP changed from 70 ± 20 U to 24 ± 11 U; $p < 0.0001$). Final DAPT consisted of ASS in combination with clopidogrel (63%), prasugrel (31%) or ticagrelor (6%).

Clinical endpoints: No definite or probable stent thrombosis (0%) occurred in the overall patient cohort at any time point. Ten (6.5%) ACS patients died during the index hospitalization, mainly due to refractory cardiogenic shock. No MACCE (cardiovascular death, myocardial infarction, stroke) occurred in SCAD patients at 30 days. MACCE rates from day 31 to 1 year or long-term FUP were 3.1% and 9.1%, respectively, without differences between SCAD and post ACS patients (p = ns for all comparisons). Ischemia driven repeat revascularization occurred in 6.6% of patients at 1 year and in 17.5% at long-term FUP, mainly driven by de-novo lesions (10.1%) or LM side branch (SB)—target lesion revascularization (5.9%). SCAD patients showed higher rates of de-novo lesion PCI compared to post ACS patients at long-term FUP (13.5% vs. 6.5%, $p = 0.05$).

Conclusions: PCI of unprotected LM stenoses with consequent personalization of DAPT in a real world all-comer setting is associated with a very favorable low rate of ischemic complications at short-, mid- and long-term FUP. The incidence of

repeat revascularization at long-term FUP is primarily triggered by the occurrence of de-novo lesions and LM-SB restenosis. We suggest that platelet reactivity should be assessed routinely, at least in high-risk PCI patents. In addition, further studies regarding optimization of medical therapy for slowing CAD progression, as well as improvements in technological aspects of bifurcations-PCI for further reduction of TLR rates seem warranted.

20-7

Prognostic relevance of the SYNTAX Score in patients with coronary multivessel disease: a one-year follow-up study

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Background: Therapeutic decisions for patients with coronary multivessel disease (CMVD) have been controversially discussed in the past. The complex atherosclerotic involvement of the coronary vessels renders it difficult to decide between percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) and conservative treatment. In 2005, the SYNTAX Score was developed, which quantifies the severity of coronary heart disease and should serve as a decision-making tool for the appropriate revascularization therapy. Although recommended by ESC guidelines, the SYNTAX score is not routinely applied in clinical practice.

Methods: In this retrospective unicentric analysis, subsequent patients with CMVD were included and angiograms were scored retrospectively according to the SYNTAX score algorithm. The following major adverse cardiac and cerebrovascular events (MACCE) were defined: death, acute coronary syndrome, acute PCI, acute CABG and stroke. The prognostic relevance of the SYNTAX score was examined within a 1-year follow-up as well as its potential as a decision-making tool between PCI, CABG and conservative treatment.

Results: One-hundred-three patients (22 females, average age 68 years) were included. A SYNTAX score 0–22 was found in 29 patients (28%), 32–32 in 29 (28%) and >32 in 45 (44%). CABG was performed in 36 patients (35%), PCI in 43 (42%) and conservative treatment in 24 (23%). During one year of follow-up, MACCE occurred in 21 patients (death $n=9$, acute coronary syndrome $n=10$, stroke $n=2$, acute revascularization $n=9$). Patients with a lower SYNTAX score tended to have less MACCE than with a higher score (MACCE rate: 17% score 0–22 vs. 24% score 23–32 vs. 20% score ≥33; $p=0.806$, mortality: 0% score 0–22 vs. 14% score 23–32 vs. 11% score ≥33; $p=0.143$). Patients receiving a CABG had a higher SYNTAX score than the other groups (CABG 36 ± 10.1 vs. PCI 28 ± 11.6 vs. conservative treatment 29 ± 12.5; $p=0.005$). Patients receiving PCI did not differ in outcome from the other groups (MACCE rate: PCI 9% vs. CABG 28% vs. conservative treatment 29%; $p=0.064$, mortality: PCI 5% vs. CABG 14% vs. conservative treatment 8%; $p=0.331$).

Conclusions: The use of the SYNTAX Score for patients with CMVD might be relevant for the prognosis and decision-making in clinical practice. There is a need to investigate the prognostic value of the SYNTAX Score, regardless of the method of treatment, in large randomized trials. The use of the SYNTAX score in interventional cardiology practice should be further supported.

20-8

Der operative Aortenklappenersatz bei degenerativen Aortenklappenvitien im hohen Lebensalter

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Grundlagen: Der interventionelle, katheterbasierte Aortenklappenersatz hat sich in den letzten Jahren von einer Methode, die nur bei high-risk PatientInnen eingesetzt wurde, zu einem etablierten Verfahren entwickelt, das zunehmend auch bei intermediate- risk PatientInnen eingesetzt wird. Im Hinblick auf diese Entwicklung müssen die Ergebnisse des konventionellen, chirurgischen Aortenklappenersatzes kritisch hinterfragt werden. Ziel dieser Studie war es, die Ergebnisse des isolierten chirurgischen Aortenklappenersatzes bei degenerativen Aortenklappenstenose zu evaluieren.

Methodik: Inkludiert wurden alle PatientInnen, die zwischen 2009 und 2017 aufgrund einer degenerativen Aortenklappenstenose an unserer Abteilung mittels Aortenklappenersatz ohne Zusatzeingriff operiert wurden. PatientInnen mit reiner Aortenklappeninsuffizienz, einer Re-Operation oder einer aktiven infektiösen Endokarditis wurden exkludiert.

Aus den lokalen Datenbanken wurden PatientInnenalter, Klappentyp, -durchmesser, -kuspidität, perioperative echokardiographische Befunde, Aortenklemm- und Bypasszeit, Euroscore (logistisch und Euroscore II ab 2012), operativer Zugang, Krankenhausaufenthaltsdauer und folgende Komplikationen evaluiert: 30 Tage-Mortalität, Schlaganfall, TIA, Vorhofflimmern, Schrittmacherimplantation, Nierenversagen, Dialysepflichtigkeit, Reoperation aufgrund von Nachblutungen und Wundinfektionen.

Es erfolgte eine Stratifizierung in Altersgruppen sowie nach Risiko (logistischer Euroscore >20 % = high-risk; Euroscore II <2 % = low-risk, 2–7 % = intermediate-risk, >7 % = high-risk). Die Datenanalyse wurde mittels deskriptiver Statistik durchgeführt.

Ergebnisse: Insgesamt wurden 517 Patienten operiert, davon 380 über eine mediane Sternotomie (73,5 %), 122 über eine Hemisternotomie (23,6 %) und 15 über eine rechtsanteriore Thorakotomie (2,9 %).

Das mittlere Alter lag bei 70,6 ± 9,0 Jahren, wobei im Verlauf ein tendenzieller Rückgang des Durchschnittsalters und der PatientInnengruppe der über 80-Jährigen bei Zunahme der Gruppe der 71- bis 80-Jährigen zu erkennen war. Von 2009 bis 2012 kam es zu einer deutlichen Abnahme des Anteils von HochrisikopatientInnen, der im weiteren Verlauf konstant blieb. Ab 2012 kam es zu einer Zunahme von PatientInnen im low-risk Bereich bei deutlicher Abnahme im intermediate-risk Bereich.

Im Gesamtkollektiv lag die 30-Tage Mortalität bei 1,5 %, das Auftreten eines Schlaganfalles bei 1 %, TIA 1,4 %, Dialyse 1,4 %, Schrittmacherimplantation 6 %, Nachblutungen 3,5 %, Wundinfektionen 2,1 %, postoperativ intermittierendem Vorhofflimmern bei 31,3 %.

Die Komplikationsraten zeigten bei den über 75-Jährigen ($n=203$) im Vergleich zu den unter 75-Jährigen ($n=314$) folgende Unterschiede: 30-Tage Mortalität 2,5 %/1,0 %, Schlaganfall 2,0 %/1,6 %, TIA 0,5 %/1,9 %, Dialyse 3,9 %/0,3 %, Schrittmacherimplantation 7,9 %/4,5 %, Nachblutung 4,4 %/3,5 %, Wundinfektion 2,0 %/2,5 %, postoperativ intermittierendes Vorhofflimmern 38,4 %/26,8 %.

Schlussfolgerungen: Im Beobachtungszeitraum nahm die Anzahl an high-risk PatientInnen erwartungsgemäß ab. Bei low- und intermediate-risk PatientInnen kann der konventionelle, chirurgische Aortenklappenersatz weiterhin mit einer sehr niedrigen Mortalitäts- und Komplikationsrate durchgeführt werden. Bei PatientInnen über 75 Jahren und erhöhtem operativen Risikoscore ist eine individualisierte und interdisziplinäre Therapieplanung unter Einbeziehung des katheterbasierten Aortenklappenersatzes (TAVI) unerlässlich.

20-9

ANP Expression after left atrial appendage occlusion in porcine model: A new marker to predict peri-device leaks?

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Background: Atrial fibrillation (AF) is the most common heart arrhythmia with high clinical relevance, especially in the elderly population with an incidence up to 10% and high risk on strokes and other thromboembolic events. On the other hand, triple anticoagulation of patients with recent vascular stent or percutaneous valve implantation and AF carries a high bleeding risk. Left atrial appendage (LAA) closure offers an alternative therapy to oral anticoagulation in patients with nonvalvular AF, who are at risk for thromboembolic or major bleeding complications. However, incomplete closure of the LAA with peri-device leaks (up to 30%) or incomplete endothelialisation may result multiple thromboembolic events with eventually fatal complications. Atrial natriuretic peptide (ANP) is released by the atrial myocytes and its level is associated with LAA function. Our aim was to measure the plasma ANP level before, immediately after and at 3-month follow-up after LAA occluder implantation, to test the prognostic value of ANP in detection of peri-device leaks.

Methods: Young adult Yorkshire pigs ($n=16$) underwent percutaneous LAA occlusion (device constructed for research purpose only) under general anaesthesia and transoesophageal ultrasound (TEE) guidance, while 6 pigs served as controls. Plasma levels of ANP were measured by porcine specific ELISA kit (Uscn Life Science Inc).

Results: Based on control angiography and TEE, 6 device showed incomplete closure of the LAA immediately after device placement (Group LAA-Leak), while 10 devices successfully occluded the LAA (Group LAA) (Figure). Baseline ANP did not differ between the groups. Plasma ANP increased significantly immediately after procedure in the Group LAA-Leak as compared to Group LAA and controls (96.5 ± 123.8 vs 13.1 ± 13.8 and 13.4 ± 14.7 pg/mL; $p<0.05$). At the 3 months follow-up, TEE and control angiography with subsequent histology confirmed the device leak and incomplete endothelialization in animals of Group LAA-Leak, while endothelialisation of the device with complete closure of the LAA was seen in the pigs in Group LAA. At the 3-month follow-up, plasma ANP was significantly elevated in Group LAA as compared to controls (71.2 ± 62 vs 41.2 ± 30.5 pg/mL, $p<0.001$), while in group LAA-Leak, ANP was further increased to 515.4 ± 204.8 pg/mL ($p<0.001$).

Conclusions: Serial measurements of plasma ANP post LAA closure procedure might predict the incomplete closure of the LAA, with the clinical relevant information of persisting risk of thromboembolic event.

POSTERSITZUNG 21 – Vitien

21-1

Determinants of bioprosthetic heart valve degeneration

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Background: Structural valve deterioration (SVD) is a major determinant of valve durability in bioprosthetic heart valves. We sought to assess incidence, mode, and associated factors of SVD in the present long-term prospective study.

Methods: 521 consecutive patients (73.4 ± 7.9 years old; 57.2% female) underwent surgical bioprosthetic aortic ($n=480$), mitral ($n=39$), or tricuspid ($n=2$) valve replacement between 1994 and 2014 and were prospectively enrolled. Patients underwent clinical assessment, transthoracic echocardiography, and laboratory testing at baseline and at follow-up visits. SVD was defined as an elevated mean transprosthetic gradient (≥30 mmHg for aortic, ≥10 mmHg for mitral valves) and/or at least moderate valvular regurgitation. Patient prosthesis mismatch (PPM) was defined as an effective orifice area indexed to body surface area ≤0.8 cm2/m2 for aortic and ≤1.2 cm2/m2 for mitral valves.

Binary logistic regression analyses were used to identify factors associated with SVD, Kruskal Wallis analysis was used to compare mean delays to SVD in different age groups.

Results: Patients were followed for a mean of 55.7 ± 42.7 months. By echocardiography, 74 patients (20.9%) developed SVD. Modes of SVD were stenosis ($n=47$), regurgitation ($n=17$), or both ($n=10$). Mean delay to SVD was 54.5 ± 49.6 months. Factors associated with SVD were PPM (odds ratio [OR] = 3.06; 95% confidence interval [CI] 1.57–5.95; $p=0.001$), glomerular filtration rate ≤45 ml/min (OR = 2.93; 95% CI 1.23–6.98; $p=0.015$) and male sex (OR = 2.16; 95% CI 1.14–4.09; $p=0.018$), whereas arterial hypertension (OR = 2.13; 95% CI 0.95–4.75; $p=0.066$) slightly failed to reach level of significance. Age (<70y: 21.3% [$n=23$], 70–80y: 19.9% [$n=38$], >80y: 24.5% [$n=13$]; $p=0.738$) was not associated with development of SVD. Mean delay to SVD, however, was significantly shorter in the elderly (<70y: 44.0 months, 70–80y: 39.0 months, >80y: 21.3 months; $p=0.008$).

Conclusions: Based on echocardiographic criteria we observed a high incidence of SVD in bioprosthetic heart valves. SVD was significantly associated with PPM, renal impairment and male sex but not with age. Mean delay to SVD was significantly shorter in elderly patients.

21-2

Long-term experience with mechanical aortic valve prostheses after one-third of a century

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Background: Mechanical valve replacement is considered a well-proven therapeutic option for aortic valve diseases in young and middle-aged adults compared to biological counterparts. However, valve related complications may impair long-term outcome. The goal of this study was to evaluate hazards focussing on mechanical prostheses in the aortic position and observing their long-term survival, rate of re-operations and the occurrence of major adverse events in a single centre analysis.

Methods: 1730 mechanical aortic valve implantations were recorded at the Medical University of Vienna/General Hospital Vienna from 1983 to 2008. Patients with acute indications, endocarditis, aortic dissections and combined procedures were not excluded. Information on patients' characteristics, risk factors, surgical details and survival were provided by the documentation system of the department and further through a cross-

Adverse event	Patients	Total records	Linearized incidence
Valve thrombosis	0.9%	14	0.1%
Endocarditis	3.1%	52	0.4%
Stroke	11.1%	204	1.4%
Transient ischemic attacks	3.9%	60	0.4%
Non-cerebral embolism	1.8%	29	0.2%
Myocardial infarction	12.2%	216	1.5%
Non-structural valve dysfunction	9.5%	152	1.1%
Structural valve dysfunction	0.1%	2	0.01%
Bleeding	28.3%	611	4.3%
Reoperation (bleeding)	6.6%	114	-
Early revisions	2.4%	38	-

Fig. 1 | 21-2 Incidences of adverse events

Adverse event		Patients	Total records	Linearized incidence
Carbomedics	Valve thrombosis	0.8%	6	0.1%
	Endocarditis	2.7%	20	0.3%
	Stroke	12.4%	102	1.4%
	Transient ischemic attacks	4.6%	34	0.5%
	Non-cerebral embolism	1.6%	13	0.2%
	Bleeding	28.7%	283	3.9%
	Re-AVR	4.4%	32	0.4%
Adverse event		**Patients**	**Total records**	**Linearized incidence**
Duromedics	Valve thrombosis	0.3%	1	0.03%
	Endocarditis	3.9%	14	0.5%
	Stroke	12.8%	47	1.5%
	Transient ischemic attacks	3.3%	11	0.4%
	Non-cerebral embolism	1.2%	4	0.1%
	Bleeding	31.8%	137	4.5%
	Re-AVR	5.0%	17	0.6%

Fig. 2 | 21-2 Incidences of adverse events for Carbomedics & Duromedics

sectional telephone follow up. Valve related adverse events and mortality were evaluated according to the current guidelines. The mean follow-up was 138 years (range 0–32 years).

Results: 625 (36%) female and 1105 (64%) male patients with a mean age of 5513 years were included. Most frequent prostheses were the Carbomedics (791; 46%) and the Duromedics (375; 22%) aortic valve with a mean size of 23.02.0 mm. 256 (15%) had a preceding cardiac surgery. 808 (47%) underwent concomitant cardiac procedures; 307 (18%) received a mitral valve in addition to the aortic valve surgery. 116 patients (6.7%) died during the first 30 days. Over-all mortality was 57.5% ($n=995$). The actuarial survival estimates were 78%, 64%, 51% and 39% at 5, 10, 15 and 20 years after surgery. Valve related adverse events are reported (Fig. 1 and 2).

Conclusions: We conclude that valve-related adverse events were increased within our real-world, all-comer study population compared to previous results in the literature. Studies with novel mechanical valve prosthesis or other surgical approaches are required to assess the outcome of current surgical therapies for young patients. However, we want to raise awareness for the long-term risk of adverse events after mechanical aortic valve replacement.

21-3

Extracellular volume by CMR for risk assessment in patients undergoing mitral valve surgery

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Background: Timing of mitral valve (MV) surgery for severe mitral regurgitation (MR) remains controversial. Structural remodeling with uncertain reversibility might already be advanced when class I triggers occur.

Aim: To study morphological, functional and prognostic impact of cardiac MR derived left ventricular extracellular volume (ECV) to predict event-free survival in Patients with class I triggers undergoing MV surgery.

Methods: 78 Patients (39% female, 61% male) with severe mitral regurgitation and class I trigger for MV surgery were prospectively enrolled. In addition to standard clinical and laboratory measurements, CMR-T1 mapping with the modified look-locker inversion recovery sequence was used to quantify ECV—a key feature of structural remodeling. Patients were stratified according to the median ECV of 28%. All patients underwent MV surgery for severe MR. Event-free survival was used as the primary endpoint.

Results: 53% of Patients with class I indication scheduled for mitral valve surgery had an ECV≥28%. There were no differences in age, sex, body surface area, symptomatic status and baseline NT-pro-BNP levels according to an ECV≥28%. CMR revealed larger left ($P=0.066$) and right atrial ($P=0.01$) size, more eccentric left ($P<0.01$) and right ventricular ($P=0.015$) remodeling and more functional impairment ($P<0.01$) in patients with an ECV≥28%. There was a trend towards longer admission times after mitral valve surgery in patients with an ECV≥28% ($P=0.08$). During a median follow-up of 1015 days (IQR 574–980) 13 events occurred. Kaplan-Meier analysis demonstrated an increased risk of events in patients with an ECV≥28% (log-rank P = 0.021, Figure). ROC AUC for event-free survival was 0.83 for ECV and 0.68 for NT-pro-BNP. Cox-regression confirmed significant increased events in patients with an ECV≥28% independently of NT-pro-BNP with an adjusted HR of 1.3 (95%CI 1.05–1.61; $P=0.015$).

Conclusions: A significant proportion of patients with class I trigger for mitral valve surgery has increased ECV suggesting structural myocardial damage with uncertain reversibility. CMR quantified cardiac size and function confirms an association of

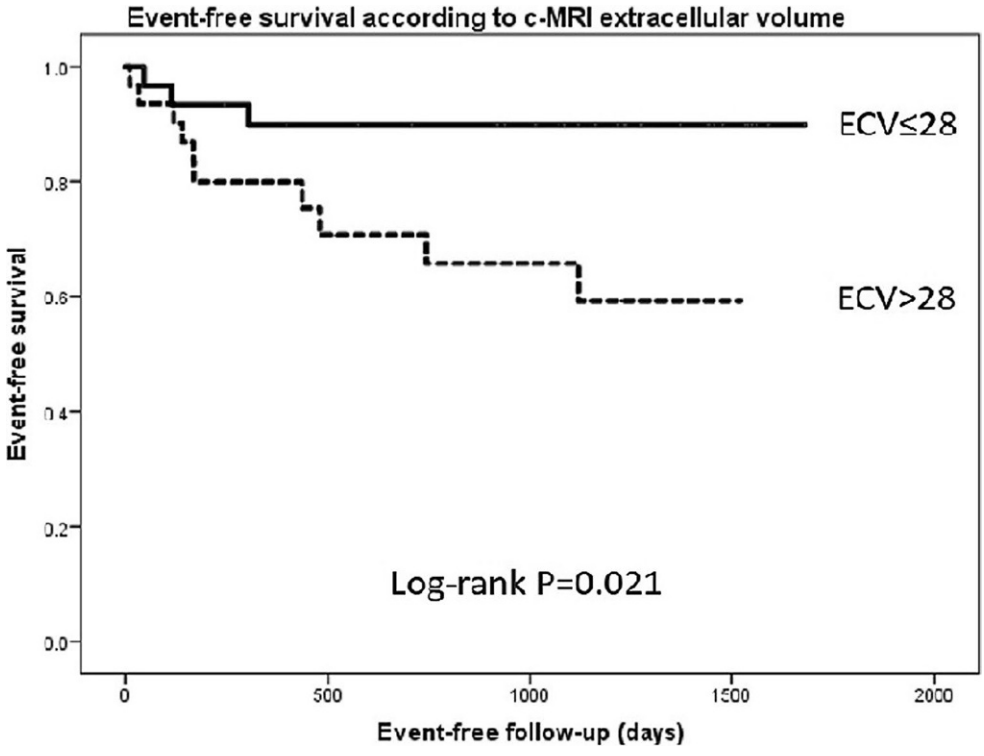

Fig. 1 | 21-3

eccentric remodeling with expansion of extracellular volume. ECV expansion conveys an increased risk, independently of NT-pro-BNP. Further research is warranted to define a possible role of ECV to optimize timing of surgery for severe mitral regurgitation in order to reduce hospital admission times and long-term morbidity and mortality.

21-4

Quantification of fluid status using bioelectrical impedance spectroscopy: a predictor of outcome in patients with valvular heart disease

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Background: Volume overload is a main cause for chronic disease burden in patients with valvular heart disease (VHD). Fluid overload requiring hospitalization is not only associated with high mortality rates but also a major economic challenge for the healthcare system. So far, clinical assessment of fluid status is limited to presence of leg edema, distension of jugular veins, progression of dyspnoea, or weight gain, lacking both specificity and reliability.

Bioelectrical impedance spectroscopy (BIS) is a validated non-invasive way to assess fluid status in patients undergoing haemodialysis. However, the usefulness of BIS in VHD patients has not been studied so far.

Methods: Patients with moderate or severe VHD by transthoracic echocardiography were invited to undergo fluid status assessment using BIS at baseline and were prospectively followed. Patients with clinically overt cardiac decompensation were excluded. The primary end-point was a composite of heart failure requiring hospitalization and cardiovascular death. Kaplan-Meier estimates and multivariable Cox-regression analysis were used to identify factors associated with outcome.

Results: 164 (53% female, 72 ±13 years) were included. 39.0% suffered from mitral regurgitation, 29.3% from aortic stenosis, and 27.4% from tricuspid regurgitation. The remaining 4.3% were patients with aortic regurgitation, mitral stenosis, or combined lesions.

The median of overhydration (OH) was +0.7 liters and patients were stratified by this cut-off into two groups. There was no association between fluid status and diabetes ($p=0.888$), arterial hypertension ($p=0.468$), coronary artery disease ($p=0.110$), the type of valve lesion ($p=0.095$), renal function ($p=0.639$), left ventricular size ($p=0.796$), or left and right ventricular function ($p=0.408$ for LVEF and $p=0.285$ for FAC). Also, age ($p=0.787$), height ($p=0.480$), and weight ($p=0.222$) had no influence on the OH status. Interestingly, NYHA class did not correlate with fluid status ($p=0.333$).

However, NT-proBNP levels were significantly elevated in patients with OH > +0.7 liters (7228 ± 7798 versus 3680 ± 4897 ng/l, $p<0.001$).

A total of 38 events (23.3%) occurred during a follow-up of 16 ± 11 weeks. Patients with a fluid overload were more likely to experience an event (32.9% in OH > +0.7 liters versus 14.3% in OH ≤+0.7 liters; log-rank, $p=0$–006; Fig. 1).

By simple Cox-regression analysis, previous myocardial infarction (HR 2.276 [1.175–4.409], $p=0.015$), NT-proBNP levels (HR 1.912 [1.386–2.638] when logarithmized, $p<0.001$), renal function (eGFR, HR 0.972 [0.948–0.998], $p=0.034$), and fluid status (HR 1.212 [1.070–1.372] per liter, $p=0.002$) were associated with outcome.

In a multivariable Cox-regression model (Fig. 2), only fluid status remained significantly associated with survival (HR 1.197 [1.006–1.424] per liter, $p=0.033$).

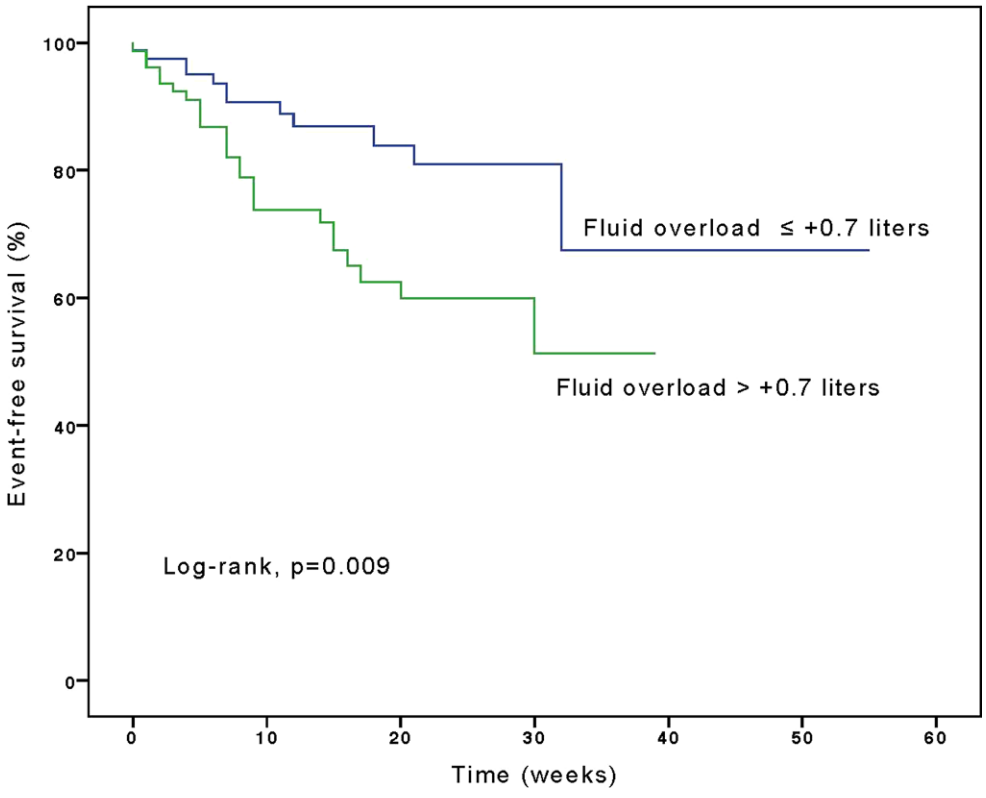

Fig. 1 | 21-4

Cox-regression analysis		Univariable	Multivariable
	p-value	Hazard Ratio (95% CI)	p-value
Clinical Parameters			
Age (yr.)	0.189	1.020 (0.990-1.052)	
Weight (kg)	0.954	0.999 (0.981-1.018)	
Hypertension	0.046	4.280 (1.026-17.858)	0.070
Atrial Fibrillation	0.687	1.151 (0.580-2.283)	
Diabetes	0.124	1.698 0.865-3.333)	
Hyerlipidemia	0.241	0.674 (0.349-1.303)	
Coronary artery disease	0.533	1.231 (0.640-2.366)	
Previous myocardial infarction	0.015	2.276 (1.175-4.409)	0.696
NYHA class	0.690	1.083 (0.733-1.599	
eGFR (ml/min/1.73m^2)	0.034	0.972 (0.948-0.998)	0.116
NT-proBNP (log; ng/l)	0.000	1.912 (1.386-2.638)	0.341
Echocardiographic Parameters			
Left atrial size (mm)	0.233	1.018 (0.989-1.048)	
Right atrial size (mm)	0.098	1.022 (0.996-1.049)	
LV end-diastolic volume (ml)	0.183	1.008 (0.996-1.020)	
RV end-diastolic diameter (mm)	0.480	1.014 (0.976-1.054)	
LV ejection fraction (%)	0.419	0.983 (0.944-1.024)	
RV fractional area change (%)	0.469	0.971 (0.895-1.052)	
Type of valvular lesion	0.505	0.918 (0.714-1.180)	
Bioelectrical Impedance Spectroscopy			
Fluid status (liter)	0.002	1.212 (1.070-1.372)	**0.033**

LV indicates left ventricle; RV, right ventricle.

Fig. 2 | 21-4

Conclusions: Quantitative assessment of fluid status using BIS is significantly associated with cardiovascular events in patients with VHD and outperformed NT-proBNP as a predictor of outcome in our cohort. Routine use of this non-invasive technique could help guiding diuretic treatment and reduce disease burden.

This study was registered at clinicaltrials.gov (NCT03372512).

21-5

Right and left heart failure due to carcinoid heart disease complicated by a PFO with right-to-left shunt: a case report with analysis of novel cardiovascular biomarkers

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Background: Carcinoid syndrome is a rare cause for acquired valvular heart failure. Carcinoid heart disease (CHD) occurs in 20–70% of the patients with carcinoid tumors leading to fibrotic remodeling of valvular structures, however due to degradation of serotonin in the pulmonary circulation usually only the right heart is involved. Here, we report the case of a 57-year-old woman presenting with heart failure due to carcinoid syndrome.

Case Report: The patient was admitted to our clinic because of dyspnea and edema of the lower extremities. Transthoracic and transesophageal echocardiography showed very severe tricuspid regurgitation and severe mitral regurgitation. The leaflets of the tricuspid valve almost showed no motion at all. This pattern is typical for carcinoid heart disease caused by direct negative effects of serotonin in the right heart circulation leading to fibrosis of the leaflets. Furthermore, a small PFO with right to left shunt was found. We performed urine analysis screening for 5-hydroxyindoleacetic acid excretion, which proved to be severely elevated. Also serotonin (596 U/l) and chromogranin A (1248 µg/l) levels were elevated more than ten-fold. Next, we conducted a PET-CT scan which revealed a tumorous mass within in the liver. The primary tumor was thought to be located in the terminal ileum. Based on these results we hypothesized that the cause for the described symptoms was heart failure due to carcinoid heart disease. A medical therapy with the somatostatin analogue lanreotide together with heart failure treatment was started.

It was also found that the mitral valve was severely affected by fibrosis. We think that this was caused by direct serotonin-related effects due to the right to left shunt through the PFO leading to fibrosis of the mitral valve leaflets. A tricuspid valve replacement (Edwards St. Jude Epic, 33 mm bioprosthesis) and mitral valve repair (Edwards Physio Ring, 30 mm) was conducted successfully together with closure of the PFO and the patient showed good convalescence. This was also documented with decreasing levels of pro-BNP over the follow-up period (from 7830 pg/ml to 982 pg/ml). Moreover, we performed an analysis of cardiovascular biomarkers (IL-8, sST-2, H-FABP and IGF-BP2). Also here a decreasing trend was documented over the whole follow-up (Fig. 1).

Two months later, a hemicolectomy and liver segment resection (segment VI/VII and III) was performed. The tumor metastasis in the liver was extirpated and the (immuno-)histological analysis confirmed the diagnosis (neuroendocrine tumor of the terminal ileum).

The patient was followed-up for further 2 years and presented herself in good health without signs of recurring heart

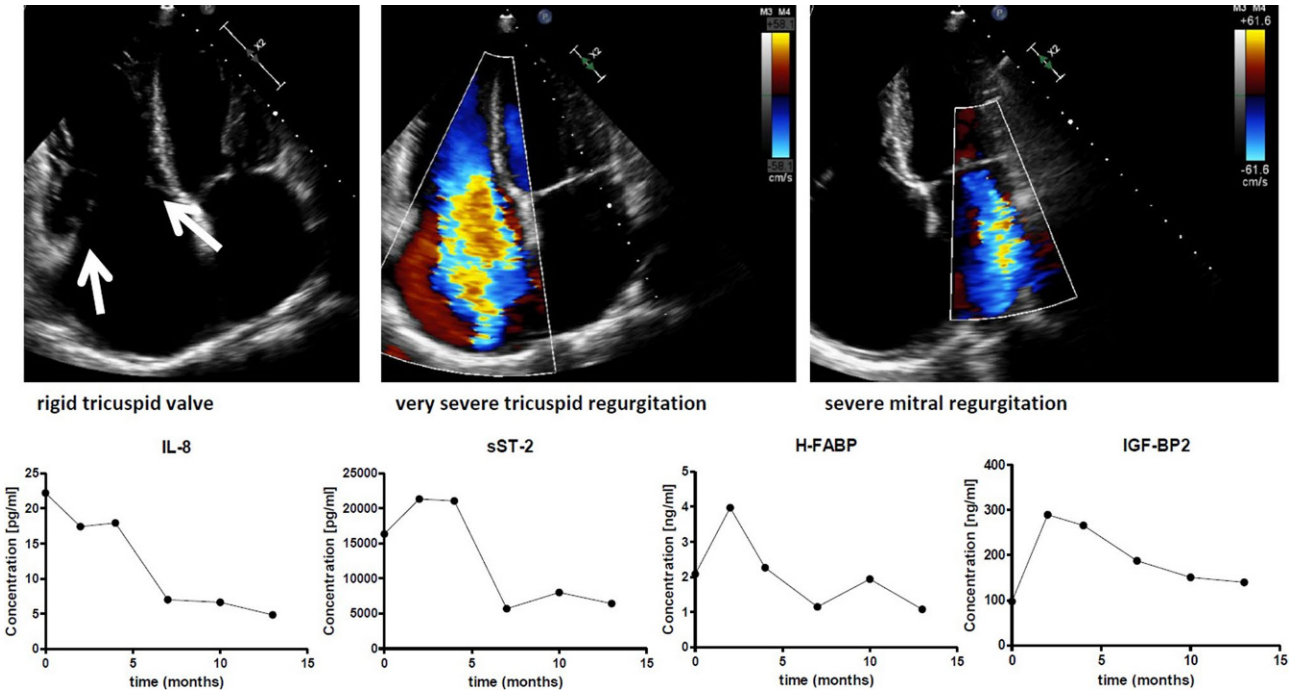

Fig. 1 | 21-5

failure. At the recent follow-up exam including MRI of the abdomen new metastases were found in the liver and the patient is scheduled to undergo another liver segment resection.

This case is unique since the patient developed both right and left ventricular dysfunction due to fibrotic remodeling of not just the tricuspid valve as usually seen in carcinoid heart disease but also fibrosis of the mitral valve because of right to left shunt through a patent PFO.

21-6

Prognostic implications of psoas muscle area in patients undergoing transcatheter aortic valve implantation

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Background: This study sought to assess the incremental prognostic value of psoas muscle area (PMA) in patients scheduled for transcatheter aortic valve implantation (TAVI).

Methods: A total of 1076 consecutive patients undergoing TAVI in two centers were prospectively included between 2010 and 2017. Computed tomography derived cross sectional area of the psoas muscle was measured at the superior border of the third (L3) and fourth (L4) lumbar vertebra and indexed to body surface area (PMAi) as well as stratified into tertiles. Multivariable logistic regression and cox regression analysis was performed to investigate the value of PMAi as predictor of 30-day and cumulative mortality. The incremental prognostic value of PMAi over the Society of Thoracic Surgeons (STS) score was assessed using net reclassification analysis.

Results: The rate of 30-day mortality was 5.8% ($n=62$). PMAi at the level of L3 (odds ratio (OR): 0.082; 95% confidence interval (CI) [0.011–0.589]; $p=0.013$) and L4 (OR: 0.049; 95% CI [0.005–0.536]; $p=0.013$) independently correlated with 30-day mortality. During a median follow-up of 435 days (interquartile range [IQR]: 139–904), 292 patients (27.1%) died. PMAi of L3 (HR: 0.200; 95% CI [0.083–0.482]; $p<0.001$) and L4 (HR: 0.083; 95% CI [0.029–0.235]; $p<0.001$) were independently associated with mortality during follow-up. The addition of PMAi to the STS score led to a net reclassification improvement for 30-day and cumulative mortality ($p<0.05$).

Conclusions: PMAi emerged as valuable outcome predictor in patients undergoing TAVI. The addition of PMAi to the established STS score leads to an incremental prognostic value over the STS score.

21-7

Recurrent prosthetic mitral valve thrombosis

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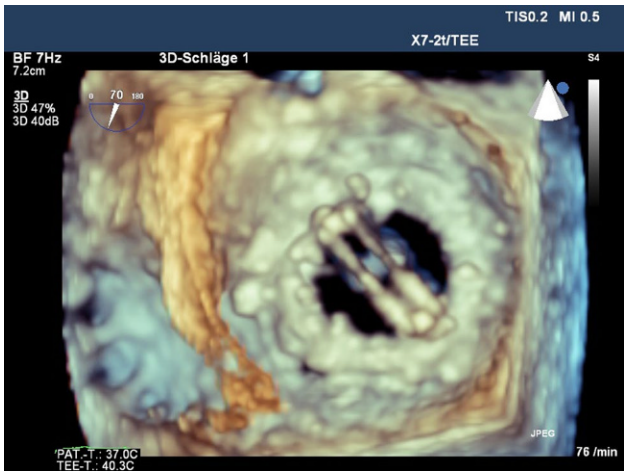

Fig. 1 | 21-7

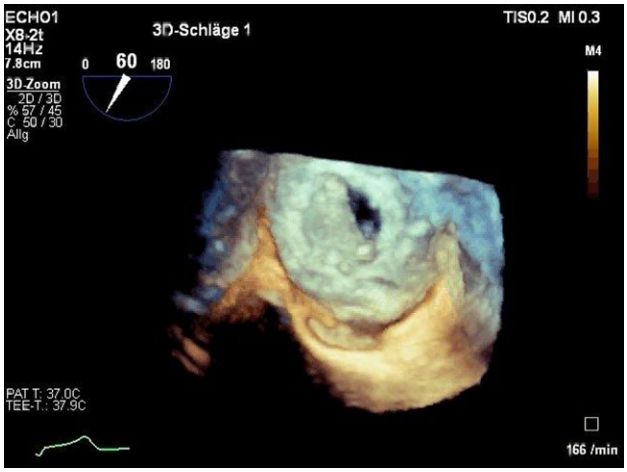

Fig. 2 | 21-7

Background: Prosthetic mitral valve thrombosis is a life threatening complication after mechanical mitral valve replacement and is associated with high morbidity and mortality. The incidence is 0.5% to 8% despite anticoagulation therapy.

We report a case of recurrent obstructive prosthetic mitral valve thrombosis, initially treated with emergency surgical valve re-replacment and at recurrence successfully treated with fibrinolysis.

Case Report: A 65 year old man with a history of mechanical prosthetic mitral valve replacement (St. Jude Medical 25 mm) 4 years earlier presented with progressive shortness of breath over the last 6 month. Transthoracic echocardiography revealed prosthetic mitral valve stenosis with a transmitral mean gradient of 25 mmHg and severe pulmonary hypertension (systolic pulmonary artery pressure 85 mmHg). Transesophageal echocardiography confirmed a frozen mitral leaflet and a 5 mm nonmobile mass adjacent to the sewing ring, highly suspicious of pannus formation. During the hospital stay the health status deteriorated with right heart failure and multi organ dysfunction. Cine fluoroscopy showed complete immobility of one leaflet and limited mobility of the other. Emergency redo mitral valve replacement was performed (St. Jude medical 27 mm). The obstructive mass on the valve was histological classified as organized thrombus. The postoperative course was uneventful.

Eight months later the patient was readmitted because of dyspnea. Transthoracic and transesophageal echocardiography again revealed prosthetic valve stenosis with a mean gradient of 20 mmHg due to immobility of a prosthetic leaflet. Intravenous unfractionated heparin (UFH) in combination with acetylsalicylic acid (ASS) over two days had no effect on prosthesis function. Therefore, despite a history of traumatic cerebral haemorrhage 10 years before, fibrinolysis with recombinant tissue plasminogen activator was initiated. The transmitral Doppler mean gradient significantly decreased to 5 mmHg within hours after initiating fibrinolytic therapy. As subtherapeutic INR values (2.0–2.5) were reported the weeks before symptoms ocurred, anticoagulation management was intensified (repeat in-hospital controls with target INR 3.0–3.5) and ASS was continued.

Discussion: Prosthetic valve obstruction can result from thrombus, pannus overgrowth, vegetations or combinations of these. A history of sub-optimal anticoagulation and the post-op time course are useful clinical characteristics for differentiation between thrombus and pannus formation.

Prosthetic valve thrombosis mainly occurs in mechanical prostheses but has also been reported in bioprostheses (surgical as well as transcatheter valves). Whereas anticoagulation using a vitamin K antagonist and/or UFH is the first line treatment for bioprostheses, urgent valve replacement is recommended for symptomatic obstructive thrombosis of mechanical valves (ESC guidelines, class I). Fibrinolysis should be considered when surgery is not available or very high risk or for thrombosis of right-sided prostheses (ESC guidelines, class IIa).

Conclusions: In case of prosthetic valve stenosis thrombus or pannus have to be differentiated. Fibrinolysis may be effective for acute and subacute obstructive valve thrombosis with acceptable risk considering the life-threatening condition. Before planning high risk redo surgery, fibrinolysis should be considered for mechanical valve thrombosis.

POSTERSITZUNG 22 – Rhythmologie 3

22-1

Regionale postinterventionelle Perikarditis nach antraler Pulmonalvenenisolation-Fallbericht

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Grundlagen: Entsprechend den ESC-Guidelines von 2015 kann eine akute Perikarditis diagnostiziert werden, wenn zumindest zwei von vier der folgenden Kriterien erfüllt sind: 1) Thoraxschmerz, 2) Perikard-Reiben, 3) neue ST-Elevation oder PR Depression im EKG, 4) Perikarderguss.

Die Perikarditis kann infektiös bedingt sein (viral, bakteriell, fungal, parasitär) oder hat eine nicht infektiöse Ursache (Autoimmunologisch, neoplastisch, metabolisch, traumatisch und iatrogen, medikamentös induziert, Amyloidose, Aortendissektion, Pulmonale Hypertonie, Herzinsuffizienz). Traumatische Ursachen können direkt (Perforation) aber auch indirekt bedingt sein (nach MCI, Postperikardiotomie-Syndrom, post PCI, nach Schrittmacher-Sondenimplantation oder auch nach Radiofrequenzablation); bei unserem Patienten traten die klinischen Zeichen einer Perikarditis Stunden nach erfolgter Pulmonalvenenisolation (PVI) auf.

Methodik: Ein 35-jähriger männl. Patient wurde bei paroxysmalen Vorhofflimmern zur geplanten PVI aufgenommen (ana-

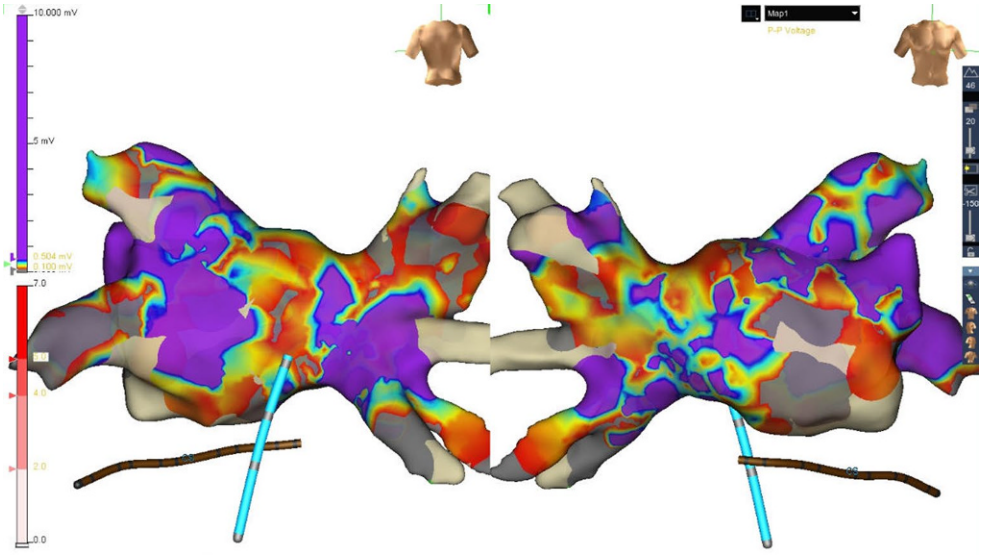

Abb. 1 | 22-1

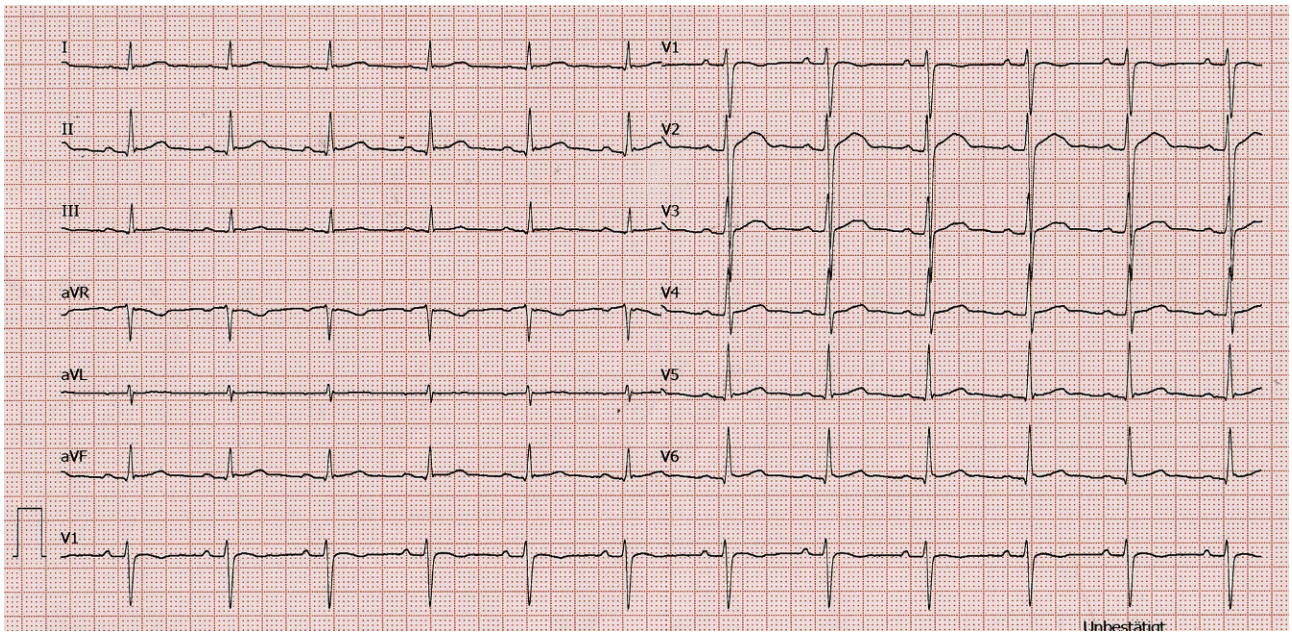

Abb. 2 | 22-1

mnestisch Tachykardiomyopathie bei primär persistierendem tachykarden Vorhofflimmern, unter Amiodarontherapie Vorhofflattern, Isthmusablation); die Indikation zur PVI wurde gestellt, da es auch unter Amiodaron zu Vorhofflimmerrezidiven kam.

Ergebnisse: Das EKG zum Aufnahmezeitpunkt zeigt Sinusrhythmus, HF 48/min, U-Welle unter Amiodaron, normale Repolarisation; in der transösophagealen Echokardiographie (TEE) kein Hinweis auf Thrombus im linken Herzohr (LAA); bei dem Patienten wird am Folgetag eine elektive PVI mittels Hochfrequenzenergie durchgeführt (66 Energieapplikationen, max. Ösophagus Temperatur 39,3° bei Ablation im posterioren Antrum der RIPV); beim primär durchgeführten elektroanatomischen Map des linken Atriums (Ensite NavX) finden sich ausgedehnte low voltage Areale als Hinweis für Fibrose (Abb. 1); bei der Kontrolle mit dem Spiralkatheter zeigen sich alle vier Pulmonalvenen elektrisch isoliert; abschließend wird der rechtsatriale Isthmusblock kontrolliert, der sich als anhaltend bidirektional blockiert erweist.

11 Stunden nach dem Eingriff klagt der Patient über Thoraxschmerzen, echokardiografisch zeigt sich bei normaler LVF kein Perikarderguss, im EKG diskrete neue ST-Elevation in I, II, aVF (Abb. 2). Troponin T 773 ng/l, CK 143 U/l, Leuko 13,3 G/l, CRP 7,4 mg/l; kein Fieber; CRP-Anstieg am Folgetag auf 53,2 mg/l, danach ohne Antibiotika-Therapie fallend; NT-pro-BNP 19 ng/l. In der Annahme einer postinterventionellen Perikarditis wird eine Colchizintherapie (0,372 mg 1-0-1) für 3 Monate eingeleitet, von einer NSAR-Gabe wird wegen des erhöhten Blutungsrisikos unter OAK (Rivaroxaban 20 mg) abgesehen. Die Amiodarontherapie wird neben einer vorbestehenden Bisoprololtherapie weitergeführt.

Die Brustschmerzen klingen rasch ab, die EKG-Veränderungen sind rückläufig; aufgrund der dargestellten low voltage-Areale im linken Atrium und der früheren TCMP wird vor der Entlassung noch eine molekulargenetische Untersuchung (DCMP) durchgeführt und eine kardiale MRT-Untersuchung geplant.

Schlussfolgerungen: Obwohl die Komplikationsrate nach Katheterablation der Pulmonalvenen mittlerweile niedrig ist (ca. 3 %), müssen auch seltene Ursachen wie eine regionale Perikarditis in der Differentialdiagnose bedacht werden; typische EKG-Veränderungen sind dabei nicht beschrieben, möglicherweise ist aber das Ausbleiben von negativen T-Wellen ein Hinweis für die nicht ischämische Genese.

22-2

Complete electrical isolation of the left atrium as a new strategy for the treatment of advanced arrhythmogenic left atrial cardiomyopathy

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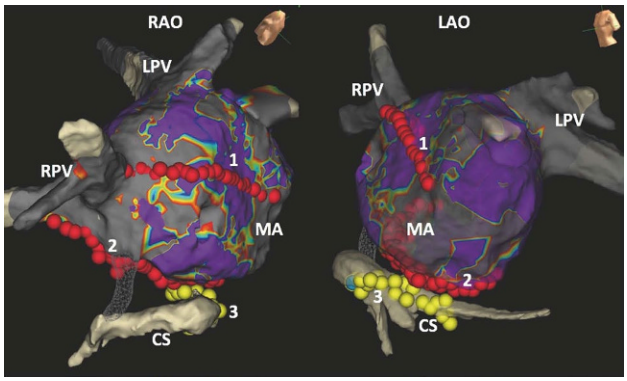

Fig. 1 | 22-2 3D map after left artial isolation. Right: *RAO* view (right anterior oblique, 20°); Left: *LAO* view (left anterior oblique, 50°); *CS:* coronary sinus; *LPV:* left pulmonary veins; *MA:* mitral annulus; *RPV:* right pulmanary veins; 1: lesion line from the anterior mitral annulus to the right suoerior PV; 2: line from the posterior mitral annulus to the anteroir part of the right inferior PV; 3: lesions at the ostium of the coronary sinus in right atrium

Background: Atrial fibrillation (AF) is one of the most common arrhythmias and nowadays pulmonary vein isolation (PVI) is the cornerstone in the treatment of AF. In many cases of patients with extensive scarred tissue in the left atrium (LA), PVI is not enough to cure complaints. Multiple procedures with substrate modification are needed and AV-node ablation after pacemaker implantation is the last resort. Unfortunately, right ventricular pacing involves an increased risk of developing heart failure. Biventricular pacing can reduce this risk nowadays but there is still a higher risk compared to intrinsic conduction. Furthermore, the implanted devices and leads are often needed for many years with their well-known complications. This case presents a new method for the treatment of AF in patients with extensive scarred tissue.

Case Report: A 79-year-old male patient was presented to our department with highly symptomatic recurrent persisting AF. He has already undergone PVI twice in 2012 and 2013. During the second PVI a gap at the left pulmonary veins (PVs) was closed and a voltage map revealed low voltage areas at the roof of the LA. Therefore, a lesion line along the roof was ablated. After that the patient remained free of symptoms for about 4 years. In June 2017 he had a relapse of persisting AF and got 3 electrical cardioversions until December 2017 during the intake of amiodarone. Unfortunately, sinus rhythm only lasted for 3 days after the last cardioversion. For that reasons we decided to perform another electrophysiological study. In case of suspect for extensive low voltage areas and low likelihood to accomplish a lasting sinus rhythm the patient agreed to a recently developed novel ablation approach with the endpoint of isolation of the left atrium and consecutive left atrial auricle (LAA) occlusion because of very high thromboembolic risk.

PVs were still completely blocked after two PVIs and so was the roof-line. High density voltage map (EnSite PrecisionTM NavXTM, Abbott) by using a novel multipolar mapping catheter (HD Grid, Abbott) revealed extensive scarring of the inferoseptal and anterior region. Therefore, disconnection was achieved by ablating a lesion line from the anterior mitral annulus to the right superior PV which is the region of Bachmann's bundle insertion. After that a line from the posterior mitral annulus to the anterior part of the right inferior PV was ablated as well as lesions at the ostium of the coronary sinus in right atrium to isolate the posterior and sinus coronarius interatrial connections (Fig. 1). Finally, a complete disconnection of the LA could be achieved which was proved by dissociated signals in LA (Fig. 2). Because of a high thromboembolic risk after this procedure LAA occlusion was indicated and was performed consecutively under TEE guidance (Amplatzer Amulet, Abbott). Oral antico-

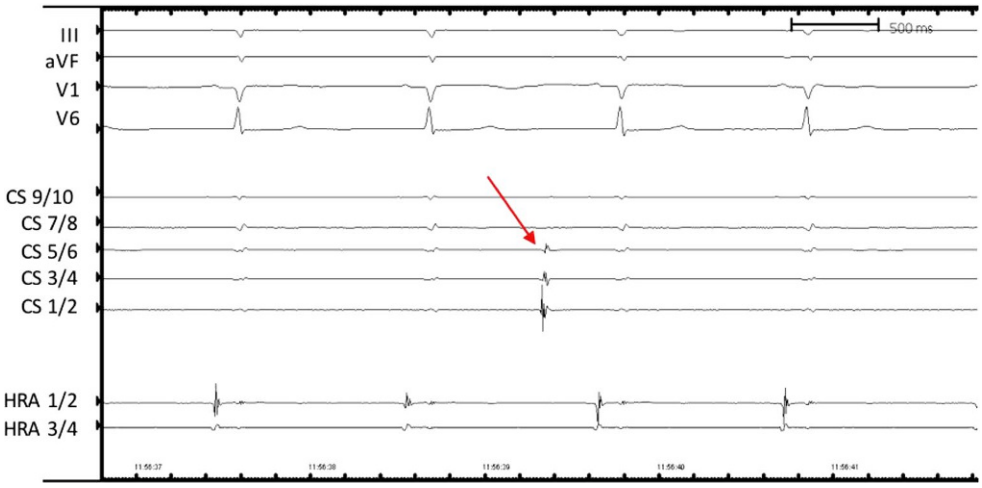

Fig. 2 | 22-2 Intracardiac ECG after complete left atrial isolation. *Red arrow:* dissociated left atrial contraction. III, aVF, V1 and V6: body surface ECG; CS 1, 2 to CS 9, 10: coronary sinus, 1/2 distal, 9/10 proximal; HRA: high right atrium, 1/2 distal, 3/4 proximal

agulation and ASS was recommended for 4 weeks followed by a single therapy with ASS.

Conclusions: This case presents a new strategy for the interventional therapy of highly symptomatic AF in patients with extensive low voltage areas and low likelihood of achieving a lasting sinus rhythm. It is an alternative for the pace-and-ablate strategy with AV-node ablation after pacemaker implantation that was the last resort so far. Benefit of this procedure is that there is no need for pacemakers with their consequences like ventricular pacing induced heart failure. The ablation and LAA occlusion can be done with relatively low interventional risk.

22-3

Gesundheitsökonomische Auswirkungen der Ablation von Vorhofflimmern

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Grundlagen: Vorhofflimmern (VHF) ist die häufigste Herzrhythmusstörung der westlichen Welt mit einer geschätzten Prävalenz von 3 % bei Erwachsenen über dem 20. Lebensjahr [Kirchhof P et al., EHJ 2016; 37:2893–2962]. VHF geht mit einer erhöhten Mortalität und Morbidität der betroffenen Patienten einher, wodurch lt. ESC 10–40 % der VHF-Patienten pro Jahr zumindest einmalig hospitalisiert werden. Gemäß Studien aus England und den USA verursacht VHF etwa 1 % der gesamten Gesundheitsausgaben dieser Länder [Stewart S et al. Heart 2004; 90:286–292 und Kim MH. Circ Cardio Qual Out 2011; 4:313–320].

Die aktuelle Behandlung von VHF zielt auf eine Prävention thrombembolischer Ereignisse sowie die Bekämpfung der Symptome durch Frequenz- oder Rhythmuskontrolle ab. Die einzige, potentiell kurative Behandlungsmethode steht mit der Pulmonalvenenisolation (PVI) zur Verfügung. Die letzten ESC Guidelines beurteilen diese Methode mit einer Klasse IA Indikation in der Zweitlinientherapie (Therapieversagen von Medikamenten) und in der Erstlinientherapie bei Patientenpräferenz als Klasse IIa B.

Gesundheitsökonomische Daten zur Auswirkung der PVI bei VHF finden sich in der Literatur fast ausschließlich als Simulation der Kosten des Eingriffes mit einer angenommenen Wirksamkeit aus Ablationsstudien gegenüber den Kosten einer konservativen, medikamentösen Behandlung mit bekannt unterlegener Wirksamkeit. Gesundheitsökonomische Echtdaten fehlen weitestgehend, Daten aus Österreich wurden bisher nicht publiziert.

Methodik: In Oberösterreich wurde die PVI bereits im Jahr 2000 im Krankenhaus der Elisabethinen gestartet und wird derzeit in 3 Krankenhäusern angeboten, welche auch wissenschaftlich im IKMF der JKU zusammenarbeiten. Über die Abteilung für Gesundheitsökonomie der JKU besteht Zugang zu gesundheitsökonomischen Daten des stationären und niedergelassenen Bereiches über die Jahre 2005 bis 2015. In dieser Studie soll die Auswirkung der PVI auf die Ausgaben im stationären Bereich (Krankenhaustage, LKF-Punkte, LKF-Beträge), niedergelassenen Bereich (Arztbesuche und Aufwendungen für Heilmittel) und auf Krankenstandstage bei Berufstätigen untersucht werden.

Ergebnisse: Es konnten insgesamt 1125 PVI-Patienten in den vorliegenden Daten identifiziert werden, von denen 261 einem mehrmaligen Eingriff unterzogen wurden (Abb. 2 a). Im Jahr vor der PVI kommt es zu einem deutlichen Anstieg der durchschnittlichen Krankenhaustage pro Patient (Abb. 1 a) und der Krankenstandstage (Abb. 1 b). Gleichzeitig können beide Werte durch die PVI wieder auf das durchschnittliche Niveau der Patienten ein Jahr vor Ablation gesenkt werden. Vergleicht man die 4 Quartale vor und nach PVI mittels T-Test (Abb. 2 b), findet sich ein signifikanter, jedoch betragsmäßig geringer Anstieg der Kosten im niedergelassenen Bereich, bei einer hochsignifikanten Reduktion im stationären Bereich. In einer weiteren Analyse konnte die Kostensteigerung im niedergelassenen Bereich auf eine häufigere Verordnung antihypertensiver Medikamente, Lipidsenker und Diabetespräparate zurückgeführt werden.

Schlussfolgerungen: In einer Analyse von 1125 OÖ VHF-Patienten können nach PVI signifikante Effekte des Eingriffes auf die nachgelagerten Gesundheitsausgaben im stationären und niedergelassenen Bereich sowie auf die Krankenstandsdauer gezeigt werden. Für eine Beurteilung der Kosteneffektivität der Behandlungsmethode wird im nächsten Schritt ein Echtdatenvergleich mit medikamentös antiarrhythmisch behandelten Patienten durchgeführt.

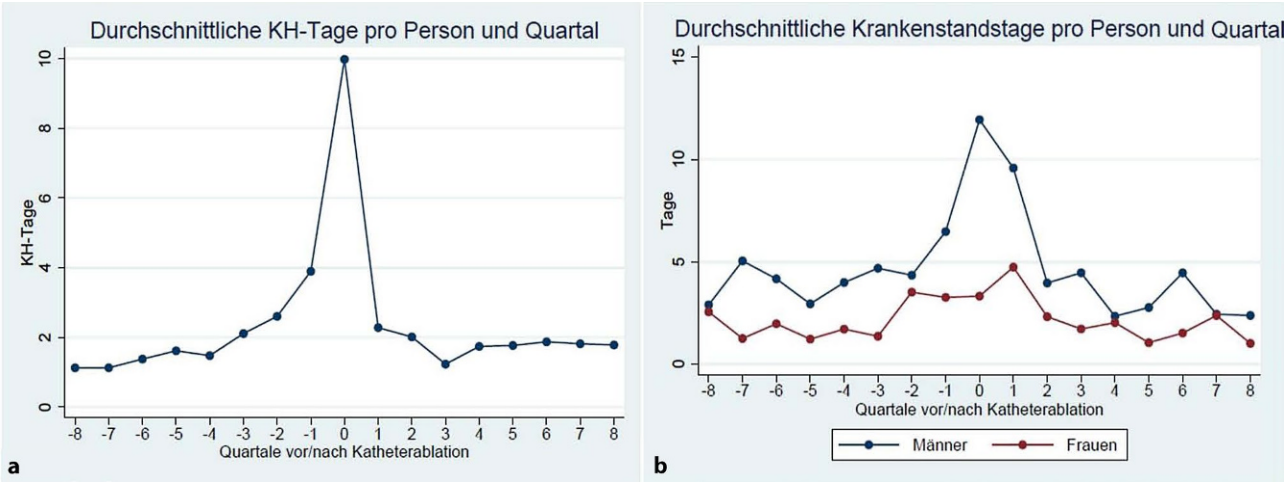

Abb. 1 | 22-3

Demographie der Personen mit Katheterablation 2005-2015

	Anteil in %
Weiblich	30,84
Alter bis 55 (bei Ablation)	31,64
Alter 55–65 (bei Ablation)	31,29
Alter über 65 (bei Ablation)	37,07
Verstorben bis 2015 (bei GKK)	2,31
Beitragsgrundlage=0	61,51
ArbeiterIn	15,73
Angestellte	23,82
PensionistIn	51,56
Rest & unbekannt	8,89
Hyperthyreose	4,18
Diabetes mellitus	10,40
Adipositas	10,58
Störungen des Lipoproteinstoffwechsels	35,82
Nikotinabusus	3,11
Hypertonie	48,27
KHK	37,78
Klappenerkrankungen	7,82
Kardiomyopathie	9,16
Herzinsuffizienz	11,38
Krankheiten des Reizleitungssystems	3,11
Insult / TIA	10,13
CAVK	2,40
PAVK	2,13
COPD	5,16
Schlafapnoe	5,60
Niereninsuffizienz	2,76

N=1.125 Personen. Es wurden alle LKF-Daten der 1.125 betroffenen Personen im Zeitraum 2005-2015 auf entsprechende ICD 10 Codes durchsucht. Sobald der jeweilige Code aufscheint, gilt die Person als betroffen.

a

Statistischer Test (t-Test) zum Vergleich der durchschnittlichen Ausgaben/Tage/Punkte 1 Jahr vor und nach der Behandlung

	Differenz der Mittelwerte	Konfidenzintervall
Heilmittel		
unpaired t-test	$+33,44^{***}$	[10, 25; 56, 64]
paired t-test	$+38,22^{**}$	[0, 05; 76, 48]
Ärztliche Hilfe		
unpaired t-test	$-4,75$	nicht signifikant
paired t-test	$+13,07^{**}$	[1, 44; 24, 70]
LKF-Punkte		
unpaired t-test	$-354,09^{***}$	$[-460,42; -247,76]$
paired t-test	$-337,81^{***}$	$[-450,87; -224,74]$
Krankenhaustage		
unpaired t-test	$-0,98^{***}$	$[-1,21; -0,74]$
paired t-test	$-0,90^{***}$	$[-1,15; -0,64]$

Differenz der Mittelwerte entspricht dem durchschnittlichen Wert in den 4 Quartalen **nach** der Behandlung pro Person und Quartal weniger dem durchschnittlichen Wert in den 4 Quartalen **vor** der Behandlung pro Person und Quartal. * $p < 0,1$; ** $p < 0,05$; *** $p < 0,01$.

b

Abb. 2 | 22-3

22-4

Prognostic relevance of early repolarization pattern in patients with left ventricular hypertrabeculation/noncompaction

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Background: Early repolarization (ER) is a common ECG finding in the general population (5.8%). ER has been associated with idiopathic ventricular fibrillation especially if ER is located in the inferior or lateral leads. Left ventricular hypertrabeculation/noncompaction (LVHT) is echocardiographically characterized by an increased number of left ventricular trabeculae and a 2-layered myocardial structure, with an outer compacted and an inner noncompacted layer. LVHT has been associated with arrhythmias and sudden cardiac death. The aim of the study was to assess if ER is associated with increased mortality in patients with LVHT.

Methods: ECG recordings of LVHT patients included in a registry were retrospectively analyzed. Patients with right bundle branch block were excluded.

Results: ECG recordings of 178 patients (mean age: 55 years, 32% female) were included. The median follow-up duration was 10 years (IQR 6-14). During that time 40 patients received cardiac electronic devices (CED) (pacemaker, loop recorder, implantable cardioverter defibrillator, cardiac resynchronization therapy). The mortality was 6% per year. Sudden death was found in 12 patients. ER was found in 86 patients (48%). ER was found most frequent in anterior ($n=74$, 42%), lateral ($n=30$, 17%) and inferior leads ($n=26$, 15%). Baseline characteristics of patients with and without ER differed regarding sex (24% women vs 38%, $p=0.05$), NYHA III (17% vs 32%, $p=0.03$), ECG left ventricular hypertrophy (40% vs 20%, $p=0.003$), and left ventricular fractional shortening (26 vs 22%, $p=0.004$). No differences were detected regarding the prevalence of neuromuscular disorders. During follow-up, no differences between patients with and without ER were found regarding mortality. Patients with and without ER differed regarding CED-therapy (14% vs 30%, $p=0.008$) during follow-up and stroke/embolism (4% vs 0%, $p=0.005$) as cause of death.

Conclusions: ER was not associated with increased mortality in our group of LVHT patients. The prevalence of ER in LVHT, however, was higher than reported in the general population. This may be due to the high rate of CED implanted during the observation period.

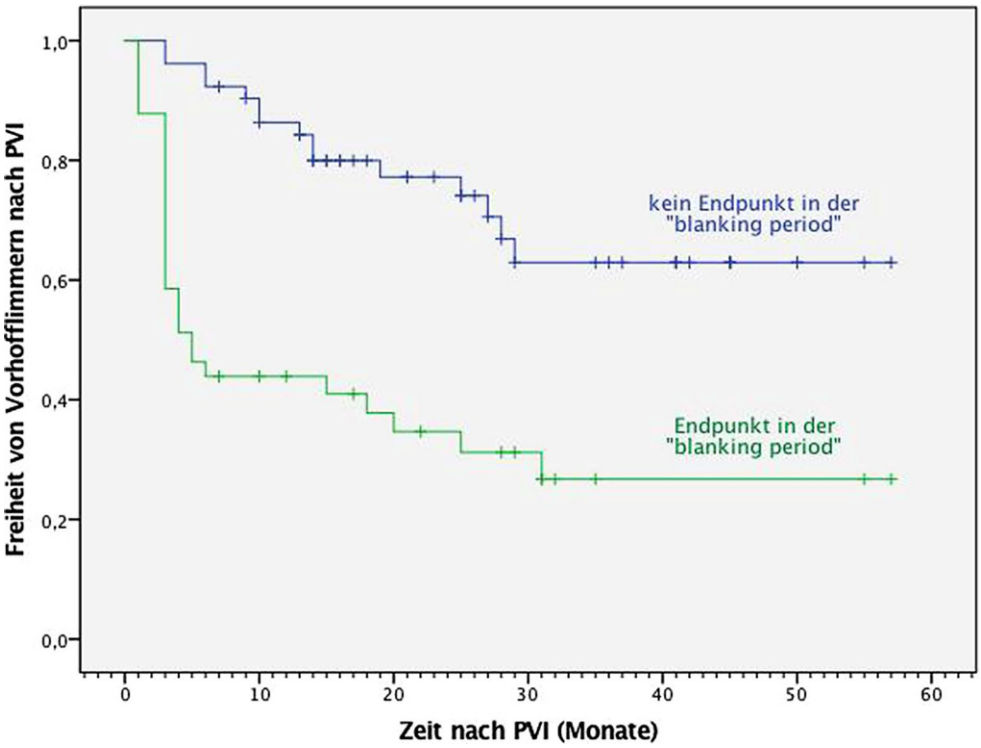

Abb. 1 | 22-5

22-5

Wiederauftreten von Vorhofflimmern in der „blanking period“ nach einer ersten Pulmonalvenenisolation ist ein negativer Prädiktor für den Langzeiterfolg

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Grundlagen: Die Pulmonalvenenisolation (PVI) entwickelte sich in den letzten Jahren zu einer wichtigen Säule in der Behandlung von Vorhofflimmern (VHFli). Während bei fast allen Patienten die primäre Venenisolation gelingt, sind die Langzeitergebnisse, wenn man die völlige Freiheit von VHFli als Erfolgskriterium heranzieht, noch nicht zufriedenstellend. Prädiktoren für den Langzeiterfolg oder für das Scheitern der Therapie wurden in mehreren Studien bereits untersucht, bislang konnte sich aber keiner der untersuchten Parameter als wesentliches Steuerelement durchsetzen.

Das Ziel der Studie war es in einer gut dokumentierten Patientengruppe unabhängige Prädiktoren für den Langzeiterfolg oder für ein Therapieversagen nach einer ersten PVI zu finden. Marker für einen Langzeiterfolg oder für einen Misserfolg könnten die Patientenselektion verbessern und damit die Erfolgsrate der Intervention erhöhen.

Methodik: Die verfügbaren Daten aller konsekutiven Patienten, die zwischen Jänner 2011 und Juni 2015 an unserer Abteilung eine erstmalige PVI mit Radiofrequenz point by point erhielten, wurden retrospektiv analysiert. Klinische Parameter wie Geschlecht, Alter, Vorhofflimmertyp, Hypertonie, Diabetes mellitus, Body-Mass-Index (BMI), Amiodaron-Therapie zur Zeit der PVI, Daten, die während der PVI gewonnen wurden wie linksatrialer Mitteldruck, linksatriales Volumen, frühzeitige Pulmonalvenenrekonnektion und die Ergebnisse eines Patientenfragebogens wurden mittels univariater und multivariater Analyse untersucht (Kaplan-Meier und Cox-Regression). Endpunkte waren dokumentiertes Vorhofflimmern oder -flattern und das Auftreten genau der gleichen Symptome wie vor der Ablation.

Ergebnisse: Nach Ausschluss von 13 Patienten gelangten die Daten von 93 Patienten, 51 mit paroxysmalem und 42 mit persistierendem VHFli zur Auswertung. Das Durchschnittsalter betrug 59 (±10,6) Jahre, 18 Patienten waren weiblich. Siebenundvierzig der Patienten (50,5 %) waren Hypertoniker, der mittlere BMI betrug 27,3 (±4,3), der mittlere linksatriale Mitteldruck betrug 15,5 (±6,3) mmHg.

Nach einem Follow-up von 33 (±14,5) Monaten hatten 43 Patienten (46,2 %) einen Endpunkt nach der „blanking period“ von 3 Monaten erreicht. Dieser Endpunkt wurde mit 55,8 % (24/42) häufiger bei Patienten mit persistierendem VHFli als bei Patienten mit paroxysmalem VHFli 44,2 % (19/51) gefunden (n. s.). Bei 41/93 (44,1 %) wurde ein Endpunkt in der definierten „blanking period“ erreicht. Von diesen blieben immerhin 13/41 (31,7 %) nach den ersten 3 Monaten ohne Endpunkt. Die übrigen 28 Patienten (68,3 %) hatten auch 3 Monate nach der PVI einen Endpunkt.

Die univariate Analyse ergab für folgende Patientendaten eine signifikant kürzere Vorhofflimmerfreiheit nach einer ersten PVI: Vorliegen einer arteriellen Hypertonie ($p = 0{,}028$), linksatrialer Druck >14 mmHg ($p = 0{,}015$), Eingriff unter Amiodaron ($p = 0{,}003$) und Erreichen eines Endpunktes in der „blanking period“ ($p < 0{,}001$). In der multivariaten Analyse war nur das Erreichen eines Endpunktes in der „blanking period“ ein signifikanter Prädiktor für das Wiederauftreten von Vorhofflimmern nach der „blanking period“. (Hazard Ratio 3,349; 95 % Konfidenzintervall 1,701-6,594).

Schlussfolgerungen: Die Dokumentation von Vorhofflimmern oder das Wiederauftreten der gleichen Symptome wie vor der PVI schon während der „banking period“ ist ein unabhängiger Prädiktor für ein schlechtes Langzeitergebnis nach einer ersten PVI mit Radiofrequenz.

22-6

Reduction of fluoroscopy dose using an ArtisQ.zen detector for procedures in the cardiac EP laboratory

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Background: The aim of this study was to evaluate the lowest possible clinical acquisition setting for fluoroscopic electrophysiological procedures on an ArtisQ.zen X-ray detector operated at a minimum of 6nGy detector entrance dose per fluoroscopy pulse.

Methods: 641 consecutive patients (407 m/234 f) underwent ablation procedures at our institution between August 2015 and December 2017. All ablations were performed using an ArtisQ.zen X-ray system (Siemens, Germany). The first 308 patients were treated using the conventional dosing program ("Fl Zen Std"), from October until December another 53 patients underwent ablations using the optimized X-ray dosing program "HDR Care3 minus". For the conventional program fluoroscopy dose was set to 18n Gy/pulse, for the minimized dosing program the dose was set to 6n GY/pulse and could be increased to 10 or 15 nGy/pulse manually.

Results: A total of 213 AV-node reentry tachycardia (AVNRT), 73 accessory pathways (AP), 71 atrial flutter and 284 atrial fibrillation (AF) ablation procedures were performed. Pulmonary vein isolation was performed using an electroanatomic mapping system (CARTO, Biosense Webster, USA) in 117 ora cryoballoon (Cryocath Medtronic, USA) in 167 patients. The total area dose could be reduced in all groups by a mean of 56.3% (2212.4 µGym² vs. 5067.6 µGym²), with a relative reduction of 50.0% for AF and 78.0%for right sided ablations. Total fluoroscopy time, ablation success and complication rate remained unchanged.

Conclusions: Cardiologists and especially cardiac electrophysiologists are among the greatest radiation exposed medical professionals.3 We already implemented a number of protective measures to reduce radiation exposure at our institution, including additional lead shielding, optimized x-ray detector angulation and protocols to reduce radiation time. After acquisition of a novel fluoroscopy system it was our subsequent objective to implement a dynamic user-controlled x-ray system to decrease the radiation exposure during ablation procedures. This could be shown to be feasible during different ablation therapies in three different operators with consistent dose reduction of up to 80%.

According to an early report by Miller and colleagues in 2002, the two main determinants beside the patient body habitus include the hardware (tube filtration, generator voltage and current), and its utilization (fluoroscopy time, field size, overlap of fields and user experience).12 The key message still holds true and has been the underlying idea for this investigation and several recent developments.

22-7

Rotational angiography for atrial fibrillation ablation

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Background: Pre-procedural 3D visualization of the left atrium (LA) and the pulmonary veins (PV) reduces fluoroscopy and procedure duration in atrial fibrillation (AF) ablation procedures. Segmentation of computed tomography (CT) or three-dimensional rotational angiography (3D RA) data is necessary to integrate images into X-ray equipment or electroanatomic mapping systems. We validated a novel automatic, model-based segmentation algorithm ("syngo LA segmentation") for 3D RA images in an AF ablation cohort by comparing its outcome with the established manual measurements performed on CT images.

Methods: 21 (15 male, 6 female; age 55.4 ± 3.3 years) patients underwent ECG-gated cardiac multislice CT and 3D RA prior to ablation of paroxysmal ($n = 17$) or persistent ($n = 4$) AF. CT acquisition was performed using Somatom Definition Flash and 3D RA acquisition using an ArtisQ.zen X-ray system and a dedicated syngoDynaCT Cardiac protocol for 3D LA imaging (Siemens Healthcare, Germany). For 3D RA images contrast agent was injected by a pigtail catheter into the pulmonary artery before transseptal puncture. After the procedure PV area and the minimal and maximal diameters of all PV ostia were measured in the segmentation results provided by the new model-based algorithm. For CT images the corresponding parameters were obtained by manual measurements in the CT slices and were used as ground truth regarding the validation.

Results: Computation time for the automatic LA segmentation was less than 5 seconds. Left PV measurements had to be excluded in 6 patients due to common ostia. Mean PV area was 285.6 ± 106.1 mm² in 3D RA images and 269.9 ± 119.4 mm² in the CT images, minimal diameter 17.8 ± 3.5 mm vs. 15.7 ± 3.5 mm, and maximal diameter 22.0 ± 4.2 mm vs. 21.3 ± 5.7 mm resp. The mean differences of the two groups were 15.7 mm² (5.6%) for the mean PV area, 2.10 mm (12.5%) for the minimal PV diameters, and 0.7 mm (1.6%) for the maximal PV diameters. Measurements of diameters and areas separated into the 4 PVs are given in the table.

Conclusions: Minimal, maximal diameters and PV ostium area are comparable in 3D RA and CT measurements using a novel segmentation algorithm. Assuming an accuracy of 3 mm required for catheter navigation in AF ablation, this analysis confirms the segmentation accuracy of the new automatic model-based segmentation algorithm. Thus, LA segmentation of 3D RA images using the new model-based syngo LA segmentation algorithm provides accurate, fast and operator independent 3D LA visualization.

Chirurgie Vorträge

CV 1-1

Impact of peripheral artery disease on mid-term mortality after transapical transcatheter aortic valve implantation

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Background: Peripheral artery disease (PAD) is a major risk factor for cardiovascular mortality. In order to avoid vascular complications, high-risk patients with severe aortic stenosis are mainly treated using transapical (TA) transcatheter aortic valve implantation (TAVI). However, the prognostic value of PAD for this subset of patients is still unknown. Therefore, this study aimed to investigate the impact of PAD on perioperative and mid-term mortality in patients undergoing TA-TAVI.

Methods: From 2008 to 2017, a total of 635 consecutive patients undergoing TA-TAVI from two centres were prospectively included. In order to assess the independent prognostic value of PAD on mid-term mortality stepwise uni- and multivariable Cox regression analysis was performed. Variables with a p-value of <0.1 in univariate analysis were included in the multivariable model.

Results: PAD was present in 17.5% ($n=111$) of patients. The rate of 30-day mortality was 9.9% ($n=63$) with no statistically significant difference between the PAD group and non-PAD group ($p=0.76$). During a median follow up of 491 days (interquartile range [IQR]: 104–1078), 287 patients (45.2%) died. In multivariable regression analysis, age (HR 1.034, 95% CI 1–1.1, $p=0.012$), chronic obstructive pulmonary disease (HR 1.508, 95% CI 1.1–2.1, $p=0.01$), mean aortic valve pressure gradient (HR 0.982, 95% CI 0.97–1, $p=0.01$) and PAD (HR 1.482, 95% CI 1.1–2.1, $p=0.018$) were identified as independent predictors of mortality.

Conclusions: The presence of PAD has no impact on perioperative mortality in patients undergoing TA TAVI. However, due to the independent association of PAD with mid-term mortality, it should be considered to optimize individualized risk prediction when caring for patients scheduled for TA TAVI.

CV 1-2

Impact of valve size on outcome after transcatheter aortic valve implantation

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Background: Residual transvalvular gradient is known as a risk factor for mortality after transcatheter aortic valve implantation (TAVI). Different valve sizes may have different flow characteristics due to their effective orifice area. Therefore, we investigated the impact of valve size on perioperative and mid-term clinical outcome.

Methods: From 2008 to 2016, 1060 consecutive patients were treated with balloon expandable transcatheter valves in two centers. The overall population was divided into two groups according valve size: small valve (SV) size ≤23 mm and big valve (BV) size >23 mm. Perioperative outcome was analyzed according to VARC-II criteria. Outcome parameters were assessed after adjustment for STS-PROM score with a mean follow-up of 536 days. The impact of valve size was investigated using log-rank test and regression analyses.

Results: Mean age was 83 [IQR: 79–86] years. Higher STS scores were observed in the SV size group (6.5 [IQR: 4.7–9.5] vs. BV size 7.2 [IQR: 5.1–10.4], $p<0.001$). After adjustment for STS score there was no difference in 30-day mortality (SV size 7% vs. BV size 7%, $p=0.803$), device success (SV size 95% vs. BV size 96%, $p=0.847$), early safety (SV size 33% vs. BV size 29%, $p=0.451$), stroke (SV size 3% vs. BV size 2%, $p=0.497$) and myocardial infarction (SV size 1% vs BV size 0%, $p=0.892$). Regression analysis revealed no differences in overall mortality after a median follow-up of 536 days.

Conclusions: Patients with smaller transcatheter aortic valve size have significantly higher STS-PROM scores. Nevertheless, neither perioperative outcome nor mid-term survival significantly differ between smaller and bigger valve sizes.

CV 1-3

Die Direct Flow Medical®-Prothese als Sutureless-Device bei nicht-kalzifierten Aortenklappenvitien – eine tierexperimentelle Projekt-Studie

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Grundlagen: Die Direct Flow Medical Prothese® (DFM) wurde als Prothese für Katheter-unterstützte Aortenklappen-Implantationen klinisch erfolgreich implementiert. Als eines

ihrer Hauptmerkmale gilt ihre Adaptionsfähigkeit an den nativen Aortenanulus. Diese tier-experimentelle Studie soll zeigen, ob eine Fixierung der Prothese bei Verwendung als Sutureless-Device im nicht-kalizifizierten Anulus möglich ist.

Methodik: Bei 17 Schweinen (39–85 kg) wurde die Prothese analog einer Sutureless-Klappenprothese am cardiopulmonalen Bypass (CPB) via partielle oder totale Sternotomie implantiert. Nach Beendigung des CPB wurde die regelrechte Position unter normo- und hypertensiven Druckbedingungen überprüft. Mittels TEE wurden präpoperativ die Anuli vermessen, postoperativ die Klappenposition überprüft.

Ergebnisse: Das Set-Up des Versuches war in 100 % erfolgreich, bei allen Schweinen konnte die Implantation zumindest einmalig durchgeführt werden. Nach Messen der Anuli in der TEE sowie mit konventionellen Prothesen-Sizern ($n=5$) wurden die korrespondierenden Prothesen mit maximal geringem Oversizing implantiert, zwei Tiere diese Kohorte erhielten außerdem eine Anuloraphie. Aufgrund des ausgeprägt elastischen Aortenanulus dislozierten alle Prothesen in dieser Kohorte in den linken Ventrikel (LV). Die Anuli der verbliebenen zwölf Tiere wurden mittels Hegar-Stiften vermessen. Aufgrund der resultierenden Perimeter wurde ein Prothesen-Oversizing durchgeführt. Es kam es zu keiner weiteren LV-Dislokation, eine stabile Verankerung konnte damit bewiesen werden. Drei Schweine zeigten einen unauffälligen post-CPB-Verlauf. In neun Tieren zeigte sich eine periphere Koronar-Kompression mit folgender Minderperfusion. Ein ausgeprägtes Oversizing resultierte in einer Kompromitierung des anterioren Mitralklappensegels.

Schlussfolgerungen: Nach adäquatem Sizing der massiv elatischen Aortenwurzel bei juvenilen Schweinen mittels Hegar-Stiften und folgendem ausgeprägten Over-Sizing kann die DFM-Prothese auch bei nicht-kalzifizierten Aortenklappenvitien sicher verankert werden. Nach entsprechendem Re-Design, vor allem der Profil-Höhe, müssen weitere Versuche in Vorbereitung auf ihren Einsatz als Sutureless-Device durchgeführt werden.

CV 1-4

Transapical TAVI in patients with complex aortic pathologies. How to deal with dissections, thoracic aneurysms or complex previous aortic surgery and transcatheter aortic valve implantation

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Background: With complex aortic pathologies like dissections or aortic arch aneurysm as well as previous surgery of the ascending aorta or aortic arch in combination with aortic stenosis or more often aortic insufficiency, we are facing an even more complex patient population.

Addressing both pathologies, the treatment is very demanding. On the one hand the high surgical risk due to open surgery can be avoided and on the other hand manipulation of the catheter devices in the injured aorta comprises and increases risk by itself.

This case series presents the treatment of patients with aortic valve disease and complex aortic pathologies through a transapical approach.

Methods: Three patients mean age 66 years, (2 female, one male) presented with aortic valve disease (insufficiency $n=2$, stenosis $n=1$) and concomitant complex aortic pathologies (type b dissection $n=1$; Ascending aortic replacement after type A dissection $n=1$ and three reoperations on the ascending aorta and the aortic arch $n=1$).

Patient 1 had an uncomplicated type b dissection and a severe symptomatic aortic stenosis, which had to be treated before evaluating for TEVAR. The patients was refused from other hospitals due to the surgical risk.

Patient 2 presented a severe aortic valve insufficiency after three operations on the ascending aorta and the aortic arch, additionally she was overweight and suffered from multiple sclerosis. Therefore the patient was rejected for conventional surgery. CT-Scan revealed an unfavorable angle of the apex to the ascending aorta and a gothic aortic arch.

Patient 3 had a history of type A dissection with tirone david repair and developed severe aortic valve insufficiency 6 month after surgery. The grafted ascending aorta had a 90° angle in the mid portion and was is close proximity to the sternum. Due to the complexity of the initial operation, the patient was rejected for open surgery.

For Patient 1 and 3 an Edwards Sapien 3 26 mm and 29 mm was used; for Patient 2 a JenaValve 27 mm. The transapical approach was chosen in all 3 patients.

Results: The transapical TAVI was performed uneventfully without any dynamics regarding the dissection membrane and with no incidence of a paravalvular leak. The postoperative course was uneventful in all patients, except Patient 1 who developed a left sided scotoma. All patients were extubated within the 1 POD and discharged within 2 weeks postoperatively.

Conclusions: For positioning of the device in patients with gothic arches the transapical approach might be favorable due to the shorter way and therefore less loss of traction through the guidewire.

Transapical TAVI is a fast and safe treatment option for patients with acute, chronic or remaining untreated type B dissections. Avoiding to pass the dissected part of the aorta with the introducer sheet or penetrating the false lumen, the transapical approach enables a safe and precise implantation of an aortic valve prosthesis without passing or manipulating the dissection membrane with the device and therefore reducing the risk of redissection, retrograde dissection or rupture.

CV 1-5

Surgical aortic valve replacement in patients aged 80 and above is safe and significantly improves quality of life

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Background: In an ageing population, an increasing number of patients aged 80 years and above require aortic valve

replacement (AVR). Aortic valve stenosis is the most frequent indication for AVR in patients aged 75 and above, with a prevalence of 6% in persons aged 85 years and above.

Objectives: The objective of this retrospective, single-centre, non-randomized comparative study was to investigate the early and mid-term outcome of isolated AVR in elective patients aged 80 years and older using a full sternotomy.

Methods: We included 288 patients aged 80 years and older (mean age: 82.5 ± 2.3 years) who underwent isolated AVR using a pericardial bioprosthesis between 1st January 2007 to the 31st December 2012. A retrospectively data collection and statistical analysis using SPSS 22 for Mac® was performed afterwards.

Results: Patients were more likely to be women (57.3%). Preoperatively, 47.6% of the study population were classified as New York Heart Association (NYHA) class III or IV. All 288 patients received a Carpentier-Edwards Perimount Magna Ease bioprothesis. The mean logistic EuroSCORE was 13.5 ± 7.9%, intraoperative mortality was 2.8%, 30-days-mortality was 7.3%. 4.2% of the patients had a postoperative stroke. The mean follow-up time was 49.3 ± 19.2 months. Postoperatively, only 14.1% of the study population were classified as NYHA-class III and IV. Whereas 85.9% were classified as NYHA-class I or II. One-year and five-year survival rates were 83.7% and 69.1% respectively.

Conclusions: According to our data, the early and mid-term outcome of operative AVR was similar to the results obtained in other surgical cohorts. Most importantly, according to postoperative NYHA classification the patients had a significant improvement in quality of life. Our data therefore demonstrate that surgical AVR is safe in patients aged 80 years and older.

CV 1-6

Concomitant transapical transcatheter aortic valve implantation and mitral valve repair with Neochords the new area of transcatheter valve surgery

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Background: Aortic valve stenosis is often accompanied with hemodynamic relevant mitral valve insufficiency. During conventional surgery, both diseased valves would be treated. In the era of TAVI procedures the hemodynamic impact of mitral valve insufficiency is often underestimated and left untreated, therefor patients may remain symptomatic. The combination of transapical TAVI and Neochord implantation offers a therapy option for patient with aortic stenosis and mitral valve insufficiency due to a prolapsed or flail leaflet who have otherwise a too high risk for conventional surgery.

Methods: Within the last year we established the concomitant procedure of transapical TAVIs and Neochords at our institution: Two patients (one male, one female) mean age 82 years were treated. Both presented with severe aortic stenosis and a prolapse of the P2 segment of the mitral valve, with severe mitral valve insufficiency. At first the transapical TAVI was implanted under angio-guidance, followed by the 3D echo-guided implantation of the Neochords, through the same approach slightly posterior and lateral to the apex.

Results: Transapical TAVI implantation with an Edwards Sapien 3 26 mm $n=1$ and 29 mm $n=1$ was successful in both patients. Postinventional angio and transesophageal echocardiography revealed no paravalvular or central insufficiency. Mitral valve repair was performed by implantation of Neochords $n=2$ in the first and $n=3$ in the second patient, resulting in an only minimal remaining mitral valve insufficiency.

Both patients had an uneventful postoperative course, they were extubated within the first 12 h and transferred to general ward on the first postoperative day. They were discharged to home after 10 days.

The discharge echo of both patients revealed both valves competent without a remaining insufficiency or stenosis.

Conclusions: Transapical TAVI and concomitant mitral valve repair with Neochords is a feasible and promising treatment option for high risk patients. Although technically demanding, the procedure is save in experienced hands with promising results.

CV 1-7

Der operative Aortenklappenersatz bei degenerativen Aortenklappenvitien im hohen Lebensalter

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Grundlagen: Der interventionelle, katheterbasierte Aortenklappenersatz hat sich in den letzten Jahren von einer Methode, die nur bei high-risk PatientInnen eingesetzt wurde, zu einem etablierten Verfahren entwickelt, das zunehmend auch bei intermediate- risk PatientInnen eingesetzt wird. Im Hinblick auf diese Entwicklung müssen die Ergebnisse des konventionellen, chirurgischen Aortenklappenersatzes kritisch hinterfragt werden. Ziel dieser Studie war es, die Ergebnisse des isolierten chirurgischen Aortenklappenersatzes bei degenerativen Aortenklappenstenose zu evaluieren.

Methodik: Inkludiert wurden alle PatientInnen, die zwischen 2009 und 2017 aufgrund einer degenerativen Aortenklappenstenose an unserer Abteilung mittels Aortenklappenersatz ohne Zusatzeingriff operiert wurden. PatientInnen mit reiner Aortenklappeninsuffizienz, einer Re-Operation oder einer aktiven infektiösen Endokarditis wurden exkludiert.

Aus den lokalen Datenbanken wurden PatientInnenalter, Klappentyp, -durchmesser, -kuspidität, perioperative echokardiographische Befunde, Aortenklemm- und Bypasszeit, Euroscore (logistisch und Euroscore II ab 2012), operativer Zugang, Krankenhausaufenthaltsdauer und folgende Komplikationen evaluiert: 30 Tage-Mortalität, Schlaganfall, TIA, Vorhofflimmern, Schrittmacherimplantation, Nierenversagen, Dialysepflichtigkeit, Reoperation aufgrund von Nachblutungen und Wundinfektionen.

Es erfolgte eine Stratifizierung in Altersgruppen sowie nach Risiko (logistischer Euroscore >20 % = high-risk; Euroscore II <2 % = low-risk, 2–7 % = intermediate-risk, >7 % = high-risk). Die Datenanalyse wurde mittels deskriptiver Statistik durchgeführt.

Ergebnisse: Insgesamt wurden 517 Patienten operiert, davon 380 über eine mediane Sternotomie (73,5 %), 122 über eine Hemisternotomie (23,6 %) und 15 über eine rechtsanteriore Thorakotomie (2,9 %).

Das mittlere Alter lag bei 70,6 ± 9,0 Jahren, wobei im Verlauf ein tendenzieller Rückgang des Durchschnittsalters und der PatientInnengruppe der über 80-Jährigen bei Zunahme der Gruppe der 71- bis 80-Jährigen zu erkennen war. Von 2009 bis 2012 kam es zu einer deutlichen Abnahme des Anteils von HochrisikopatientInnen, der im weiteren Verlauf konstant blieb. Ab 2012 kam es zu einer Zunahme von PatientInnen im low-risk Bereich bei deutlicher Abnahme im intermediate-risk Bereich.

Im Gesamtkollektiv lag die 30-Tage Mortalität bei 1,5 %, das Auftreten eines Schlaganfalles bei 1 %, TIA 1,4 %, Dialyse 1,4 %, Schrittmacherimplantation 6 %, Nachblutungen 3,5 %, Wundinfektionen 2,1 %, postoperativ intermittierendem Vorhofflimmern bei 31,3 %.

Die Komplikationsraten zeigten bei den über 75-Jährigen ($n = 203$) im Vergleich zu den unter 75-Jährigen ($n = 314$) folgende Unterschiede: 30-Tage Mortalität 2,5 %/1,0 %, Schlaganfall 2,0 %/1,6 %, TIA 0,5 %/1,9 %, Dialyse 3,9 %/0,3 %, Schrittmacherimplantation 7,9 %/4,5 %, Nachblutung 4,4 %/3,5 %, Wundinfektion 2,0 %/2,5 %, postoperativ intermittierendes Vorhofflimmern 38,4 %/26,8 %.

Schlussfolgerungen: Im Beobachtungszeitraum nahm die Anzahl an high-risk PatientInnen erwartungsgemäß ab. Bei low- und intermediate-risk PatientInnen kann der konventionelle, chirurgische Aortenklappenersatz weiterhin mit einer sehr niedrigen Mortalitäts- und Komplikationsrate durchgeführt werden. Bei PatientInnen über 75 Jahren und erhöhtem operativen Risikoscore ist eine individualisierte und interdisziplinäre Therapieplanung unter Einbeziehung des katheterbasierten Aortenklappenersatzes (TAVI) unerlässlich.

CV 2-1

3D enabled totally endoscopic surgery in training of mitral valve repair

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Objective: To evaluate the impact of 3D totally endoscopic mitral valve repair on training, and to compare outcomes in contrast to 2D assisted minimal invasive mitral valve repair.

Methods: Between 2010 and 2017 a total number of 499 minimal invasive mitral valve procedures were performed (3D: $n = 154$; 2D: $n = 345$). In the totally endoscopic 3D cases a periareolar incision in male or submammary incision in female patients was performed. In 2D cases a 4–5 cm thoracotomy with a rib spreader to allow direct vision was used.

Results: Teaching was accomplished in 78 cases of 3D surgery (51%), but only in 58 cases of 2D surgery (17%). Repair rates were higher in 3D cases than in 2D cases, as well in teaching (94% vs. 91%, $p = 0.23$) as in the non-teaching situation (95% vs. 87%, $p = 0.05$). 52% of all patients presented with isolated P2 prolapse, the use of neo-chords was more pronounced in 3D surgery (86% training, 76% non-training). Mean cross clamp times in the teaching situation were longer in 2D cases compared to 3D (123 vs. 119 $p = 0.52$). Complications occurred more often in 2D cases compared to 3D teaching or 3D non-teaching situation (conversion to mitral valve replacement: 2.3% vs. 1.3% and 1.3%; residual mitral regurgitation > grade 1: 3.2% vs. 1.3% and 1.3%; revision for bleeding: 6.4% vs. 1.3% and 4.5%; 30-d-mortality: 1.7% vs. 0% and 1.3%).

Conclusions: 3D enabled totally endoscopic mitral valve repair is safe and provides even better results than 2D assisted minimal invasive mitral valve repair. Training is feasible and more often possible in 3D cases resulting in excellent outcomes. The endoscopic view gives identical images for surgeon and assistant and therefore is an ideal tool for teaching.

CV 2-2

Clinical outcomes of patients undergoing coronary artery bypass grafting (CABG) surgery with VEST supported venous grafts

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Background: Vein external support is a concept, which aims to reduce long-term neointima hyperplasia of saphenous vein grafts (SVG) in coronary surgery. Previous attempts of the concept with similar devices showed increased graft occlusion due to technical issues. The VEST 1 study showed decreased neointima hyperplasia at 1 year after CABG. The VEST 2 study evaluated the use of clips in supported vein grafts at the right coronary artery. The protocol of the currently presented VEST 3 Study is based on the clinical and angiographic comparison of supported and unsupported vein grafts which were accordingly randomized for the left and the right coronary system.

Objective: The primary objective of this study is to present the angiographic and clinical outcomes of CABG using Vein External supported SVGs of a single center participating in the VEST 3 study.

Methods: Ten patients with median (min, max) age of 67 years (52, 76), m/f: 8/2, EuroSCORE II: 0.99% (0.55%, 3.00%), with multi-vessel coronary artery disease were randomized in a prospective, multi-center study to VEST implantation on one

GRAFT	PATENT	STRING-SIGN	OCCLUDED
LIMA	7	1	1
RIMA	6	0	0
SVG-VEST	7	0	2
SVG	9	0	1

Fig. 1 | CV 2-2 six months CTA results

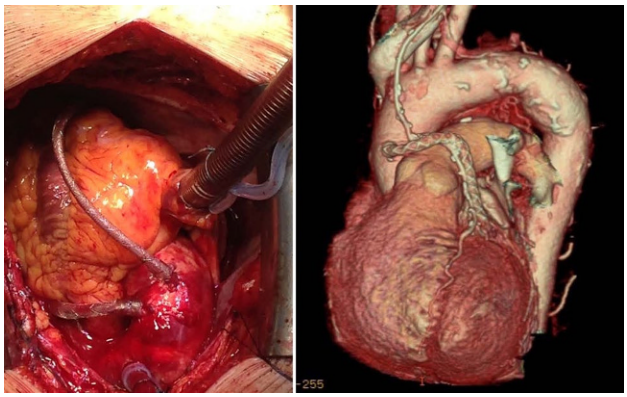

Fig. 2 | CV 2-2

of the SVGs to the right or the left coronary system in addition to single or double mammary artery grafts. Each patient received an externally supported and a non-supported SVG and acted as his/her own control. Every patient postoperative received the same medication of aspirin, beta-blocker and statin. The patients underwent clinical follow-up at 6 weeks, 6 months and 1 year. Additional CT angiography was performed at 6 months post CABG.

Results: There was no mortality observed at this case series. In all clinical use to date the VEST device has not been associated with any device related adverse events. Intubation time was 14 hours (10, 24), ICU stay was 1 day (1, 5) and hospital stay was 8 days (5, 12). There were no perioperative myocardial infarctions, acute kidney injuries or strokes. Perioperative enzyme release was: CK 444 U/l (246, 838), CK-MB 44 U/l (23, 74), Troponin 681 ng/l (318, 1313). The follow-up period was uneventful and all patients were symptom free at 1 year. The CT angiographic results at 6 months are shown in Fig. 1. One patient was excluded from the study after CABG procedure due to wound healing disorders for a patient safety reasons.

Conclusions: There was no device associated morbidity in the short-run. Angiographic follow-up showed no increased risk of graft occlusion due to technical issues at 6 months. Medium and long-term results are required to confirm the results of preclinical data.

CV 2-3

Early and intermediate outcome after bioprosthetic and mechanical aortic valve replacement in an under 60-year old patient collective—a single-center retrospective study

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Background: Aortic valve diseases are at increasing incidence the most acquired valvular heart diseases in western industrial countries. According to ESC-Guidelines, mechanical aortic valve replacement (M-AVR) should be considered in patients under 60 years and bioprosthetic aortic valve replacement (B-AVR) in patients over 65 years. Nevertheless, recent studies show acceptable outcome of B-AVR in younger patient collectives and many patients prefer the calculated risk for reoperation to a life-long Vitamin-K antagonist therapy.

Objectives: In this retrospective, single-center, non-randomized comparative study we aimed to compare the perioperative and the intermediate outcome of M-AVR vs. B-AVR in an under 60 year old patient collective.

Methods: Between 01.01.2007 and 31.12.2012, a total of 157 patients (M-AVR: $n=33$, B-AVR: $n=124$) aged under 60 years underwent aortic valve replacement at our institution. Follow-up with a mean follow-up period of 58.1 ± 20.5 months was performed from January to December 2015 and completed in 95.5%. All data were entered into the institutional database (Cardiac 2, S2 Engineering, Wels, Austria) and statistically analyzed using IBM SPSS Statistics 23. Data are presented as mean ± SD. A p-value of <0.05 was considered to be statistically significant.

Results: We found comparable baseline characteristics, except for a higher age (M-AVR: 48.3 ± 7.9 years, B-AVR: 54.6 ± 5.4, $p<.001$), as well as higher rates of COPD (M-AVR: 3.0%, B-AVR: 21.0%, $p<.05$) and dyslipidemia (M-AVR: 33.3%, B-AVR: 51.6%, $p<.05$) in the B-AVR group. Additionally, aortic cross clamping time (M-AVR: 98.4 ± 37.0 min, B-AVR: 81.3 ± 31.1 min, $p<.01$) as well as cardiopulmonary bypass time (M-AVR: 123.6 ± 45.4 min, B-AVR: 103.8 ± 37.5 min, $p<.05$) were significantly longer in M-AVR due to a higher rate of combined procedures.

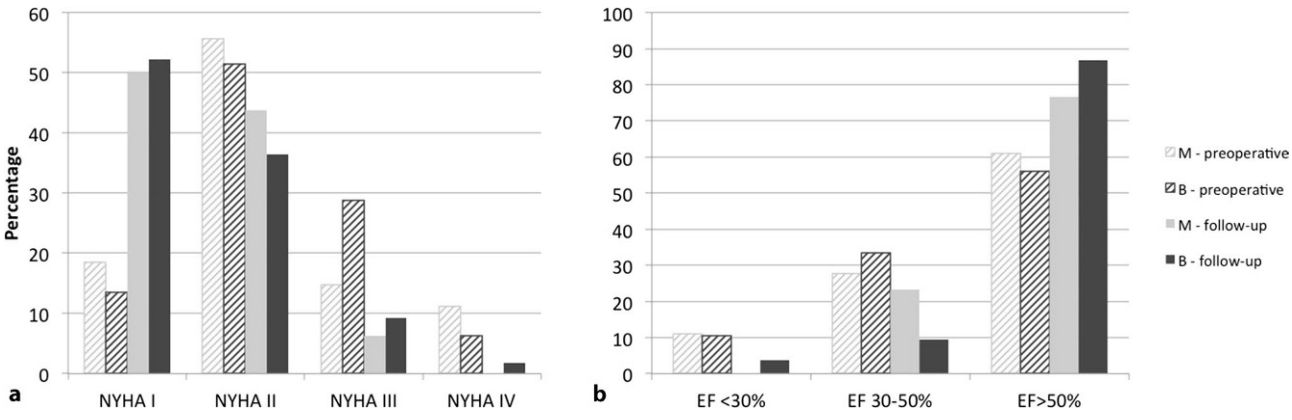

Fig. 1 | CV 2-3

No intraoperative deaths occurred. 30-day mortality (M-AVR: 0, B-AVR: 1 (0.8%), n. s.) and mortality at follow-up (M-AVR: 0, B-AVR: 8 (6.5%), of the latter only one due to cardiac pathology, n. s.) showed no significant differences. Moreover, in hospital reoperation rates (M-AVR: 2 (6.1%), B-AVR: 15 (12.7%), n. s.), mainly caused by hemorrhage, as well as late valve related reoperation rates (M-AVR: 1 (3.1%), B-AVR: 4 (3.4%), n. s.) did not show significant differences.

Additionally, at follow-up the groups showed comparable NYHA classes (Fig. 1 a, n. s.) as well as ejection fractions (Fig. 1 b, n. s.) and maximal transvalvular flows (M-AVR: 2.27 ± 0.51 m/s, B-AVR: 2.35 ± 0.47 m/s, n. s.) in echocardiography.

Conclusions: We could observe a comparable early and intermediate outcome in patients younger than 60 years with biological and mechanical prosthetic aortic valve replacement. The long-term follow-up will further elucidate possible differences.

CV 2-4

Early and mid-term results of new rapid deployment and sutureless valves for aortic valve replacement

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Background: As a result of a continuously ageing population the prevalence of age-related cardiac diseases is steadily increasing. This is certainly also true for degenerative calcified aortic valve stenosis. Surgical aortic valve replacement (AVR) is still the standard treatment for symptomatic calcified aortic valve stenosis. As surgical procedures in elderly multimorbid patients are related to a significantly increased perioperative risk, a lot of efforts have been made to find alternative methods of treatment such as transcatheter aortic valve interventions (TAVI). Recently, "rapid deployment valves" (Intuity and Intuity Elite®, Edwards Life Science) and "sutureless valves" (Perceval® Liva Nova)" have been introduced to reduce duration of surgery, cardiopulmonary bypass time and aortic cross clamp time. It was the aim of this monocentric, retrospective registry to evaluate the intraoperative, early postoperative and midterm outcome of this new technology.

Methods: Between the 20th of September 2012 and the 31st of December 2015, 132 patients with AVR using Edwards Intuity/Intuity Elite ($n = 97$) or Liva Nova Perceval ($n = 35$) were included in this study. Besides demographic data, operative mortality, hemodynamic performance and the duration of surgery, cardiopulmonary bypass time (CBP) and aortic cross-clamp time (ACC) have been monitored. Subsequently, 30d mortality as well as 12 and 50 months postoperative follow-up was analyzed. All data were entered into the institutional database (Cardiac 2, S2 Engineering, Wels, Austria) and statistically analyzed using IBM SPSS Statistics 24. Data are presented as mean±SD. A p-value of <0.05 was considered to be statistically significant.

Results: Mean age was 75 ± 7 years (55% male). Out of the total cohort, 76 patients (58%) received isolated AVR, 49 patients (37%) had a combined operation of AVR and coronary bypass surgery and 7 patients (5%) had additional procedures. There was no difference in preoperative demographic data and NYHA staging. According to the preoperative €-score, 76 patients (60%) were considered to be "high risk". In total, 48 patients (36%) were operated minimal-invasively using upper-hemisternotomy. Average operation time of the entire cohort was 157 ± 50 min, average CBP time was 90 ± 32 min, and average ACC time was 68 ± 24 min. For minimal invasive AVR, average operation time was 127 ± 28 min, average CBP time was 70 ± 19 min and average ACC time was 55 ± 15 min. Four patients needed reoperation due to paravalvular leak ($n = 2$, 1.5%) or instable valve position ($n = 2$; 1.5%), 6 patients (5%) needed perioperative pace makers. The postoperative Pmax returned to physiological values in 90% of patients, Vmax in 84% and both remained stable over the first

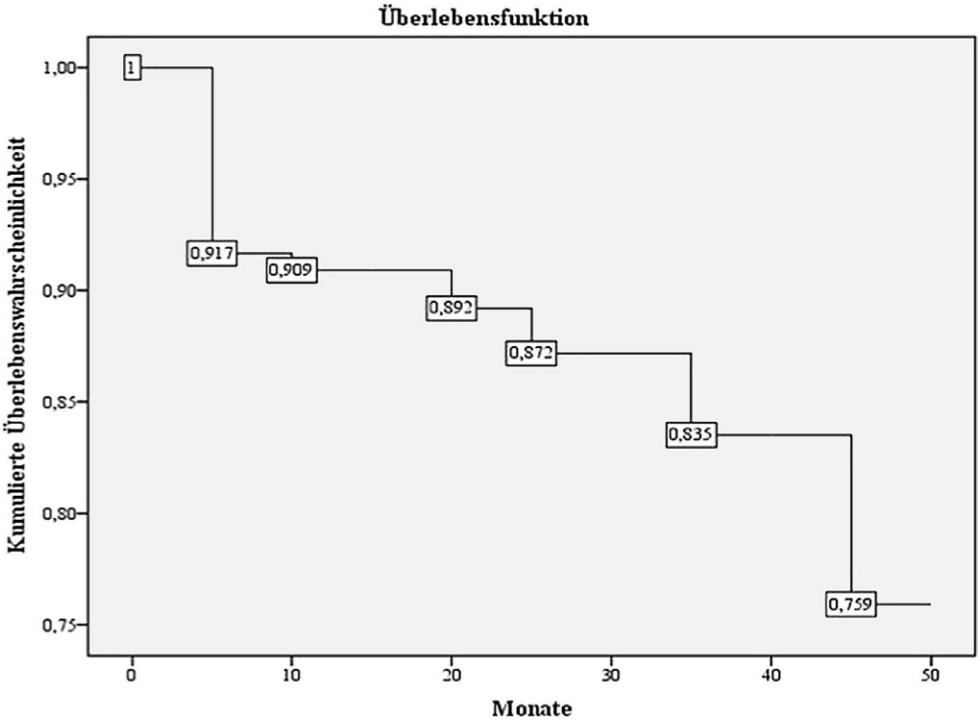

Fig. 1 | CV2-4

year of follow up. Overall 30d mortality was 5% ($n=7$). At one year follow-up 112 patients (85%) were alive, 12 patients died for cardiac reasons, 8 patients for non-cardiac. After 50 months culmulative survival was 76% (Fig. 1).

Conclusions: The new devices are safe and can easily be used also for minimal-invasive access. Therefore they are a valuable alternative for the treatment of symptomatic aortic valve stenosis in elderly and multimorbid patients. Randomised controlled trials should be performed with a longer observation period to determine ultimate superiority to standard valve procedures.

CV 2-5

Ein Jahr TEVAR-Programm Herzchirurgie St. Pölten – the good, the bad and the ugly

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Grundlagen: Die Therapie vieler Herzerkrankungen entwickelt sich weg von großen, invasiven Eingriffen hin zu minimalinvasiven und interventionellen Eingriffen. Dies gilt insbesondere für die chirurgische Versorgung der Aorta Descendens, die weitgehend durch die endovaskuläre Stenttherapie (TEVAR) abgelöst wurde. Gleichzeitig gewinnt die endovaskuläre Versorgung des Aortenbogens zunehmend an Bedeutung.

In St. Pölten werden die Diagnostik, Indikationsstellung, stationäre Aufnahme sowie die prä- und postoperative Betreuung von Patienten mit Pathologien an der thorakalen Aorta von der herzchirurgischen Abteilung durchgeführt. Aus diesem Grund wurde mit Juni 2017 im UK St. Pölten auch der eigentliche operative Eingriff in den herzchirurgischen Leistungskatalog übernommen.

Methodik: Statistische Aufarbeitung des ersten Jahres TEVAR an der herzchirurgischen Abteilung St. Pölten. Vorstellung der Eckpunkte unserer Programm-Vorbereitung und Durchführung, Erfahrungen beim Erlernen der Wire skills, Strahlenschutz, Aufbau eines eigenen Warenlagers, Komplikationsmanagement und kritische Interpretation unserer Lernkurve werden diskutiert.

Ergebnisse: Im Zeitraum 06/2017 bis 03/2018 (260 Tage) wurden 27 thorakale Stentgrafts (20 Patienten) implantiert (Abb. 1).

Schlussfolgerungen: Die operative Versorgung von Pathologien der Aorta Ascendens und des Aortenbogens wird primär von herzchirurgischen Abteilungen durchgeführt. Um die Weiterentwicklung der endovaskulären Therapie mit unserer chirurgischen Expertise optimal zu unterstützen und unseren Patienten auch in Zukunft alle Therapiemöglichkeiten der thorakalen Aortenpathologien anbieten zu können, sollte die endovaskuläre Versorgung Teil des herzchirurgischen Spektrums sein. Auch im Hinblick auf zukünftige interventionelle Therapieformen ist neben der offenen und minimal-invasiven Herzchirurgie der Ausbau einer interventionellen Herzchirurgie dringend erforderlich.

Die Integration eines endovaskulären Programmes in das herzchirurgische Routineprogramm ist mit einem überschaubaren Aufwand sehr gut möglich und ist eine ausgezeichnete Möglichkeit, Wire-skills zu verbessern. Eckpunkte eines erfolgreichen TEVAR-Programmes sind die Zusammenstellung eines interventionellen Teams, gute Kommunikation mit allen an der Patientenversorgung beteiligten Abteilungen, ausgearbeitete und vorbereitete Notfall- und Bail-out-Pläne, eine sorgfältige präoperative Planung sowie eine intensive postoperative Betreuung der Patienten.

Follow-up	100%
30d Mortalität	0%
Alter	62±8 Jahre
Geschlecht	33% weibl.
Strahlungsdauer	21±5 min.
KM-Verbrauch	146±46 ml
Liquordrainage (LD)	40 %
Indikation	
High Risk B-Diss	14/20 (60%)
Restdissektion Typ A	3/20 (15%)
Trauma/SINE/Malperfusion	3/20 (15%)

Komplikationen:	
Paraparese	1/20 (5%)
Endoleak	2/27 (7,4%)
Leistenrevision	3/20 (15%)
SINE	1/27 (3,7%)
Komplikationen LD	2/20 (10%)

Abb. 1 | CV 2-5

CV 2-6

Modification of the frozen elephant trunk implantation technique

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Background: The frozen elephant trunk (FET) technique has evolved as an accepted treatment modality for various acute and chronic aortic pathologies involving the aortic arch. Aim of this study is, to compare a modified implantation technique with an aortic anastomosis between the origin of the brachiocephalic branch and the left common carotid artery (zone 2) and an extraanatomic revascularisation of the left subclavian artery after moderate hypothermic circulatory arrest with the conventional implantation technique for the Thoraflex Hybrid prosthesis (Vascutek, Inchinnan, Scotland).

Methods: Between May 2014 and March 2018 40 patients underwent complete aortic arch replacement with the thoraflex hybrid prosthesis in our institution. 17 patients underwent conventional arch replacement and 23 patients the modified procedure.

Results: Perioperative mortality was 12.5%. Acute indication for FET implantation was given in 11 patients (64.7%) in the conventional group and in 16 patients (69.6%) in the modified group. Neurologic complications occurred in 3 patients (13.0%) in the modified group (3 strokes) and in 3 patients (17.6%) the conventional group (1 stroke, 2 spinal cord ischemia). Moderate hypothermic circulatory arrest time was shorter in the modified group (44.5 ± 15.2 vs. 50.2 ± 9.6 minutes p=ns). The stent-graft of the thoraflex hybrid prosthesis ended between the thoracic vertebra (Th) 6 and Th 8 in the conventional group and between vertebra Th 5 and Th 7 in the modified group (median 7.5 (6.75–8.0) vs. 6.0 (5.0–6.0) $p<0.004$) depending on the height of the patient. Two patients in the conventional group experienced a spinalis anterior syndrome but none of the patients in the modified group.

Conclusions: In our small series we could show that a modification of the implantation technique is safe and results

in shorter DHCA times and fewer neurologic complications with no spinal cord injuries. In combination with significantly shorter coverage of the descending aorta the modified implantation technique seems to be protective for spinal cord injury.

CV 2-7

Moving up to zone 2 in Frozen elefant Trunk procedures: The next step in the evolution of aortic arch surgery

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Background: The frozen elephant trunk (FET) procedure has facilitated the treatment of various acute and chronic aortic arch pathologies. We describe herein our initial experi-ence with a modification of this technique characterized by a distal aortic anastomosis be-tween the origin of the the left common carotid and the left subclavian artery (zone 2) in-cluding an extra-anatomic bypass to the left subclavian artery.

Methods: Between March 2017 and February 2018, 16 patients underwent total aortic arch replacement employing the FET technique with zone 2 anastomosis (FET in zone 2—F. I.2) with either the E-vita Open Plus (Jotec GmbH, Hechingen, Germany, $n=14$) or Tho-raflex (Vascutek, Inchinnan, Scotland, $n=2$) hybrid prosthesis. Direct canulation of the right axillary artery and a lowest core (bladder) temperature of 28 °C was used in all patients. Indications for surgery included redo-procedures for chronic dissections ($n=9$), acute type A aortic dissections ($n=4$), and degenerative aneurysms ($n=3$).

Results: There was no perioperative death or 30-day mortality. Mean cardiopulmonary bypass time was 178 ± 23 min, and the myocardial ischaemic time reached 109 ± 14 min. Selective antegrade cerebral perfusion time accounted for 36 ± 7 min. Ventilation time was 13 ± 7 h, whereas intensive care unit stay was 3 ± 5 days. No new onset postoperative permanent neurological complication occurred. Two patients (13%) experienced temporary delirium with complete resolution of symptoms prior to discharge from the hospital and temporary hemofiltration was necessary in another two patients (13%).

Conclusions: Our preliminary experience with the F. I.2 procedure suggests that this ap-proach is safe, feasible and helps to reduce selective antegrade cerebral perfusion time. By simplifying the sometimes cumbersome distal aortic anastomosis the F. I.2 procedure will become our future standard approach in patients requiring total arch replacement.

CV 2-8

Preoperative neurologic dysfunction in acute aortic dissection type A: Does immediate surgery improve neurologic outcome and long-term survival?

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Objective: To evaluate the impact of preoperative neurologic dysfunction on postoperative outcome and long-term survival and to identify predictors postoperative neurologic injury.

Background: Despite improvement in operative and cerebral perfusion techniques, cerebral malperfusion and neurological injury remain dreaded complications of acute type A aortic dissection (AAD). Outcomes for patients presenting with preoperative neurologic dysfunction (PND) on postoperative status remain to be clarified.

Methods: Between 02/2000 and 12/2017 338 patients (mean age 59.3 ± 13.7 years; 70% male) were admitted for surgical repair for acute type A aortic dissection. Patient cohort was screened for patients with preoperative neurologic dysfunction (PND). PND was defined as the presence of syncope, seizure, somnolence or coma, dysarthria, amaurosis fugax, paresthesia or paresis.

Results: Fifty patients (14.9%) presented with neurologic symptoms. Out of these 50 patients with preoperative PND, 25 were primarily consulted by a neurologist at the emergency department. Immediate preoperative cranial CT scan was performed in 48 patients (96%) which revealed cerebral ischemia in 5 patients (10%). Median time from symptom onset to surgery was 415 minutes (min 115 minutes; max 9 days) in the entire cohort. 5 patients (10%) with PND died from aortic rupture before cardiopulmonary bypass could be installed. In the remaining 45 patients aortic repair could successfully be performed. Postoperative imaging and neurologic examination revealed neurologic injury in 20 patients (42.2%). Multivariate analysis of all surgically treated patients identified PND (HR = 2.379, 95% CI = 1.065–5.314, $p=0.035$) and preoperative CPR (HR = 4.285; 95% CI = 1.103–16.639, $p=0.036$) as an independent risk factors for postoperative) neurologic injury. Patients with preoperative neurologic dysfunction had higher a hospital mortality (PND: 32.7% vs. no PND: 15.7%, $p=0.008$) and impaired long-term survival ($p=0.004$).

Conclusions: PND acts as a strong precursor of neurologic injury. Despite immediate emergent surgery, PND is associated with impaired short- and long-term outcome after surgical repair for AAD.

CV 2-9

Perkutane Versorgung eines gothischen distalen Aortenbogens mit Postdissektionsaneurysma durch Einsatz einer innovativen endoluminalen Prothese mit aktiver Angulation in Zone 2 bei einem 2-fach voroperierten 62-jährigen Patienten

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Größenprogrediente Postdissektionsaneurysmata, insbesondere des distalen Aortenbogens, nach notfallmäßigem Aorta ascendens oder Teilbogenersatz bei akuter Typ A Dissektion sind ein beschriebenes Problem.

In diesem Fallbericht eines 2-fach voroperierten 62-jährigen Patienten mussten mehrere anatomische und patientenspezifische Aspekte bedacht und gegeneinander abgewogen werden, um zu einer bestmöglichen Behandlungsstrategie zu finden. Im Jahr 2000 erhielt der Patient zunächst einen elektiven mechanischen Aortenklappenersatz. In 2006 musste dann notfallmäßig bei akuter Typ A Dissektion in einer technisch sehr komplexen Reoperation ein Aortenwurzel und ausgedehnter Teilbogenersatz (Zone 3 mit Interponat zum Truncus brachio-cephalicus) durchgeführt werden. Der postoperative Verlauf gestaltete sich komplex. In den Folgejahren entwickelte sich eine Postdissektionsaneurysma mit einem maximalen Durchmesser von über 60 mm und zuletzt deutlicher Dynamik der Größenprogredienz. Der initiale Plan zur Durchführung eines offenen Dritteingriffes unter Einsatz der Frozen Elephant Trunk Technik wurde aufgrund des komplizierten Verlaufes bei der Zweitoperation sowie zahlreicher Komorbiditäten des Patienten wieder verlassen.

Eine weitere Herausforderung stellte der ungewöhnlich spitze Winkel des distalen Aortenbogens („gothischer Bogen“) dar. Dadurch schien zunächst auch eine endovaskuläre Versorgung sehr schwierig zu sein. Nach interdisziplinärem Konsens mit unseren Kollegen der interventionellen Radiologie entschieden wir uns für die in Österreich zuvor erst zweimal eingesetzte Gore CTAG Prothese (W. L. Gore & Associates, Inc., Newark, Delaware USA) mit Möglichkeit zur aktiven Angulation. Nachdem im gleichen Eingriff in unserem Hybrid OP Saal zunächst ein carotido-subclavialer Bypass angelegt und anschließend der native Abgang der linken Arteria subclavia mittels eines plugs verschlossen wurde, konnte die innovative Prothese sicher in Zone 2 abgesetzt werden und führte zu einem sehr zufriedenstellenden Ergebnis (siehe auch postoperativer CT Kontrolle). Der Patient konnte nach völlig unauffälligem Verlauf ohne neurologische und klinische Auffälligkeiten nach Hause entlassen werden.

CV 3-1

Mitral valve redo surgery using a transcatheter balloon-expandable pericardial heart valve–case report

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Background: Mitral valve reoperations due to failing bioprostheses or failing mitral valve repair are associated with high morbidity and mortality, especially in patients who are at very high or prohibitive surgical risk. Transcatheter mitral valve-in-valve (TMViVI) and valve-in-ring (TMViRI) procedures have emerged as a potential alternative for these patients. Here, we report one case of successful TMViVI and one case of successful TMViRI using a balloon-expandable pericardial heart valve (SAPIEN 3; Edwards Lifesciences, Inc., Irvine, California, United States).

Case Description: First case: A 77-year-old female patient was referred with dyspnea according to New York Heart Association (NYHA) functional class III–IV, after mitral valve replacement 2010 (25 mm CE Magna), transcatheter aortic valve replacement (CoreValve, Medtronic, Inc., Minneapolis, Minnesota, United States) in 2015 and CRT-P implantation 2014 due to severe reduced left ventricular ejection fraction. Now she had a failed mitral valve bioprothesis with a mean transprosthetic gradient of 20 mm Hg. Second case: A 65-year-old female patient with dyspnea (NYHA III) due to a combined mitral vitium after mitral valve repair 2003 (30 mm Physioring C. E.) with a severe reduced left ventricular ejection fraction.

Methods: After evaluation by a Heart team in both patients, a transapical approach was performed in 10/2017 with general anaesthesia, transoesophageal echocardiography guidence and fluoroscopy. Procedures were performed with rapid pacing, using a balloon-expandable pericardial heart valve (Edwards SAPIEN 3).

Results: For the TMViVI a Sapien 3 26 mm and for the TMViRI a Sapien 3 26 mm with an additional inflation of 2 ml was used. Implantation was successful in both patients with mean transvalvular gradients of 7 mm Hg and no paravalvular or central regurgitation in both patients. Discharge from hospital was at day 15 in the first patient and at day 17 in the second patient without any major complication.

Conclusions: Transapical, transcatheter mitral valve-in-valve or mitral valve in ring implantation can be considered as a complementary approach to reoperative mitral valve surgery in select patients.

CV 3-2

Mitral valve surgery on the fibrillating heart

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Objective: To evaluate feasibility, safety and outcomes of mitral valve surgery via lateral mini-thoracotomy without aortic cross clamping.

Methods: Between 2010 and 2017 a total number of 499 minimal invasive mitral valve procedures were performed. In 19 cases (3.8%) the operation was accomplished without aortic cross clamp on the fibrillating heart. Either 2D or 3D video assistance after lateral mini-thoracotomy was used in all cases.

Results: Mean age was 64 years, 12 (63%) were male, 7 (37%) female. All patients had underwent at least one prior cardiac surgery, covering a broad spectrum of different procedures. Cannulation for extracorporeal circulation was performed via femoral vessels in 11 (58%) patients, in 8 (42%) the axillary artery was used due to severe aortic sclerosis. After preparing the left atrium ventricular fibrillation was induced and maintained throughout the procedure. Mean bypass time was 215 minutes,

mean fibrillation time was 124 minutes. In 12 patients (63%) successful mitral valve repair was accomplished, in 7 (37%) the mitral valve was replaced. Concomitant tricuspid valve repair was performed in 4 (21%) patients, in 2 (10.5%) patients additional atrial ablation was done. Major complications occurred in few patients (1 ECMO due to lung edema, 2 revisions due to bleeding), 18 patients (94.8%) were discharged home, 1 (5.2%) patient died from intracerebral bleeding. No further mitral valve intervention was necessary in all survivors.

Conclusions: Mitral valve surgery without aortic cross clamp via lateral thoracotomy is feasible with acceptable repair rates. Perioperative morbidity is low, procedural survival is excellent. This type of surgery is an attractive alternative in redo patients in a specialized center.

CV 3–3

Short term follow-up after off-pump transapical mitral valve repair with the NeoChord™ DS 1000 device

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Background: At the last year meeting of ÖKG, we reported our first initial results with the new NeoChord™ device for mitral valve prolapse repair through trans-apical approach in patients with severe mitral incompetence. Until October 2017 we operated on 5 patients and performed clinical and echocardiographic follow-up (mean FU-time: 15 months; range 4–25 months).

Methods: Since January 2016 five patients (mean age: 85 years; range 75–92 years) underwent implantation of expanded neo-chordae (polytetrafluoroethylene ePTFE) with the NeoChord™ DS 1000 device. The left ventricular apex is accessed via standard triple purse string ventriculotomy through a left "TAVI" mini-thoracotomy. The device is inserted towards the mitral valve into the left atrium. Intra-cardiac orientation is achieved with both 2D and 3D echocardiographic guidance. With expandable jaws, the prolapse is captured and its effectiveness confirmed by observing the four fiber optic monitor lights changing from red (blood) to white (leaflet). Now the leaflet is penetrated with a needle with subsequent retrieval of the NeoChord™ ePTFE suture. After implantation of the necessary number of sutures, final assessment of the operative results is achieved using echocardiography. Now the properly tensioned NeoChords™ are secured to the LV apex with pledgets and knots.

Results: With the use of several ePTFE sutures (mean number of chordae 3.4; range 2–4), all mitral valves were repaired successfully. One patient with posterior annular calcification and prolapse P2 had mild residual MI = II at discharge. No patient had conversion to sternotomy, reoperation or complications from apical bleeding. A 92 year old lady died after discharge from pneumonia and right heart failure in another department. She already had several events of right heart failure preoperative and a systolic PAP of 87 mm Hg. Four patients were examined at follow-up. All patients are in NYHA class I-II; no patient established an increase in mitral incompetence.

Conclusions: NeoChord™ implantation without HLM via trans-apical approach is feasible and leads to significant reduction of mitral incompetence in patients with mitral valve prolapse. Short term follow-up showed stable results and good quality of live in all patients. However right heart failure is a challenging issue in the postoperative care.

CV 3-4

One valve stenosis, one valve regurgitation, and one simultaneous, off pump approach to treat them both

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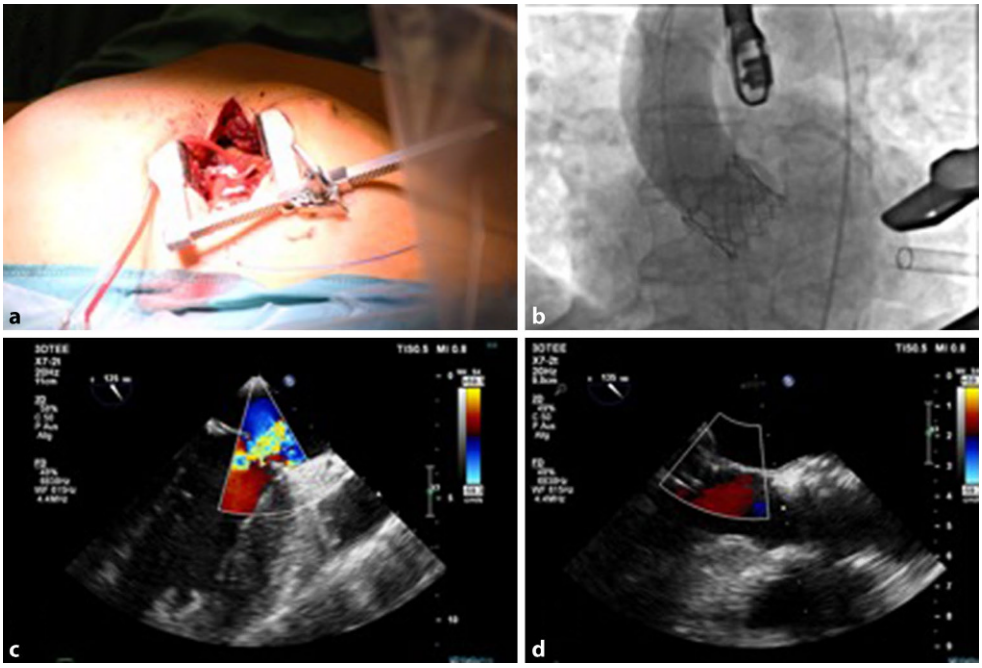

Fig. 1 | CV 3-4

Herein we describe of a single surgical procedure combining a trans-apical trans-catheter aortic valve implantation (TAVI) with an off-pump implantation of artificial chords with the NeoChord™ device. In a 89-year-old male patient severe aortic stenosis with a mean gradient of 45 mmHg (calculated valve orifice area of 0,8 cm^2) and a severe mitral regurgitation due to chordal rupture in the P2 segment of the posterior mitral leaflet (PML) was found. The institutional Heart Team decided to treat both valves simultaneously with a trans-apical approach. At first, a TAVI (29 mm SAPIEN 3/XT™, Edwards Lifesciences, Irvine, CA, USA) was implanted in aortic position. Then, three Gore-Tex CV-4 sutures (Gore-Tex; W. L. Gore & Associates, Inc, Flagstaff, AZ, USA) were attached to the free edges of the P2 segment of the PML under 3D transoesophageal echocardiographic guidance using the NeoChord™ DS 1000 device (NeoChord Inc., St. Louis Park, MN, USA). When combining these procedures, choosing the optimal access site at the apex of the left ventricle is challenging. Whereas the ideal TAVI ac-cess point is located apically, the access site best suited for the NeoChord™ procedure is slightly more laterally. Perfect interplay of cardiac surgeons and cardiologists is necessary to find this „perfect hy-brid access site". In our patient, the echocardiographic outcome for both valves was excellent (Fig. 1), with no residual mitral insufficiency and a good result after TAVI (mean gradient: 12 mmHg; no paravalvular leak). The clinical course was uneventful and the patient was discharged the ninth day after surgery. We would like to present the according video of this case and discuss current and potential future simultaneous interventional multi-valve therapies with the audience.

CV 3-5

Evaluation of cardiovascular implantable device infections: a single-center experience with 250 patients

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Background: Growing evidence suggests that infection rates after cardiovascular implantable electronic device (CIED) procedure are continously increasing. In literature infection rates after primary device implantation vary between 0.68 and 2.8% identifying different causes. Aim of this study was to evaluate infection rates after CIED procedure at our department and the role of prophylactic measures to avoid postoperative infection.

Methods: In this single center analysis a retrospective study of pacemaker surgeries performed between January and June 2015 was compiled.

Results: A total of 250 patients (63% males) received a CIED (dual-chamber pacemaker $n=87$, single-chamber pacemaker $n=21$, CRT-P $n=6$, CRT-D $n=21$, ICD $n=27$, sICD $n=2$, box change $n=54$, lead replacement $n=28$ and epicardial lead $n=4$). Mean age was 74 years (30–94). Overall infection rate was 2.8% ($n=7$). Infection rates between primary procedures ($n=4$) and reinterventions ($n=3$) were comparable (2.65 vs. 3.03%; n. s.). More than one local antiseptic measure (including wound irrigation with antiseptic solutions, local antibiotics, pocket excision and submuscular relocation of the pocket) was applied significantly more often in re-interventions compared to 18.5% in primary implantations (30.78 vs. 18.5%; $p=0.02$).

Conclusions: General infection rates of our cohort after primary implantation and revision are low and comparable with described numbers in literature. Infections after primary procedures and reinterventions were comparable, which we attribute to a significantly increased use of combined antiseptic measures. Our results show that more than one local antiseptic measures should be applied to maintain a low infection rate even in reinterventions. More data are needed to identify those preventive actions which play the most important role in infection prophylaxis.

CV 3-6

Long-term heart transplant outcomes after lowering fixed pulmonary hypertension using left ventricular assist devices

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Background: Fixed pulmonary hypertension (fPH) is a contraindication for heart transplantation. Left ventricular assist device (LVAD) implantation as a bridge to candidacy can reverse fPH in patients with terminal heart failure by chronic left ventricular (LV) unloading. We report our institutional experience with terminal heart failure patients and fPH that were successfully bridged to candidacy and underwent subsequent heart transplantation (HTX).

Methods: We retrospectively reviewed the data of 79 patients with terminal heart failure and fPH who were successfully bridged to candidacy for HTX at our center from 11/1998 to 09/2016 with six different LVAD devices (Novacor $n=4$, MicroMed DeBakey $n=29$, DuraHeart $n=2$, HeartMate II $n=13$, HVAD $n=30$, MVAD $n=1$). Median duration of LVAD support was 288 days (range 45–2279 days). Within the same timeframe a control group of 48 patients underwent HTX after bridge-to-transplant LVAD therapy for reasons other than PH. Study endpoints were, (1) development of fPH after LVAD implantation, (2) post-transplant outcome, and (3) incidence of severe adverse events.

Results: Pulmonary vascular resistance (PVR), assessed by vasodynamic catheterization, was 4.3 ± 1.8 Wood Units (WU) before LVAD implantation. After an average support period of 106 ± 136 days, PVR decreased to 2.0 ± 0.9 WU ($p < .0001$) and patients were listed for HTX. Median duration of LVAD-support in the study group was 288 days (45–2279). We observed two cases (2.5%) of acute right heart failure that required extracorporeal mechanical support after HTX in the study group. Long-term post-transplant survival between the study group (3 year: 83.5%, 5 year: 81.0%) and the control group (3 year: 87.5%, 5 year: 85.4%) were comparable (log-rank: $p=.585$).

Conclusions: LVAD implantation as a bridge to candidacy reverses fPH in patients with terminal heart failure. Post HTX survival is excellent and is comparable to results obtained in patients without fPH at the time of HTX listing.

CV 3-7

Outcomes after surgical ventricular restoration for left ventricular aneurysms

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Background: Effectiveness of surgical ventricular restoration ("Dor procedure", SVR) is a matter of debate. We evaluated the long term outcome after SVR for left ventricular aneurysm (LVA) in patients operated at our institution.

Methods: Between 2010 and 2018 34 patients were operated for dyskinetic LVA. A Dacron patch was implanted into the scarred region of the left ventricle to reshape ventricular geometry and to achieve akinesia instead of dyskinesia. Additional procedures were added as required.

Results: Mean age was 62 years, patients were predominantly male (25 male patients, 9 female patients). They presented on average in NYHA stage 3 with mean NT pro-BNP levels of 2486 ng/l. Echocardiography or magnetic resonance imaging showed mean ejection fraction of 30%. An anterior wall patch was implanted in 28 (82%) patients, a posterior wall patch in 6 (18%) patients. Coronary bypass was added in 27 (79%) cases, other concomitant procedures were mitral valve repair or replacement, ventricular septum defect closure, aortic valve replacement or tricuspid valve repair. Extracorporeal membrane oxygenation was needed in one patient, all patients were discharged alive. Early assessment of LV function showed improvement to mean ejection fraction of 39%. During long term follow up four patients deceased after 17, 30, 53 and 54 months. The remaining 30 (88%) survivors have a mean survival of 42.8 months. As of March 2018 patients present predominantly in NYHA stage 1.

Conclusions: SVR is a safe and effective procedure in properly selected patients presenting with dyskinesia of the LV aneurysm. Even extensive concomitant procedures do not add significant morbidity. Early and long term survival are excellent. Significant functional improvement is maintained over years.

CV 3-8

Patient blood management in Jehovah's Witnesses undergoing cardiac surgery

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Background: Jehovah's Witness (JW) patients refuse allogeneic blood transfusions and pose therefore a unique challenge in case of major surgery. In the present study, we reviewed our 10-year experience with JW patients undergoing cardiac surgery.

Methods: Between October 2008 and April 2017, 35 consecutive JW patients with a mean age of 68.0 ± 9.5 years underwent a cardiac operation at our institution. The follow-up is 100% complete.

Results: The mean logistic EuroSCORE was 6.9% (range: 1.1–42.4%). Performed procedures included coronary artery bypass grafting in 16 patients, aortic valve replacement in 11 patients, mitral valve repair/replacement in 6 patients and aortic surgery in 2 patients. Erythropoietin/iron were administered preoperatively to 12 patients (34.3%) for anemia, with an increase in hemoglobin by 2.0 g/dl. The mean hemoglobin concentration on admission was 14.1 ± 1.1 g/dl, and the nadir hematocrit during cardiopulmonary bypass was 30.1 ± 4.9%. None of the patients received allogeneic blood transfusions. Fatal postoperative bleeding occurred in 1 patient, leading to 2.9% in-hospital mortality. The median stay on the intensive care unit was 1 day, and the mean length of hospital stay was 17 ± 8 days. The hemoglobin concentration at discharge was 11.5 ± 1.5 g/dl. Survival probability at 5 years was 77.6%.

Conclusions: Cardiac surgery in JW patients can be performed with a low morbidity and mortality by adherence to a multi-disciplinary patient blood management program, including preoperative optimization of hemoglobin concentration.

CV 3-9

Subclavian vs. femoral artery access in venoarterial extracorporeal membrane oxygenation: a single center experience

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Background: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is an important tool in the armamentarium for the treatment of cardiogenic shock. Several approaches exist for arterial cannulation, including femoral artery, subclavian artery and central aortic access. In this study we present our institution's experience with VA-ECMO with regard to the cannulation strategy.

Methods: We conducted a retrospective analysis of 65 consecutive patients undergoing VA-ECMO implantation at our institution between January 2011 and December 2016. Subclavian artery cannulation (SAC) and non-subclavian artery cannulation (NSAC) were compared with regard to mortality, oxygenation level, ECMO blood flow and the rate of complications, defined as bleeding requiring intervention, limb ischemia, stroke, wound infection, plexus brachialis pain syndrome and hemolysis.

Results: Between January 2011 and December 2016 a total of 21 female and 44 male ($n=65$) patients required VA-ECMO support at our center. Indication for ECMO support was cardiac failure prior to or after cardiac surgery in 58 (89.2%) patients, while 7 patients (10.8%) received VA-ECMO support for other reasons, such as major myocardial infarction with cardiogenic shock ($n=3$), massive pulmonary embolism ($n=2$), pneumonia ($n=1$) and hypothermia ($n=1$). Overall 30-day mortality was 36.7%. Primary cannulation of the subclavian artery was performed in 55 patients (84.6%). While right-sided cannulation

was the preferred method in 49 patients (89.1%), six patients received left-sided subclavian artery cannulation due to pre-existing right-sided pacemaker implantation ($n=5$) or radiation ($n=1$). Ten patients (15.4%) were primarily cannulated via a femoral artery access ($n=6$) or direct insertion into the ascending aorta ($n=4$). Sufficient oxygenation was achieved via subclavian (PaO2: 301 ±130 mmHg) and non-subclavian (PaO2: 292 ±172 mmHg) arterial access and did not differ between both groups ($p=0.349$). The maximum ECMO flow was comparable between the SAC-group (4.3 ± 0.6 L/min) and the NSAC-group (4.5 ± 0.4 L/min). The number of complications per patient was lower in SAC-group compared to the NSAC-group (16/57, 28.1%] vs. 10/14, 71.4%; $p=0.043$). The need for surgical revision of the cannulation site did not differ between the two groups ($p=0.180$). Switching from a non-subclavian to a subclavian access was performed in 3 patients because of limb ischemia, switching from subclavian to non-subclavian access was necessary in 2 patients due to uncontrollable right arm hyperperfusion or substantial bleeding. Mean follow-up for the entire ECMO cohort was 234 days. Of 41 (63.3%) survivors, 13 (20%) were discharged home, 23 (35.4%) were transferred to a secondary hospital or rehabilitation center and 5 (12.1%) patients were transferred to a primary care center for LVAD-implantation or heart transplantation.

Conclusions: Our data show comparable results between subclavian artery and femoral artery cannulation for VA-ECMO support in terms of mortality, oxygenation, blood flow, hemolysis and bleeding complications. However, subclavian artery access bears the advantage of avoiding possibly disastrous limb ischemia. Therefore, subclavian artery cannulation is considered the method of choice for ECMO cannulation at our institution.

CV 3-10

The duration of the pre-operative hospitalization is associated with an increased risk of healthcare-associated infections after cardiac surgery

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Background: Nosocomial infections are a common complication in clinical practice that proved to have a major impact on the surgical success and patient outcome. While it is known, that the probability of the development of nosocomial infections is rapidly increasing during the course of hospitalization, the impact of a prolonged pre-operative hospitalization has not been investigated so far. Therefore, we aimed to investigate the impact of a prolonged pre-operative hospital stay on the development of a post-operative infection.

Methods: Within this prospective observational study, we enrolled 200 patients scheduled for elective cardiac surgery without any signs of infections at admission. Participants were stratified into groups depending on their length of pre-operative hospitalization in <2 days (surgery on time; $n=56$), 2–7 days (delayed surgery; $n=63$) and >7 days (extensive delay of surgery; $n=76$). Reasons for the delay were independently of administrative nature. Patients were followed during their total hospital stay and continuously screened for the development of a nosocomial infection. Binary logistic regression analysis was performed to elucidate the impact of a prolonged pre-operative hospital stay on the development of any infection. The multivariate model was adjusted for potential confounders: type of surgery and EuroScore II.

Results: Out of a total of 195 patients (median age: 69 years [IQR: 61–75]; 69.2% male gender) that were suitable for analysis, 32.8% ($n=64$) received coronary artery bypass graft (CABG) surgery, 44.1% ($n=86$) cardiac valve surgery and 23.1% ($n=45$)

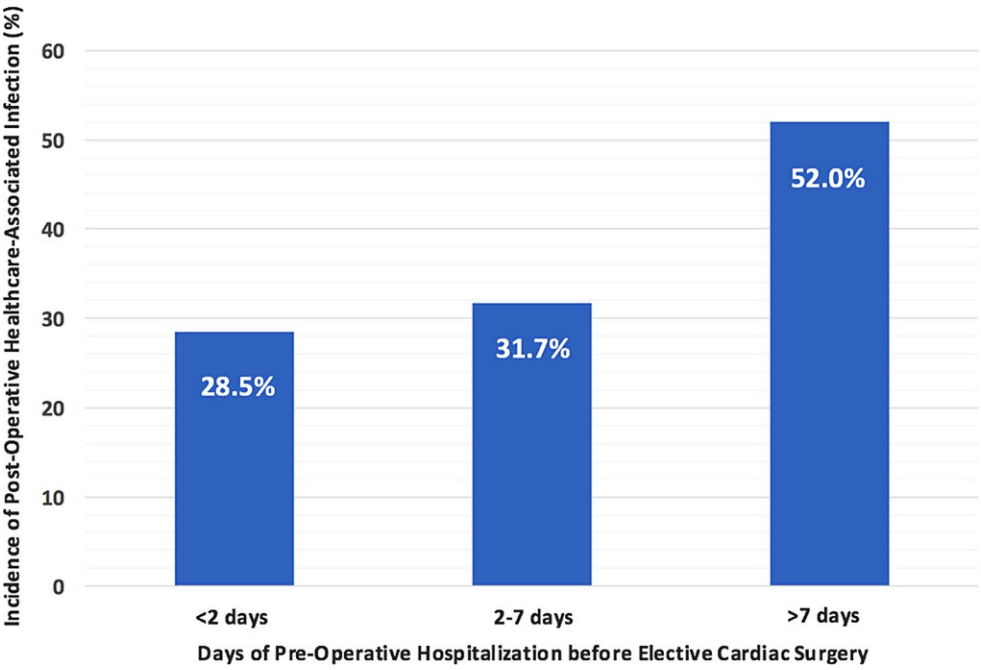

Fig. 1 | CV 3-10

a combined CABG and valve procedure. We observed that more than one third of patients (38.5%; $n=75$) developed any nosocomial infection after surgical intervention with a median pre-operative hospitalization of 6 days (IQR: 2–12). Of utmost interest, comparing patients that received surgery on time (<2 days) to individuals with extensive delay of surgery (>7 days) we found a strong and direct association of the duration of pre-operative hospitalization and the fraction of patients developing an infection (+23.5%; $p=0.006$). Interestingly, stratified by the respective types of infection there was a significant increase in surgical site infection (+7.9%; $p=0.034$) and pneumonia (+7.4%; $p=0.049$), while central venous catheter infections ($p=0.245$) and urinary tract infections ($p=0.346$) remained particularly stable. Additionally, the length of the patients' pre-operative hospital stay was independently associated with the development of any post-operative infection, with an adjusted OR per day of 1.38 (95%CI: 1.02–1.86; $p=0.036$).

Conclusions: A prolonged pre-operative hospital stay was significantly associated with the development of nosocomial infections. These findings need to be considered for future referral patterns in clinical patient management, to prevent unnecessary antibiotic use and a potential harm of patients.

CV 3-11

The Mond® RVOT Stylet improves septal positioning of the right ventricular lead during pacemaker implantation

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Background: There is strong evidence that septal positioning of the right ventricular (RV) lead improves outcome after pacemaker implantation due to a lower incidence of pacemaker induced cardiomyopathy and myocardial lead perforation. The Mond® RVOT Stylet (Abbott) is designed to facilitate septal RV lead positioning due to its three-dimensional curvature. The aim of this study was to evaluate the efficacy of the Mond® stylet compared to regular stylets.

Methods: A retrospective database analysis of pacemaker implantations, performed by one surgeon between January 1st 2017 and January 31st 2018 at our department, was conducted. A total of 125 patients (59% males) were included in this study. All pacemaker implantations, performed until June 30th 2017 were carried out using regular stylets. With July 2017, the Mond® stylet was introduced and adopted for all pacemaker implantations. Two groups were compiled: The control group (standard stylet) and the Mond group (Mond® stylet). The Mond group comprised 70 patients, the control group 55 patients. Inclusion criteria were postoperative chest x-ray in two planes (anterior-posterior, side view) for verification of RV lead position.

Results: Mean age at surgery was 74 years (range 43–96 years). Surgeries involved implantation of 119 new devices (67 DDD, 11 VVI, nine dual-chamber ICDs, one single-chamber ICD, 12 CRT-P and 19 CRT-D) and six revisions involving RV-leads. Septal position of the RV lead was significantly more often observed in the Mond vs. the control group (47% vs. 15%; $p<0.0001$).

Conclusions: Using the Mond® stylet was associated with a markedly higher rate of septal positioning of the RV lead and, therefore, should be adopted for all pacemaker implantations to improve long-term outcome.

CV 3-12

Toll-like receptor (TLR)-3 – A novel target for the prevention of ischemia-A-reperfusion injury in cardiac transplantation

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Background: Toll-like receptor (TLR)-3 represents a pattern recognition receptor involved in the innate immune response. Recently it has been proposed as a candidate molecule for the modulation of cardiac ischemia reperfusion (IRI) in vitro.

Methods: In order to investigate the detailed effects of TLR3 on cardiac IRI in vivo, syngeneic heart transplantation was performed in either C57BL/6 wild type (WT) or TLR3 knockout (TLR3-/-) mice following 9 h of cold ischemia.

Results: TLR3 knockout significantly diminished IRI-related injury 48 h after reperfusion as demonstrated by a cumulative histological damage score (TLR3-/-: 5.8 ± 0.8 vs. WT: 8.8 ± 0.3; $p=0.006$). In particular, epicardial and myocardial damage was alleviated ($p<0.05$, respectively). Furthermore, the presence of infiltrating lymphocytes significantly decreased ($p=0.0009$). This was accompanied by reduced intragraft (CCL3, CCL4) and splenic mRNA expression of pro-inflammatory cytokines (TNFα, IL1b, CCL4, CXCL10; all $p<0.05$). Whereas elevated levels of anti-inflammatory factors (TGFβ) were observed, those indicating hypoxia (HIF1α) significantly declined ($p<0.05$, respectively). Importantly, in contrast to the depletion of TLR3 expression in TLR3-/- recipient grafts and spleens, other toll-like receptors (TLR2, TLR4) remained unaffected, indicating that the observed protective effects were solely due to TLR3 deletion.

Conclusions: This study outlines for first time the detrimental influence of TLR3 signaling on the development of IRI after cardiac transplantation. Our data indicate that TLR3 represents a possible novel target for future pharmacologic therapies in solid organ transplantation.

CV 3-13

Tricuspidalklappeninsuffizienz nach Laser Sondenextraktion

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Grundlagen: Eine neu aufgetretene Tricuspidalklappeninsuffizienz (TRINS) nach Sondenextraktion ist eine nicht so

seltene Komplikation und wird in der Literatur mit einer Häufigkeit von 3,5–15 % angegeben. Bekannte Risikofaktoren sind weibliches Geschlecht, Schrittmachersonden häufiger als ICD-Sonden und die Verwendung eines Laser Extraktionsheats. Die Prognose und Therapie einer sekundären schweren TRINS ist nicht gut etabliert und richtet sich in erster Linie nach der Klinik und Entwicklung einer rechtsventrikulären Funktionsstörung. Die Problematik wird anhand eines Fallberichts erörtert.

Fallbericht: Ein 53 jähriger Patient nach Schrittmacherimplantation im Jahre 2005 bei kongenitalem AV-Block (Schrittmacher: St.Jude Identity, Sonden: Tendril SDX) wird wegen eines chronischen Infekts trotz langdauernder Antibiotikatherapie vorgestellt. Die Blutkultur war mehrmals positiv mit Staphylokokkus capitis ohne Hinweis auf systemische Infektionszeichen, in der Echokardiographie (TEE) fanden sich Vegetationen in der Tricuspidalebene ohne begleitende Tricuspidalinsuffizienz. Wir führten im Dezember 2016 die Laserextraktion der Sonden durch. Alle Sonden konnten entfernt werden, in der intraoperativen TEE fand sich aber eine mittelgradige Tricuspidalinsuffizienz mit akzeptablen Druckwerten im rechten Atrium. Zusätzlich wurde ein epikardialer Schrittmacher implantiert. Nach inital unauffälligen Verlauf entwickelte sich dann am 3. postoperativen Tag eine massive Leberfermenterhöhung mit Übelkeit. Erstdiagnose war ein toxischer Leberschaden durch die Antibiotikatherapie. Am 5.Tag entwickelte sich eine akute Rechtsherzinsuffizienz mit schwerer TRINS und hämodynamischer Instabilität weshalb ein Tricuspidalklappenersatz und eine epikardiale CRT Implantation notwendig war. Intraoperativ fand sich ein Abriss des septalen und vorderen Klappensegels. Der weitere postoperative Verlauf war dann weitgehend unauffällig und der Patient bei einer Kontrolle 6 Monate postoperativ infektfrei und klinisch gut belastbar.

Schlussfolgerungen: Eine neu auftretende Tricuspidalklappeninsuffizienz nach Sondenextraktion stellt eine schwerwiegende Komplikation dar und auch bei initial guter hämodynamischer Toleranz sollte eine Tricuspidalrekonstruktion/Trikuspidalklappenersatz eher frühzeitig erwogen werden.

CV 3-14

Validierung des EuroSCORE II für den Aortenklappenersatz – Ist der neue EuroSCORE II im Vergleich zum bereits verwendeten EuroSCORE das probate Mittel zur Qualitätssicherung bei prothetischem Aortenklappenersatz in der Herzchirurgie?

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Grundlagen: Der EuroSCORE wurde entwickelt, um das Risiko eines Patienten oder einer Patientin, innerhalb von 30 Tagen nach einer Herzoperation zu versterben, anhand seiner oder ihrer individuellen Risikofaktoren zu berechnen. Aufgrund des sich verändernden Risikoprofils und der neuen Techniken und Möglichkeiten in der Herzchirurgie machte sich der Bedarf nach einem überarbeiteten, moderneren System bemerkbar. Dabei handelt es sich um den EuroSCORE II. In unserer Studie wurde die prädiktive Aussagekraft des logistischen EuroSCORE mit der des EuroSCORE II in Bezug auf Aortenklapeneratzoperationen verglichen.

	AUC (95% KI)	Sensitivität	Spezifität	Cut Off	p-Wert
Add. EuroSCORE	0,837 (0,752-0,921)	0,889	0,682	7,5	<0,001
log EuroSCORE	0,847 (0,761-0,933)	0,889	0,721	8,95	<0,001
EuroSCORE II	0,829 (0,733-0,926)	0,889	0,665	2,65	<0,001

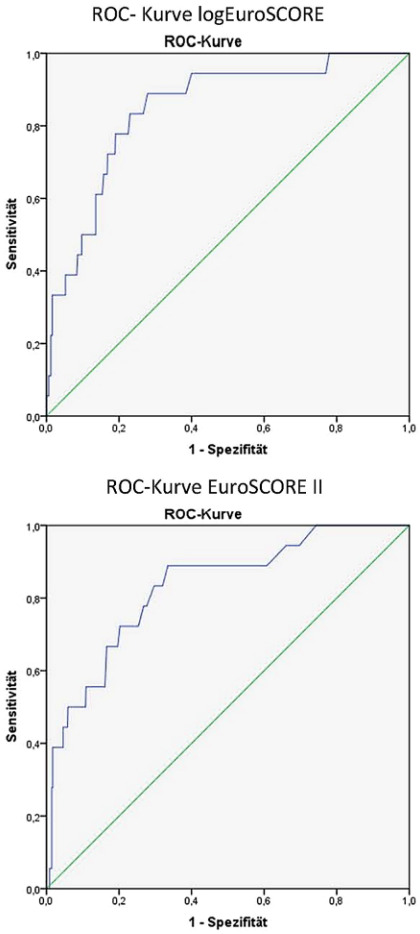
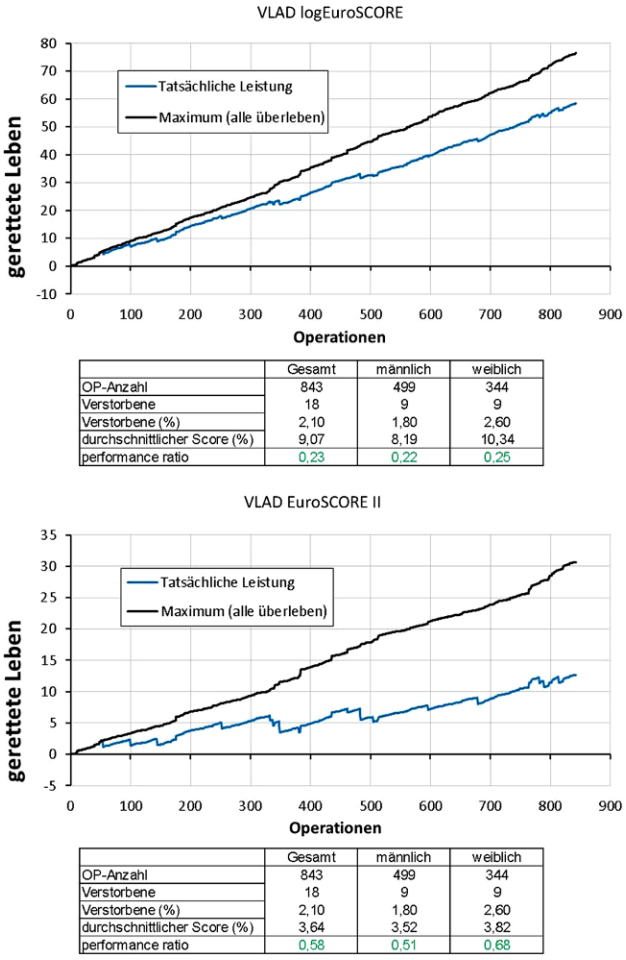


Abb. 1 | CV 3-14

Methodik: Anhand der Daten von 843 Patienten und Patientinnen, welche in den Jahren 2012 bis 2016 an unserer Abteilung einem Aortenklappenersatz unterzogen wurden, wurden die Ergebnisse der beiden Scores überprüft. Receiver Operating Characteristic (ROC) Analysen wurden in Bezug auf die 30-Tages Mortalität erstellt. Es wurden mithilfe des Youden-Index Cut-Off Werte definiert, um Aussagen über Sensitivität und Spezifität zu erhalten und so die Diskriminationskraft zu beurteilen. Variable-Life-Adjusted-Display (VLAD) und Funnel Plots (FP) wurden verwendet um die Performance Ratio darzustellen. Diese stellt das brauchbarste Tool dar, um die Leistung eines Zentrums retrospektiv grafisch zu präsentieren und zu beurteilen.

Ergebnisse: Die tatsächliche 30-Tage-Sterblichkeit für den gesamten Beobachtungszeitraum betrug 2,1 %. Die durchschnittliche vorausgesagte 30-Tage-Mortalität für den logistischen EuroSCORE und den EuroSCORE II betrug 9,07 % (Performance Ratio 0.23) bzw. 3,64 % (Performance Ratio 0,58). Die Diskriminationskraft für die 30-Tage-Mortalität – ermittelt mittels Area Under the Curve (AUC) – für den logistischen EuroSCORE und den EuroSCORE II ergab 0,847 (0,761–0,933 95 % KI) bzw. 0,829 (0,733–0,926 95 % KI). In weiteren Analysen wurden der logistische EuroSCORE und der EuroSCORE II



	Gesamt	männlich	weiblich
OP-Anzahl	843	499	344
Verstorbene	18	9	9
Verstorbene (%)	2,10	1,80	2,60
durchschnittlicher Score (%)	9,07	8,19	10,34
performance ratio	0,23	0,22	0,25

	Gesamt	männlich	weiblich
OP-Anzahl	843	499	344
Verstorbene	18	9	9
Verstorbene (%)	2,10	1,80	2,60
durchschnittlicher Score (%)	3,64	3,52	3,82
performance ratio	0,58	0,51	0,68

Abb. 2 | CV 3-14

verglichen, wobei eine hochsignifikante Korrelation ($p < 0{,}001$) festzustellen war. Der EuroSCORE II zeigte insgesamt eine etwas bessere absolute Voraussage- und Diskriminationskraft in Bezug auf den Faktor 30-Tage-Mortalität.

Schlussfolgerungen: Beide Scores zeigten eine ähnliche und außerordentlich gute Diskriminationskraft, die für die 30-Tages-Mortalität bei Aortenklappenoperationen signifikant war. Der EuroSCORE II zeigte jedoch eine bessere Kalibrierung als der logistische EuroSCORE, obwohl beide weit von einer performance ratio von 1 entfernt waren. Der EuroSCORE II, als Verbesserung des logistischen EuroSCORE, stellt einen guten Prädiktor der 30-Tages-Mortalität bei Aortenklappenoperation dar und kann in sämtlichen Situationen verwendet werden.

CV 3-15

Valve-sparing root replacement for failed pulmonary autografts

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Background: Dilatation of the pulmonary autograft (AG) is the main long-term complication of the Ross procedure using the complete root replacement technique. We reviewed our 25-year experience with a special emphasis on valve-sparing reoperations.

Methods: From 1991 to 2016 153 patients (29.4% pediatric) with a mean age of 29.6 ± 16.6 years underwent a Ross procedure at our institution with implantation of the AG as complete root replacement. The follow-up is 98.7% complete with a mean of 12.2 ± 5.5 years.

Results: The mean aortic cross clamp time was 124 ± 22 minutes, and the median stay on the intensive care unit was 1 day. Mortality at 30-days was 2.0% (3 patients). Echocardiography at hospital discharge documented no or trivial aortic regurgitation in 99.3% of the patients. Survival probability at 15 years was 89.7%. No case of AG endocarditis occurred during the study period. A reoperation on the AG was required in 37 patients (24.2%) at a mean interval of 10.9 ± 4.7 years after the Ross procedure, leading to 75.3% freedom from AG reoperation at 15 years. AG dilatation (54.7 ± 4.2 mm) was the indication for AG reoperation in 35 patients. In 77% of those patients, a valve-sparing root replacement was performed, including 17 Yacoub and 10 David procedures with no early mortality. In 3 patients a conduit was implanted within 2 years after a Yacoub operation because of progressive aortic valve regurgitation. At latest follow-up, 92% of all surviving patients still carry the pulmonary AG valve, and freedom from AG valve replacement was 92.1% at 15 years.

Conclusions: In the majority of patients with AG dilatation, prosthetic valve replacement can be avoided by a valve-sparing root replacement. Reoperations can be performed with no early mortality, an excellent early valve function, and an acceptable rate of re-intervention.

CV 3-16

Die Ross-Konno Operation beim Neugeborenen und Säugling mit hochgradiger linksventrikulärer Ausflußtraktstenose

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Grundlagen: Patienten mit hochgradiger angeborener linksventrikulärer Ausflusstraktstenose leiden oft unter eingeschränkter Linksventrikelfunktion, Endokardfibroelastose und grenzwertig großen linksseitigen Strukturen. Die Ross-Konno Operation im Neugeboren- oder frühen Säuglingsalter kann eine anhaltende biventrikuläre Korrektur bieten und eine Alternative zur univentrikulären Palliation bei grenzwertigen Strukturen darstellen. Diese Operationsmethode kann durch radikale Beseitigung der Ausflußtraktstenose zu funktioneller Erholung des druckbelasteten Ventrikels und Wachstum von hypoplastischen Strukturen führen.

Methodik: Zwischen 2008 und März 2017 wurden 44 frühe Ross-Konno Operationen an unserem Zentrum durchgeführt. 35 Patienten waren Neugeborene mit duktusabhängigem Systemkreislauf, 9 weitere Patienten waren jünger als 3 Monate. Unsere retrospektive Single Center Analyse untersucht Früh- und Spätmortalität, postoperative Komplikationen, die Reoperationsrate und funktionelle Parameter während der Follow up Periode. Weiters wurden mögliche prognostische Einflussfaktoren wie fetale Aortenklappenintervention, zusätzliches

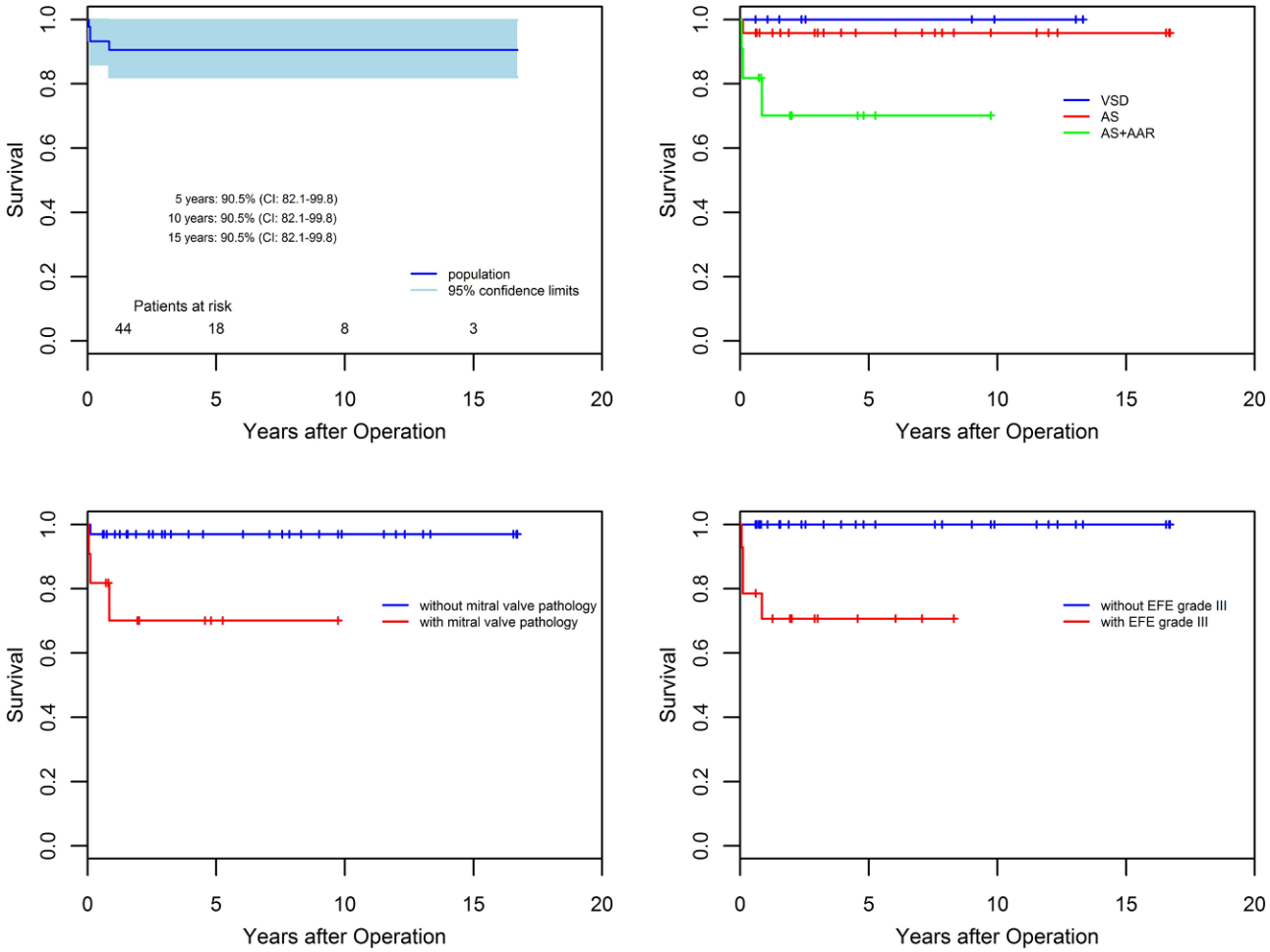

Abb. 1 | CV 3-16

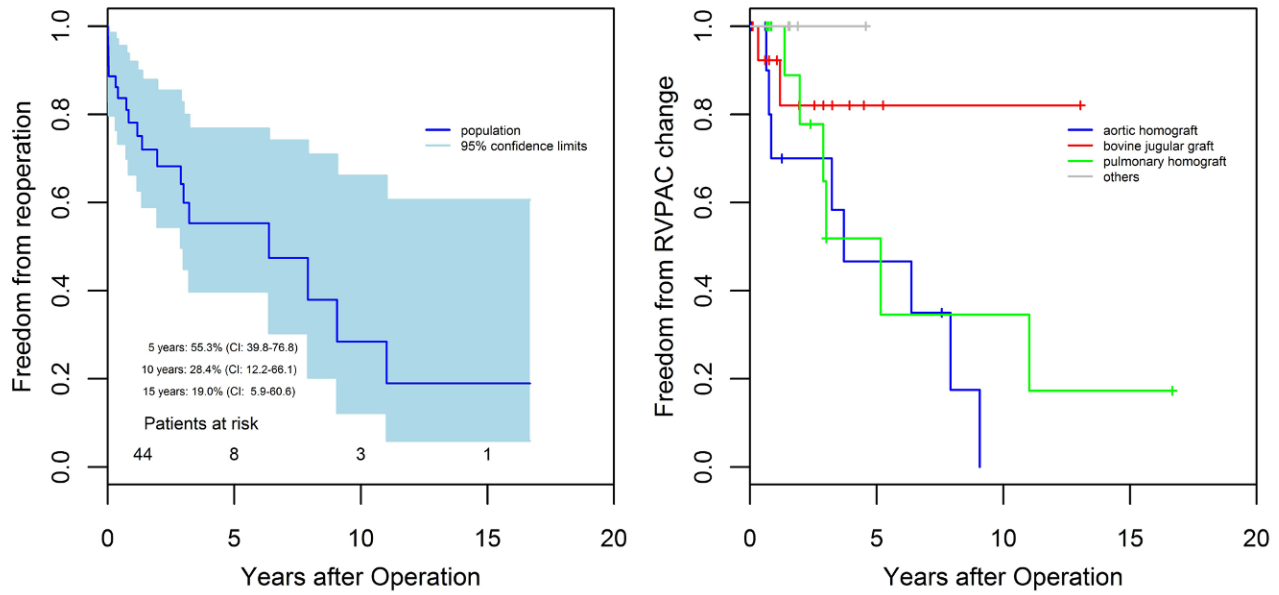

Abb. 2 | CV 3-16

Vorliegen eines Ventrikelseptumdefekts, einer Aortenbogenhypoplasie, einer Mitralklappenpathologie, sowie einer Endokardfibroelastose Grad III untersucht.

Ergebnisse: Die Frühmortalität war 7 % (3/44), ein weiterer Patient verstarb im Alter von 10 Monaten nach Umstieg auf Single Ventricle Palliation (1/41). Kein Todesfall ereignete sich in der Gruppe mit Ventrikelseptumdefekt und hypoplastischem oder unterbrochenem Aortenbogen (9 Fälle). Ein Todesfall war aus der Gruppe mit kritischer Aortenstenose ohne Aortenbogenhypoplasie (1/24), jedoch 3 Todesfälle betrafen Patienten mit kritischer Aortenstenose und hypoplastischem Aortenbogen (3/11). Ross-Konno Patienten mit Zustand nach fetaler Aortenklappenintervention hatten eine mittlere Überlebensrate von 87 %.

Eine univariate Risikofaktorenanalyse betreffend Exitus zeigte das Vorliegen von Aortenbogenhypoplasie bei intaktem Ventrikelseptum, assoziierte Mitralklappenpathologie sowie eine Endokardfibroelastose Grad III als signifikante Einflussfaktoren auf die Überlebensrate.

Während des durchschnittlichen Beobachtungszeitraums von 5,9 Jahren waren keine Reoperationen im Bereich des pulmonalen Autografts oder linksventrikulären Ausflusstrakts nötig. 19 Patienten hatten Reoperationen, vorwiegend im Bereich des RV-PA Conduits.

Die Neoaortenklappe zeigte zuletzt bei allen überlebenden Patienten keine oder nur triviale Insuffizienz und keine Einengung des linksventrikulären Ausflusstrakts. Die Linksventrikelfunktion wurde zuletzt bei 83 % als gut oder sehr gut beurteilt (FS > 28 %). 2 Patienten haben eine mechanische Mitralklappe.

Schlussfolgerungen: Die frühe Ross-Konno Operation kann eine biventrikuläre Reparatur auch bei grenzwertig großen linksseitigen Strukturen ermöglichen und Erholung der Ventrikelfunktion und nachhaltige Stenosefreiheit des Ausflusstrakts gewährleisten. Das höchste Operationsrisiko zeigten Patienten mit kritischer Aortenstenose und assoziierter Aortenbogenhypoplasie ohne Ventrikelseptumdefekt, sowie Patienten mit schwerer Endokardfibroelastose und Mitralklappenpathologie.

CV 3-17

Erfahrung mit der chirurgischen Behandlung von subaortalen Stenosen bei Kinder und jungen Erwachsenen

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Grundlagen: Die subvalviläre Aortentenose (SAS) ist die zweithäufigste Form der Aortenstenose. Sie ist für 14 % der LVOT Stenosen verantwortlich. SAS kann als dünnes fibröses Gewebe, fokal lokalisiert oder als tunnelartige diffuse Einengung, meist im Rahmen von komplexen Herzfehlern auftreten. Entsprechend der Morphologie werden verschiedenen Operationstechniken angewandt. Das Ziel dieser Studie ist es die Operationen auf ihre Ergebnisse zu überprüfen.

Methodik: Im Zeitraum von Jänner 2002 bis Februar 2017 wurden bei 52 Patienten (m = 3 Jahre; IQR [1–8,5]) 64 Operationen, mit dem Ziel eine SAS zu beheben, durchgeführt, 24 modifizierte Konno-Operationen, 25 subaortale Resektionen, 10 Myektomien nach Morrow und 5 andere Eingriffe. Die Daten dieser Patienten wurde retrospektive analysiert. Die zugrundeliegenden Herzfehler waren eine primäre SAS bei 13 (25 %), ein kompletter AV-Kanal bei 14 (29,9 %), ein Shonekomplex bei 6 (11,5 %), ein VSD bei 5 (9,6 %), ein DORV bei 5 (9,6 %), eine TGA bei 4 (7,8 %), ein partieller AV-Kanal bei 3 (5,8 %) und andere Ursache bei zwei Kindern. Die statistische Auswertung erfolgte mittels SPSS Version 23 (IBM, Ehningen, Deutschland).

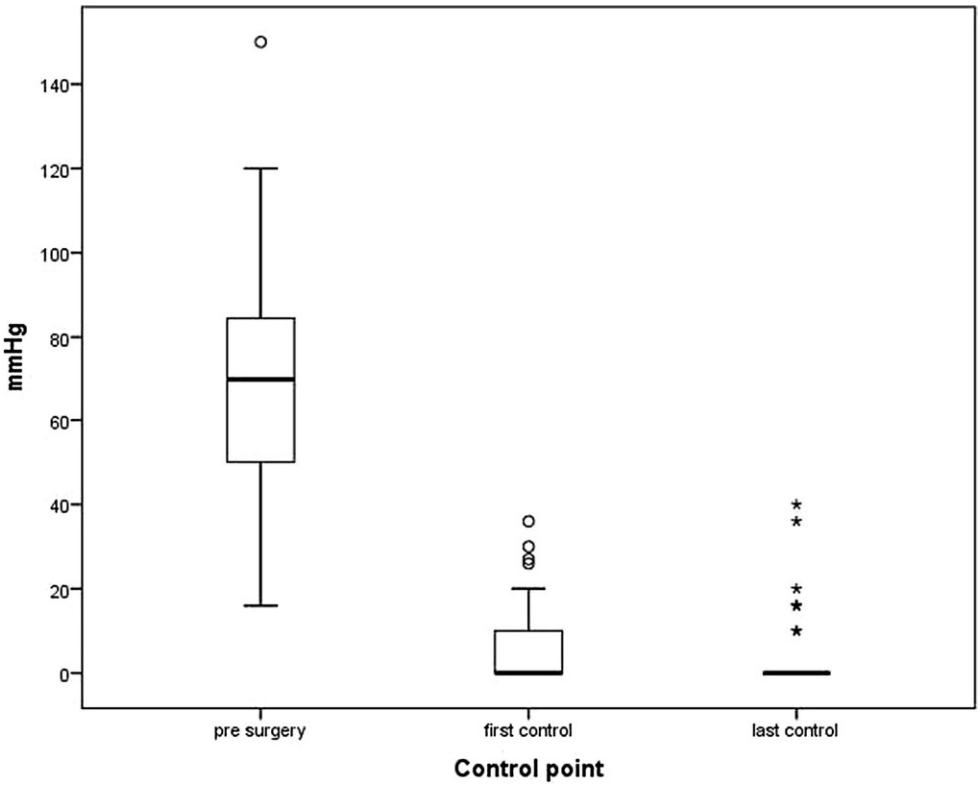

Abb. 1 | CV 3-17 LVOT Gradienten: vor Op, nach Op und bei Kontrolle

Ergebnisse: Der mediane Beobachtungszeitraum betrug 3 Jahre (IQR [0,4; 8,5]). Kein Patient verstarb. Zwei Patienten benötigten einen Schrittmacher bei postoperativen AV-Block. Die Operation führte bei allen Patienten zu einer Reduktion des LVOT Gradienten ($p<0{,}001$) (Abb. 1). Zwölf Patienten (23,1 %) mussten aufgrund einer neuerlichen SAS nach 2 Jahren (IQR: [1,5; 4,2]) reoperiert werden. Diese Patienten hatten einen höheren präoperativen LVOT Gradienten ($p=0{,}02$) (Abb. 2). Die Art der Erstoperation oder das Alter erhöhten das Risiko eines SAS Rezidivs nicht.

Schlussfolgerungen: In dem untersuchten Patientenkollektiv konnten wir eine signifikante Reduktion des LVOT Gradienten bei niedriger Mortalität und Morbidität nachweisen. Die beobachtete Rezidivrate von 23,1 % entspricht, der in der Literatur beschriebenen. Ein hoher initialer LVOT Gradient war ein Risikofaktor für ein Rezidiv der SAS. Andere Gründe, wie Art der Erstoperation oder junges Alter waren keine Risikofaktoren.

CV 4-1

Transcatheter aortic valve implantation—which determinants of outcome remain? Data from the extended VIenna CardioThOracic Aortic Valve RegistrY (eVICTORY)

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Background: TAVI has advanced to a viable treatment option in high-risk patients presenting with aortic valve stenosis. To the present, detailed knowledge about factors predisposing adverse outcomes of this high-risk subgroups remains scarce. The present study gives a detailed analysis of a large TAVI cohort.

Methods: Since 2009 a total of consecutive 1.861 patients underwent TAVI in both study centers. Mean patient's age was 80.8 +/– 5.6. Common risk scores confirmed a predominantly high-risk subgroup (EuroSCORE 20.0 +/– 14%; EuroSCORE II 7+/– 5%). The majority of the patients were female (58.2%). Patient's baselines were characterized by a broad spectrum of relevant comorbidities, such as chronic kidney disease (33.9%), COPD (9.3%), extracardiac arteriopathy (21.3%), pulmonary hypertension (14.3%) and diabetes (32.3%). Mean follow-up was 2.92 years, ranging up to 6.8 years. Data were retrospectively analyzed out of the hospital's database. A uni- and multivariate

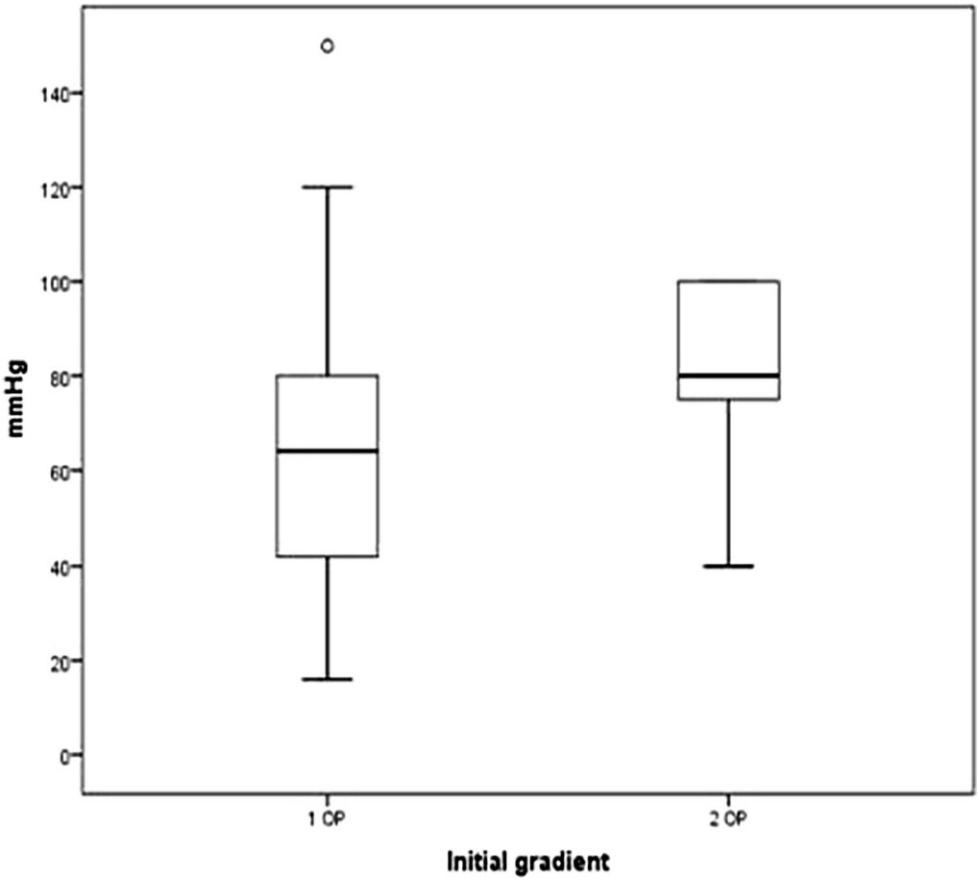

Abb. 2 | CV 3-17 1 OP: Initiale LVOT Gradienten von Patienten mit einer Operation; 2 OP: LVOT Gradienten von Patienten (N=12), die reoperiert wurden

analysis of risk factors for mortality during primary hospital-stay and further follow-up was performed.

Results: Hospital mortality was 4.1%. Survival rates for 1-, 2- and 6-years were 86.8%, 68.3% and 37.9% respectively. Univariate risk factors for hospital mortality were LV-EF <30% ($p=0.03$), extracardiac arteriopathy ($p=0.023$), chronic kidney disease ($p=0.002$), postoperative LCOS ($p<0.01$), re-exploration ($p<0.01$), respiratory failure ($p<0.01$), postoperative stroke ($p<0.01$), postoperative delirium ($p<0.01$), CVVH ($p<0.01$), prolonged ventilation ($p<0.01$), transfusion ($p<0.01$), prolonged ICU-stay ($p<0.01$), postoperative stroke ($p<0.01$). After multivariate analysis respiratory failure needing reintubation (HR 2.3 +/- 0.4; $p<0.01$), postoperative stroke (HR 1.4 +/- 0.6; $p=0.02$) and postoperative renal failure needing CVVH (HR 1.1 +/- 0.4; $p<0.01$) remained as factors for hospital mortality. Univariate risk factors for mortality during follow-up of the hospital survivors were pulmonary hypertension ($p<0.01$), COPD ($p=0.02$), postoperative stroke ($p<0.01$), postoperative CVVH ($p<0.01$), transfusion ($p<0.01$), postoperative respiratory failure needing reintubation ($p<0.01$), postoperative stroke ($p<0.01$). After multivariate analysis pulmonary hypertension (HR 2.8 +/- 0.2; $p<0.01$) and postoperative stroke (HR 1.7 +/- 0.7; $p=0.02$) remained as significant factors for mortality during follow-up.

Conclusions: Hospital mortality of TAVI-patients is decoupled from patients baseline characteristics. Significant factors for hospital mortality mainly were generated out of post-procedural complications. Different patterns were observed for long-term survival. Regarding the hospital survivors, patients with pulmonary hypertension or post-procedural stroke had an inferior outcome. In conclusion, TAVI provides good results in this particular high-risk subgroup. Further investigations are needed to identify patients benefiting or not-benefiting from TAVI distinctively.

CV 4-2

Cui bono?—Old vs. young. A propensity score matched comparison between transcatheter aortic valve implantation in younger and older high-risk patients. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: As the indication for transcatheter aortic valve implantation (TAVI) is continuously expanding towards a low-risk population, it will doubtlessly become a valuable alternative for younger high-risk patients with symptomatic severe aortic stenosis (AS) in the near future. The aim of the study was to compare the outcome and survival of a young inoperable TAVI cohort with a matched older population.

Methods: From June 2009 through December 2017 data of 532 TAVI patients (transapical access $n=266$ [50%], female $n=335$ [63%]) were analyzed in our institution. Propensity score matching analysis was used to adjust for baseline characteristic differences between the two groups (1-to-1 matching). Matching variables were: BMI, left ventricular function, sPAP, serum creatinine, re-operation, stroke, diabetes, history of myocardial infarction, peripheral vascular disease, COPD, and sex. After propensity score matching, we compared 96 high-risk patients (mean STS 6.3 +/- 2.9) above 75 years against 96 high-risk patients under 75 years (mean STS 4.1 +/- 2.9). Mean patient age in the older cohort was 82.1 +/- 3.9 years, in the younger cohort 68.7 +/- 5.9 years. The transapical (TA) access route had been chosen in case of severe kinking or calcification of the iliac vessels. The younger cohort received TAVI procedure as a measure of last resort, as any other kind of conservative or surgical treatment was declined by the patient. 30-day mortality, device success, and a combined safety endpoint were chosen as primary endpoints.

Results: Preoperative characteristics were comparable in the older and younger cohort. Overall mortality at 30 days (3 [3.1%] vs. 1 [1.0%]; $p=0.311$) as well as device success (79 [82.3%] vs. 85 [88.5%]; $p=0.146$) did not differ significantly. However, the combined safety endpoint was more often met in the younger cohort (85 [88.5%] vs. 74 [77.1%]; $p=0.027$). Life-threatening bleedings (14 [14.6%] vs. 3 [3.1%], $p=0.037$), new atrial fibrillation (15 [15.6%] vs. 6 [6.3%], $p=0.031$), and reoperation (17 [17.7%] vs. 6 [6.3%], $p=0.012$) occurred more often in the older cohort, whereas new left bundle branch block (9 [9.4] vs. 2 [2.1%] $p=0.01$) was more often observed in the younger cohort.

Conclusions: Evaluating our findings, we can conclude TAVI can be performed safely in younger patients. The only limiting factor for endorsing TAVI in a younger population is valve durability. Once transcatheter valves are proven to be as durable as surgical valves, the indication for TAVI can expand safely towards younger patients.

CV 4-3

Cut-down outperforms complete percutaneous transcatheter valve implantation. Data from the extended VIenna CardioThOracic Aortic Valve RegistrY (eVICTORY)

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Background: The ideal approach for transfemoral transcatheter aortic valve implantation (TAVI) is still widely debated. The objective of the present study was to compare access and bleeding complications of complete percutaneous versus surgical cut-down approach for transfemoral TAVI in a real-world all-comers setting.

Methods: The study included 667 consecutive patients from November 2008 to December 2016, 466 patients in the percutaneous and 201 patients in the cut-down group. Mean patient's age was 81.5 ± 5.2 years [percutaneous] vs. 80.5 ± 4.7 years [cut-down] ($p=0.351$). Calculated logistic EuroSCORE correlated an increased surgical risk (19.3 ± 13.3 vs. 17.8 ± 7.4%, $p=0.488$). Primary study endpoints were vascular access site as well as bleeding complications according to the VARC-2 criteria.

Results: There were no significant differences regarding baseline characteristics between both groups. Mean procedure time was significantly shorter in the cut-down group (93.5 ± 22.0 min [percutaneous] vs. 69 ± 19 min [cut-down]; $p<0.001$). Overall rate of VARC-2 access complications were more frequent

in the percutaneous group (20.4% [95/466] vs. 8.5% [17/201]; $p=0.037$); with predominantly minor complications in the percutaneous cohort (14.4% [67/466] vs. 2.5% [5/201]; $p=0.04$). Overall bleeding complications were more frequent in the percutaneous group (21.9% [102/466] vs. 4.5% [9/201]; $p=0.01$). Hospital mortality was 5.2% in the percutaneous group and 1.9% in the cut-down group ($p=0.075$).

Conclusions: Surgical cut-down provided controlled access resulting in less access site and bleeding complications. Nonetheless, major access complications were not significantly different between the two cohorts. Both approaches must be seen as complementary techniques. A portfolio containing both techniques is the exclusive way to provide a tailor-made and patient-orientated approach warranting the safest access based on the individual vessel condition.

CV 4-4

Dosis non fecit venerum—Is contrast medium dosage a true predictor of acute kidney injury following transcatheter aortic valve implantation? Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: Recent studies suggested that the contrast medium (CM) volume is associated with acute kidney injury (AKI) after TAVI. Several scores and risk ratios had been proposed as predictors of AKI. Nevertheless, in a high-risk elderly TAVI population, the prognostic value and ideal threshold of CM dosage on AKI persist to be unclear. The study aimed to investigate AKI in our TAVI cohort and define cut-off values of contrast medium dosages.

Methods: Data of 532 successive TAVI patients (age 89.3 +/– 7.3 years, Euro- SCORE II 6.9% +/– 6.0%) were analyzed. AKI was defined by Valve Academic Research Consortium 2 criteria. Based on a recently published formula, the renal function (preprocedural serum creatinine: SCr) corrected ratio of CM and body mass index (CM*SCr/BMI) was calculated to determine the risk of postprocedural AKI. Furthermore the incidence of AKI but also predictive factors and prognosis of AKI were analyzed.

Results: AKI occurred in 78 patients (15.2%). A significant difference in 1-year mortality between the AKI and non-AKI groups (47.9% vs. 15.7%, p 0.001) was shown. In contrast to recent findings, our study showed no association between CM dosage or the CM*SCr/BMI ratio and the occurrence of AKI ($p=0.872$ and $p=0.258$, respectively). By multivariate analysis the only predictors of AKI were EuroScore 2 ($p=0.010$), STS Score ($p=0.002$), preprocedural myocardial infarction ($p=0.006$) transfemoral access ($p=0.012$), bleeding complications ($p<0.001$). Moreover, a strong correlation between AKI and 30d mortality was observed ($p<0.001$). A threshold value of CM*SCr/BMI for predicting AKI was not identified due to lack of association.

Conclusions: In our all-comers, all-access cohort we found no relationship between preprocedural renal function, CM dosage, nor the established ratio occurrence of postprocedural AKI. Bleeding complications were the only postprocedural complication associated with AKI; hence AKI can be predicted well by preprocedural risk assessment.

Larger studies will be needed to settle the discussion if AKI is truely caused due to the nephrotoxic effect of contrast medium. Subsequently, the need for sufficient nephroprotection needs to be addressed, since this cohort features an almost 50% mortality rate at 1-year.

CV 4-5

Save your breath—Update on the impact of COPD on outcome in 1871 patients undergoing transfemoral vs. transapical transcatheter aortic valve implantation. Data from the extended VIenna CardioThOracic Aortic Valve RegistrY (eVICTORY)

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Background: Notably, a large number of patients undergoing transcatheter aortic valve implantation (TAVI) have been diagnosed with concomitant chronic obstructive pulmonary disease (COPD) as this distinct population is generally regarded to be at high-risk in conventional cardiac surgery.

Objectives: The purpose of this study was to evaluate the impact of COPD on clinical outcomes in patients referred for transfemoral (TF) as well as transapical (TA) aortic valve implantation in two European centers and furthermore to discuss possible advantages considering the selection of access evaluation.

Methods: In total, 1871 patients undergoing TAVI procedure were included in the present study between June 2008 and December 2017: 231 (12.3%) suffered from concomitant COPD, whereas 1611 (86.1%) did not. The severity of airflow limitation in COPD was assessed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) definition based on spirometry results (FEV1 <70% predicted) and/or the requirement for bronchodilator therapy. Furthermore, a TF (54.1%) or TA (45.9%) approach was selected primarily depending on size, degree of calcification as well as kinking of iliofemoral arteries. Spirometry was performed prior to intervention and at discharge. New York Heart Association (NYHA) functional status was evaluated at baseline and at 6- respectively 12-months follow-up. The outcome was measured and classified according to VARC-II criteria. Survival was estimated by Kaplan-Meier-Plot.

Results: The present extended analysis suggests that patients with concomitant COPD featured no significant differences in 30-day mortality (COPD 6.2% vs. non-COPD 5.2%, $p=0.655$) as well as long-term survival over five years (log-rank $p=0.773$) after TAVI.

Furthermore, ventilation times and post-procedural pneumonia rates were not increased in COPD patients (7.4% vs. non-COPD 4.2%, $p=0.483$). Post-procedural spirometry at 6-months follow-up did not differ from pre-procedural results in the TA-cohort (FEV1: 73.7% vs. 75.4%, $p=0.843$; FVC: 82.1% vs. 81.8%, $p=0.847$). Comparing TF to TA approach, no significant difference on the impact of COPD on post-procedural outcomes especially pneumonia rates (TF 6.4% vs. TA 7.9%, $p=0.314$), res-

piratory insufficiency (TF 4.2% vs. TA 7.9%, $p=0.114$), or reintubation (TF 1.0% vs. TA 3.9%, $p=0.184$) could be found. Both cohorts featured significant improvement in NYHA functional class after performing TAVI, although COPD patients experienced less progress.

Conclusions: COPD patients are still considered a high-risk population regarding any type of aortic valve replacement, although our updated data show no significant difference in short-term mortality as well as long-term survival after TAVI procedure. Besides, the access site does not implicate a significant difference in VARC II-defined clinical outcomes in COPD patients. Evaluating these results, COPD cannot be considered a contraindication for a transapical approach.

CV 4-6

BNP and Troponin I—biomarkers of prognostic value after transcatheter aortic valve implantation. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: Brain natriuretic peptide (BNP) is known to be an established biomarker in various heart conditions and correlates with the severity of aortic valve stenosis. Troponin I indicates myocardial injury and transcatheter aortic valve implantation (TAVI) is associated with increased postprocedural Troponin I levels.

Objective: This present analysis aimed to investigate the significance of these biomarkers predicting clinical outcomes after TAVI focusing on mortality as a primary endpoint.

Methods: In total, 532 patients undergoing TAVI procedure were included in the present study between June 2009 and December 2016. Retrospective analysis of BNP and Troponin I levels was performed at baseline, on the first and third postprocedural day, at discharge as well as at one-year follow-up. Outcomes were measured and classified according to VARC-II criteria. Survival was estimated by Kaplan-Meier-Plot.

Results: Baseline BNP levels had no impact on outcome or survival, however patients with elevated baseline Troponin I levels were associated with a higher rate of re-operation as well as higher long-term mortality rates. A significant increase of BNP after the procedure was associated with the use of a balloon-expandable valve ($p=0.04$), the need of postprocedural pacemaker implantation ($p=0.04$) and a higher rate of postprocedural atrial fibrillation ($p=0.03$). Furthermore, significantly elevated Troponin I levels were associated with stroke ($p=0.022$), bleeding complications ($p=0.024$), new AV-Block ($p=0.016$) as well as the use of a balloon-expandable valve ($p<0.001$). A significant increase in Troponin I was furthermore observed in all transapical TAVI patients ($n=263$; 100%) but only in 153 (65.7%) of transfemorally treated patients indicating myocardial injury during TAVI ($p<0.001$). A higher degree of myocardial injury—a 15 fold increase in Troponin I at the first postprocedural day—was an independent predictor of 30-day mortality, but not long-term survival.

Conclusions: With Troponin I measured at baseline, this marker seems to be a strong predictor of postprocedural complications as well as long-term mortality, and may help to identify patients with limited life-expectancy at risk of futile treatment. With BNP and Troponin I being predictors of various postprocedural complications, it's role needs to be clarified in larger studies with particular focus on valve type and access route.

CV 4-7

Which regimen is the best choice? The impact of antiplatelet and antithrombotic therapy on outcome and survival transcatheter aortic valve implantation. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: Thromboembolic complications and stroke are two of the main concerns of transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement. The correct choice of antiplatelet or antithrombotic treatment is therefore crucial. We compared procedural and follow-up outcomes and complications of our TAVI patients based on the type of antiplatelet and antithrombotic treatment (single-antiplatelet [SAPT] vs. dual-antiplatelet [DAPT] vs. anticoagulation [VKA] vs. none [NT]).

Methods: From June 2009 through December 2017 data of 532 TAVI patients (transapical access $n=266$ [50%], female $n=335$ [63%]) underwent TAVI in our institution. There were 120 patients without any antiplatelet or antithrombotic treatment, 197 with SAPT, 139 with DAPT, and 76 with VKA referred for TAVI. As main study endpoints, the VARC-2 defined bleeding, vascular access and neurological complications had been chosen as well as a composite safety endpoint, defined as freedom from death at 30-days, bleeding, myocardial infarction and stroke. Secondary endpoints were 30-day mortality and long-term survival. Long-term outcome was assessed for 37 patients without treatment, 150 patients under SAPT, 216 under DAPT and 87 under VKA treatment, with a complete follow-up for 92% (490/532).

Results: Preprocedural antithrombotic or anticoagulation treatment had limited impact on VARC-2 defined postprocedural complications or 30-day mortality. Access related complications were more often reported for patients under DAPT vs. patients without any treatment prior to TAVI (DAPT: 19 [13.7] vs. NT: 3 [2.5%]; $p=0.012$). Apart from that, patients under DAPT were at higher risk for re-operations due to bleeding or cardiac tamponade (DAPT: 6 [4.3%] vs. NT: 0 [0%]; $p=0.008$) and showed a trend towards a higher rate of pacemaker implantations (DAPT: 18 [12.9%] vs. VKA: 2 [2.6%]; $p=0.080$). There were no differences between the groups regarding the main study endpoints bleeding ($p=0.179$), stroke ($p=0.465$) and composite safety ($p=449$), and for the secondary endpoint mortality at 30-days ($p=0.915$). Long-term survival differed significantly between the different regimens. NT showed significantly reduced long-term survival compared to the other cohorts (NT vs. SAPT $p=0.005$: NT vs. DAPT $p<0.001$, NT vs. VKA $p=0.001$). DAPT showed improved long-term survival over SAPT (log rank: $p=0.012$) but did not differ to patients treated with VKA (log rank: $p=0.111$), whereas VKA was not superior to SAPT ($p=0.518$).

Conclusions: It is evident from the results that patients under DAPT bore the highest risk for adverse events among the studied cohorts. DAPT prior to TAVI is associated with a higher rate of access related complications as well as reoperations for bleeding or cardiac tamponade. The superior long-term survival curves of patients treated with DAPT or VKA after TAVI warrant considerable attention in further recommendations of antithrombotic regimens after TAVI.

CV 4-8

Platelets count–predictors of major bleeding events after transcatheter aortic valve implantation. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: Postprocedural thrombocytopenia is frequently observed after transcatheter aortic valve implantation (TAVI). The aim of this study was to investigate its incidence and impact on postinterventional complications.

Methods: In total, 532 patients undergoing TAVI procedure via transapical or transfemoral approach were included in the present study between June 2009 and December 2016. Thrombocytes counts (TC) were performed at baseline and daily postprocedural until the third day and at discharge. Primary study endpoints were 30d mortality and bleeding events according to VARC-II criteria. Survival was estimated by Kaplan-Meier-Plot.

Results: We observed an relevant drop in thrombocytes (>100.000/µl) in 71 (13.3%), 113 (21.3%) and 16 (3.0%) patients at 1st postoperative day (POD), 3rd POD and at discharge respectively. Laboratory results identified 35 (6.6%) patients on 1st POD, 76 (14.3%) patients on 3rd POD and 11 (2.1%) patients at discharge with thrombocytopenia (TC <100.000/µl). The present analysis suggests that early severe thrombocytopenia, as well as a significant drop in thrombocytes up until 3rd POD, does correlate with the occurrence of bleeding events ($p=0.047$ and $p=0.004$ respectively). However, these findings were not associated with access-related complications ($p=0.478$ and $p=0.471$). Moreover, patients with a significant drop during the 1st POD ($p=0.012$) and 3rd POD ($p=0.002$) as well as maintained thrombocytopenia until discharge ($p=0.037$) were at higher risk for 30-day mortality.

Conclusions: Evaluating these results, we conclude that severe and persistent thrombocytopenia post TAVI can serve as an independent predictor of mortality and bleeding events, which are not related to access site complications. Even though the driving pathophysiological factor behind this phenomenon is still heavily debated, its occurrence has a significant impact on the clinical outcome. More studies, especially in context with hypo-attenuated leaflet thickening and reduced leaflet motion will be needed to reveal the true kernel of this clinical phenomenon.

CV 4-9

The impact of new-onset atrial fibrillation on the outcome and survival after transcatheter aortic valve implantation. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: Atrial fibrillation is one of the most common comorbidities among patients undergoing transcatheter aortic valve implantation (TAVI). This study aimed to investigate the importance of new-onset atrial fibrillation (NOAF) as a risk factor for adverse clinical outcomes and mortality in patients selected for either transapical (TA) or transfemoral (TF) TAVI.

Methods: A total number of 532 (266 TA/266 TF) patients undergoing TAVI between June 2009 and December 2016 were included in this retrospective study, out of which 163 (30.7%) patients had a history of AF before surgery. The mean CHAD1DS2-VASC score was 5.3 +/– 1.4 with a HAS-BLED bleeding score of 1.5 +/– 0.7 and 233 (43.7%) on antithrombotic treatment prior to the procedure.

Cardiac rhythm was assessed by continuous electrocardiographic (ECG) follow-up until the third postprocedural day, as well as on individual ECG readings on the fifth postprocedural day, at discharge and at one-year follow-up. Furthermore, postprocedural adverse events defined according to the VARC-2 criteria were evaluated for both groups.

Results: 55 patients (10.3%) were diagnosed with NOAF during their hospital stay or after discharge, with 36 (13.5%) in the TA cohort but only 19 (7.5%) in the TF cohort ($p=0.012$). The transapical access (OR 4.96, 95% CI 1.9–13.2; $p=0.003$) was an independent predictor for the development of NOAF. Overall neurological adverse events did not differ between the NOAF cohort and those without (8 [1.7%] vs. 2 [3.6%]; $p=0.288$). However, adjusted for the degree of severity the NOAF cohort showed a significantly higher rate of TIA and minor strokes (2 [3.6%] vs. 3 [0.6%]; $p=0.018$). 30-day mortality rates as well as long-term survival was not significantly higher in the NOAF cohort (25 [5.4%] vs. 2 [3.6%]; $p=0.437$; log-rank: $p=0.997$).

Conclusions: Evaluating the results of the study, minor neurological events were more often seen in the NOAF cohort, suggesting that major events resulted mostly from embolic events during the implantation rather than thromboembolic events caused from AF. Nevertheless, this has to be seen in context with the latest findings of hypoattenuated leaflet thickening (HALT) and reduced leaflet motion (RELM) as a potential risk factor. Larger multicenter trials focusing on this complex clinical problem will be needed to thoroughly elucidate the nature of this problem to make TAVI safer for potentially younger and low-risk patients.

CV 4-10

Soften the blow—A comparison of semi- and non-compliant balloon systems in transcatheter aortic valve implantation. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: The benefit of percutaneous balloon aortic valvuloplasty (BAV) during transcatheter aortic valve implantation (TAVI) has recently been questioned. Therefore, due to the growing relevance of TAVI-procedures, there is intensified research on the role of BAV during TAVI. However, there has been little focus on the difference in the outcome of compliant- and non-compliant-balloon use. The aim of this study was the evaluation of possible differences in mortality and complication rates between compliant- and non-compliant-balloon use during TAVI-procedures.

Methods: Between June 2009 and December 2016, 532 TAVI patients were examined throughout this retrospective single-center cohort study. The primary endpoint of the study was the grade of residual paravalvular leak (PVL) after TAVI. Secondary endpoints were 30-day mortality as well as a composite safety endpoint. Furthermore, complication rates of VARC-2 defined endpoints had been investigated. Non-compliant-ballons (NCB) (True Dilatation, Bard Inc.) were compared to (semi-)compliant-ballons (CB), such as Nucleus, Z-MED or Z-MED II by NuMed Inc., VACS II and III by Ospyka or the standard Edwards Transfemoral Balloon Catheter. Pre- and post-dilatation (PreD/PostD), as well as inflation time, had been measured during the implantation.

Results: A postprocedural paravalvular leak was not influenced by balloon type or inflation time; however the overall incidence of PVL was more often observed after pre-dilatation (no PreD: 59 [38.1%] vs. PreD: 181 [52.8%]; $p=0.002$). Clinically relevant PVL (more than trace) on the other hand was more often observed after post-dilatation (no PostD: 30 [7.3%] vs. PostD: 14 [15.7%]; $p=0.014$).

Balloon type nor pre-dilatation or post-dilatation had any effect on 30-day mortality, however, during long-term follow-up, the use of post-dilatation had a trend towards impaired long-term survival (log rank: 0.064).

Evaluating adverse events, predilatation was associated with a higher rate of pacemaker implantation (no PreD: 12 [7.4] vs. PreD: 58 [16.5%]; $p=0.003$), conversion to open surgery (no PreD: 0 [0%] vs. PreD: 8 [2.3%]; $p=0.047$), the need for valve-in-valve (VIV) implantation (no PreD: 0 [0%] vs. PreD: 8 [2.3%]; $p=0.047$) and less often met the criteria for the composite safety endpoint (no PreD: 116 [69.9%] vs. PreD: 216 [59.0%]; $p=0.010$).

The use of non-compliant balloons during predilatation led to a higher rate of VIV-implantations during index procedure (CB: 2 [0.6%] vs. NCB: 5 [5.7%]; $p=0.005$) and conversions to open surgery (CB: 1 [0.3%] vs. NCB: 3 [3.4%]; $p=0.030$). Furthermore a trend towards neurological adverse events had been observed (CB: 6 [1.7%] vs. NCB: 5 [5.5%]; $p=0.058$).

Conclusions: Reviewing our results, pre-dilatation entails serious operational risk factors as well as a higher rate of postprocedural PVL—mainly consisting of minimal or trace regurgitation. And even though post-dilatation generally reduces PVL, a significant difference in clinically relevant PVL remains, thus leaving balloon- and THV companies room for improvement on sealing and valve expansion. The use of non-compliant balloon systems during predilatation must be discouraged in the light of a higher rate of VIV implantations and conversion to open surgery as well as a trend towards neurological adverse events in our study.

CV 4-11

Spoilt for choice—Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transcatheter aortic valve replacement. Data from the VIenna CardioThOracic Aortic Valve RegistrY (VICTORY)

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Background: In contrast to surgical technique, transcatheter aortic valve implantation (TAVI) relies either on the expansion of a pre-mounted balloon or on self-expanding material properties of the prosthetic valve. Our objectives were to elucidate potential differences in clinical outcomes as well as long-term mortality between these two different valve systems.

Methods: We retrospectively categorized our TAVI patients into either being treated with a balloon-expanding valve (BEV; $n=264$ [49.6%]) or a self-expanding valve (SEV; $n=268$ [50.4%]). Between June 2009 and December 2016 data of 532 TAVI patients (transapical access $n=266$ [50%], female $n=335$ [63%]) were analyzed. Balloon-expandable valves were more often implanted via transapical access (TA: 197 [71.4%] vs. TF: 67 [25.5%]; $p<0.001$). The primary endpoint was device success, which is a composite endpoint including the absence of procedural mortality, correct position and good performance of a single valve during the index procedure. Furthermore, the study compared early clinical safety endpoints defined by the Valve Academic Research Consortium 2 (VARC-2).

Results: VARC-2 defined device success occurred in 87.9% ($n=232$) patients in the BEV cohort and in 89.6% ($n=240$) of patients in the SEV cohort respectively ($p=0.300$). Postoperative paravalvular leak did not differ between the two cohorts with 1.2% ($n=3$) of moderate or severe aortic regurgitation in the BEV group vs. 1.5% ($n=4$) SEV group ($p=0.168$). Regarding safety outcomes, neurological adverse events (SEV: 11 [4.1%] vs. BAV: 0 [0%]; $p=0.009$), overall bleeding events (SEV: 59 [22.0%] vs. BAV: 47 [17.8%]; $p=0.007$), acute kidney injury (SEV: 46 [17.2%] vs. BAV: 38 [14.4%]; $p=0.006$) and post-procedural pacemaker implantations (SEV: 54 [20.1%] vs. BAV: 19 [7.2%]; $p<0.001$) appeared more often in the self-expanding cohort. However, reoperations for non-cardiac problems were more often reported in the balloon-expandable cohort (SEV: 15 [5.6%] vs. BAV: 28 [10.6%]; $p=0.024$). Both cohorts showed no difference between 30-day mortality (SEV: 14 [5.2%] vs. BAV: 13 [4.9%]; $p=0.504$) and long-term survival (log-rank: $p=103$)

Conclusions: With device success as a surrogate parameter for the feasibility of implantation and no difference between short- and long-term mortality, the method of expansion seems to have limited impact on valve performance. However, the access site as a potential bias for safety endpoints after TAVI has to be taken into consideration during valve selection.